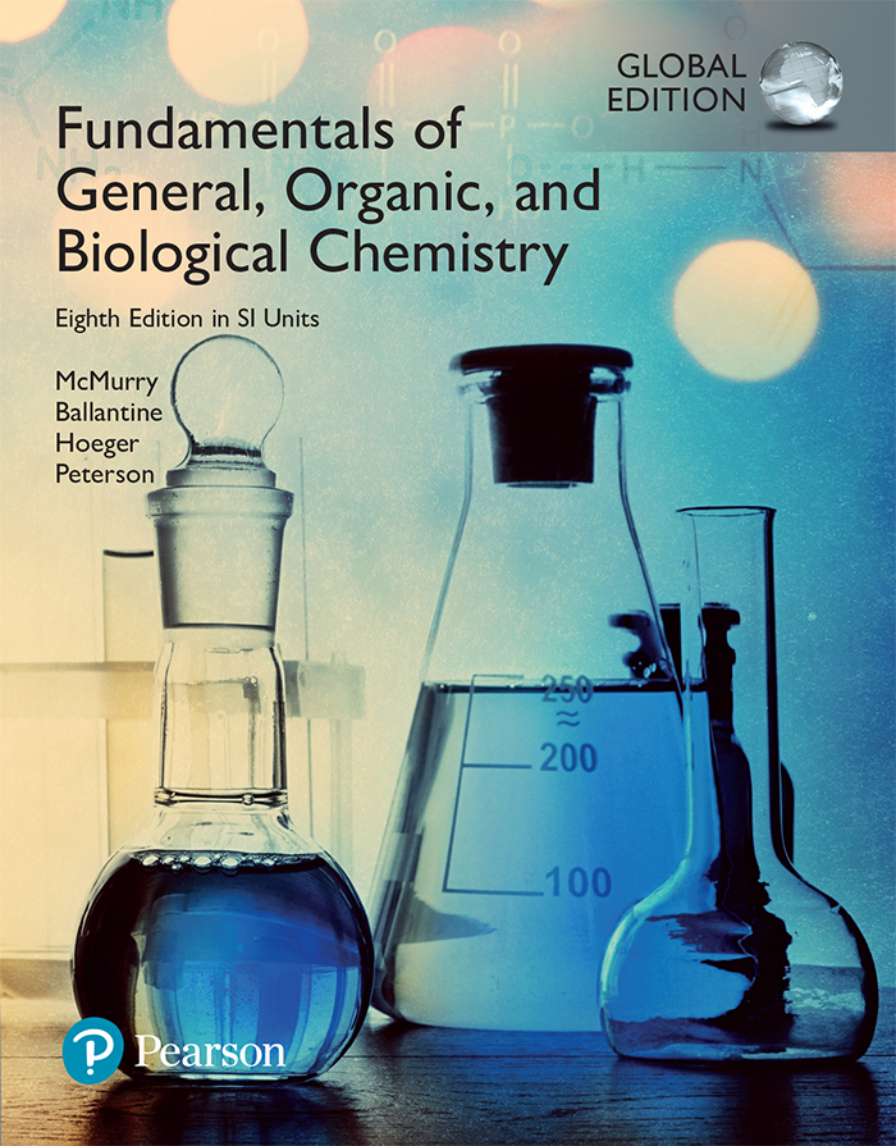
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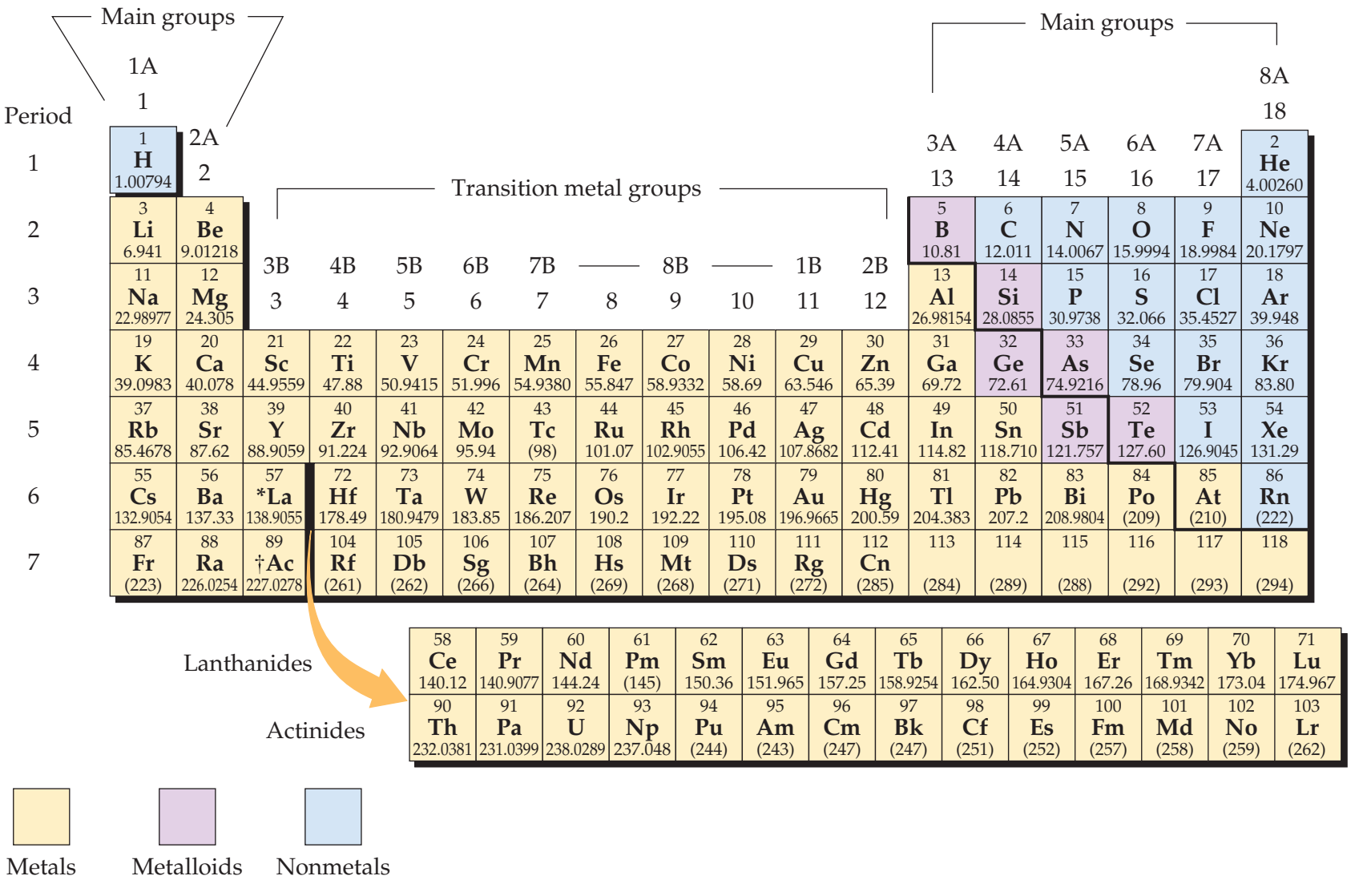

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Fundamentals of General, Organic, and Biological

CHEMISTRY

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Fundamentals of General, Organic, and Biological

CHEMISTRY

Eighth Edition in SI Units

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Authorized adaptation from the United States edition, entitled Fundamentals of General, Organic, and Biological Chemistry, *8th Edition, ISBN 978-0-13-401518-7, by John E. McMurry, David S. Ballantine, Carl A. Hoeger, and Virginia E. Peterson published by Pearson Education © 2018.*

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

10 9 8 7 6 5 4 3 2 1

ISBN 10: 1-292-12346-X
ISBN 13: 978-1-292-12346-2

Typeset by Lumina Datamatics, Inc.

Printed and bound in Malaysia

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John McMurry, educated at Harvard and Columbia, has taught approximately 17,000 students in general and organic chemistry over a 30-year period. A professor of chemistry at Cornell University since 1980, Dr. McMurry previously spent 13 years on the faculty at the University of California at Santa Cruz. He has received numerous awards, including the Alfred P. Sloan Fellowship (1969–1971), the National Institute of Health Career Development Award (1975–1980), the Alexander von Humboldt Senior Scientist Award (1986–1987), and the Max Planck Research Award (1991).

David S. Ballantine received his B.S. in Chemistry in 1977 from the College of William and Mary in Williamsburg, VA, and his Ph.D. in Chemistry in 1983 from the University of Maryland at College Park. After several years as a researcher at the Naval Research Labs in Washington, DC, he joined the faculty in the Department of Chemistry and Biochemistry of Northern Illinois University, where he has been a professor since 1989. He was awarded the Excellence in Undergraduate Teaching Award in 1998. Since then, he has served as the coordinator for the Introductory and General Chemistry programs, with responsibilities for supervision of supervising the laboratory teaching assistants. He served as the departmental director of undergraduate studies from 2008 to 2014 and is currently the associate dean for undergraduate affairs in the College of Liberal Arts and Sciences. He continues to teach in the Department of Chemistry and Biochemistry.

Carl A. Hoeger received his B.S. in Chemistry from San Diego State University and his Ph.D. in Organic Chemistry from the University of Wisconsin–Madison in 1983. After a postdoctoral stint at the University of California–Riverside, he joined the Peptide Biology Laboratory at the Salk Institute in 1985, where he supervised the NIH Peptide Facility while doing basic research in the development of peptide agonists and antagonists. During this time, he also taught general, organic, and biochemistry at San Diego City College, Palomar College, and Miramar College. He joined the teaching faculty at University of California–San Diego (UCSD) in 1998. Dr. Hoeger has been teaching chemistry to undergraduates for 30 years, where he continues to explore the use of technology in the classroom; his current project involves the use of video podcasts as adjuncts to live lectures, along with the use of tablets to deliver real-time lectures with slide annotations. In 2004, he won the Barbara and Paul Saltman Distinguished Teaching Award from UCSD. He is deeply involved with both the general and organic chemistry programs at UCSD and has shared partial responsibility for the training and guidance of teaching assistants and new instructors in the Chemistry and Biochemistry department.

Virginia E. Peterson received her B.S. in Chemistry in 1967 from the University of Washington in Seattle and her Ph.D. in Biochemistry in 1980 from the University of Maryland at College Park. Between her undergraduate and graduate years, she worked in lipid, diabetes, and heart disease research at Stanford University. Following her Ph.D., she took a position in the Biochemistry Department at the University of Missouri in Columbia and is now professor emerita. When she retired in 2011, she had been the director of undergraduate advising for the department for 8 years and had taught both senior capstone classes and biochemistry classes for nonscience majors. Although retired, Dr. Peterson continues to advise undergraduates and teach classes. Awards include both the college-level and the university-wide Excellence in Teaching Award and, in 2006, the University's Outstanding Advisor Award and the State of Missouri Outstanding University Advisor Award. Dr. Peterson believes in public service and in 2003 received the Silver Beaver Award for service from the Boy Scouts of America. In retirement, she continues her public service activities by participating in a first-year medical student mentoring program and her more than 25-year commitment to the Boy Scouts of America as an active adult volunteer.

Sara K. Madsen received her B.S. in Chemistry at Central Washington University in Ellensburg, Washington, in 1988 and her Ph.D in Inorganic Chemistry at the University of Wyoming in 1998. She has been teaching since 2001. The beginning of her teaching career started with a one-semester survey course and moved from there to courses in general, organic, and biochemistry, general chemistry, organic and inorganic chemistry for undergraduates, and inorganic chemistry for graduate students. She loves helping students develop the connections between ideas and concepts and, above all, exposing their realization about how chemistry is involved in their program of study or professional path.

Brief Contents

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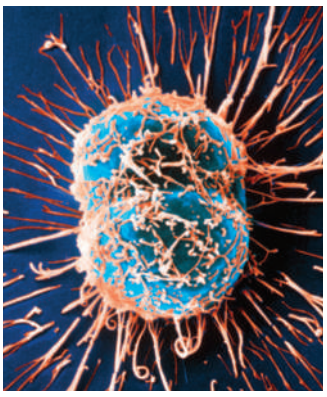

Features

CHEMISTRY IN ACTION

MASTERING REACTIONS

HANDS-ON CHEMISTRY

Preface

This textbook and its related digital resources provide students in the allied health sciences with a needed background in chemistry and biochemistry while offering a general context for chemical concepts to ensure that students in other disciplines gain an appreciation of the importance of chemistry in everyday life.

To teach chemistry all the way from "What is an atom?" to "How do we get energy from glucose?" is a challenge. Throughout our general chemistry and organic chemistry coverage, the focus is on concepts fundamental to the chemistry of living things and everyday life. In our biochemistry coverage, we strive to meet the further challenge of providing a context for the application of those concepts in biological systems. Our goal is to provide enough detail for thorough understanding while avoiding so much detail that students are overwhelmed. Many practical and relevant examples are included to illustrate the concepts and enhance student learning.

The material covered is ample for a two-term introduction to general, organic, and biological chemistry. While the general and early organic chapters contain concepts that are fundamental to understanding the material in biochemistry, the later chapters can be covered individually and in an order that can be adjusted to meet the needs of the students and the duration of the course.

The writing style is clear and concise and punctuated with practical and familiar examples from students' personal experience. Art work, diagrams, and molecular models are used extensively to provide graphical illustration of concepts to enhance student understanding. Since the true test of knowledge is the ability to apply that knowledge appropriately, we include numerous worked examples that incorporate consistent problem-solving strategies.

Regardless of their career paths, all students will be citizens in an increasingly technological society. When they recognize the principles of chemistry at work not just in their careers but in their daily lives, they are prepared to make informed decisions on scientific issues based on a firm understanding of the underlying concepts.

New to This Edition

The major themes of this revision are active learning, an increased focus on clinical examples, updates based on current teaching and research findings, and digital innovations designed to engage and personalize the experience for students, all of which are accomplished in a variety of ways:

- **NEW! Chapter opening photos and vignettes** with an increased clinical focus have been added to provide a theme for each chapter and to strengthen connections between the concepts and applications in Chemistry in Action features in the chapter.
- **NEW! Chapters now have a more focused roadmap** that begins with specific learning objectives and ends with a summary study guide that addresses these initial goals and offers students targeted problems designed to help them assess their ability to understand those topics.
- **NEW! Hands-On Chemistry** boxes offer students an opportunity to solidify their understanding of chemistry through elementary experiments that can be safely done in their living spaces with household items. Many students strongly benefit from kinesthetic activities, and regardless of whether this is their "preferred" style, the evidence suggests that variety in exposure to concepts is by itself tremendously valuable.
- **NEW! Interactive Worked Examples** have been developed and are identified in the text with special icons.
- **NEW! In-chapter questions have been added to the Chemistry in Action and Mastering Reactions** features to reinforce the connection between the chapter content and practical applications.

- **NEW! Concept Maps** have been added to most chapters, and others have been modified to draw connections between general, organic, and biological chemistry.
- **Updated Concept Links** offer visual reminders for students that indicate when new material builds on concepts from previous chapters or foreshadow related material that will be explained in more detail in future chapters.
- **Updated questions in the end-of-chapter section build on Concept Links** and require students to recall information learned in previous chapters.
- **Chemistry in Action** features (many with a clinical focus) extend the discussion of major chapter topics in new ways, providing students with enhanced perspective on core concepts relevant to their future careers.
- **All Learning Objectives tied to EOC problem sets:** Chapter summaries include a list of EOC problems that correspond to the learning objectives for a greater connection between problems and concepts.
- **NEW! Group Problems** at the end of every chapter are ideally used in class to get students to carefully think about higher level problems, such as how concepts fit together, or to put the concepts they have learned to use in a clinical application.
- **Chapters 1 and 2** have been restructured: Chapter 1 focuses on building math skills, while Chapter 2 focuses on matter, atomic structure, and the periodic table.
- **An expanded discussion of stereochemistry and chirality** has been moved to Chapter 14 to allow instructors and students more time to get used to this challenging topic before coming across it again in biochemistry. The concept of symmetry has also been introduced in this section.
- **Chapter 16 is now the chapter on amines**, allowing the discussion of organic bases and acids (Chapter 17) to flow together, whereas in the seventh edition, they were separated by the ketone and aldehyde chapter, which is now Chapter 15.
- **Chapter 20 is now the chapter on carbohydrates**, preceding the discussion of energy generation (now Chapter 21) and carbohydrate metabolism.
- **Chapter 25 is now the chapter on protein metabolism**, completing the discussions of metabolism before addressing DNA (Chapter 26) and Genomics (Chapter 27).
- **The Use of SI Units:** All the units in this edition have been converted to SI units, except where a non-SI unit is commonly used in scientific, technical, and commercial literature in most regions.

Organization

General Chemistry: Chapters 1–11 The introduction to elements, atoms, the periodic table, and the quantitative nature of chemistry (Chapters 1 and 2) is followed by chapters that individually highlight the nature of ionic and molecular compounds (Chapters 3 and 4). The next three chapters discuss chemical reactions and their stoichiometry, energies, rates, and equilibria (Chapters 5, 6, and 7). Topics relevant to the chemistry of life follow: Gases, Liquids, and Solids (Chapter 8); Solutions (Chapter 9); and Acids and Bases (Chapter 10). Nuclear Chemistry (Chapter 11) closes the general chemistry sequence.

Organic Chemistry: Chapters 12–17 These chapters concisely focus on what students must know in order to understand biochemistry. The introduction to hydrocarbons (Chapters 12 and 13) includes the basics of nomenclature. Discussion of functional groups with single bonds to oxygen, sulfur, or a halogen (Chapter 14) is followed by introducing aldehydes and ketones (Chapter 15), where a double bond between carbon and oxygen plays a key role in their chemistry. A short chapter on organic bases, the amines, which are so important to the chemistry of living things and drugs (Chapter 16) follows. Finally, the chemistry of carboxylic acids and their derivatives (esters and amides) is covered (Chapter 17), with a focus on similarities among the derivatives. Attention to the mechanisms by which organic reactions occur and the vernacular used to describe them has been retained in this edition. Stereochemistry, which is key to the understanding of how biological molecules function as they do, has been moved to Chapter 14 in this edition, allowing students more exposure to this complicated topic before reaching the biological chemistry section of this text.

Biological Chemistry: Chapters 18–29 Rather than proceeding through the complexities of protein, carbohydrate, lipid, and nucleic acid structure before getting to the roles

of these compounds in the body, structure and function are integrated in this text. Protein structure (Chapter 18) is followed by enzyme and coenzyme chemistry (Chapter 19). Next, the structure and functions of common carbohydrates are introduced (Chapter 20). With enzymes and carbohydrates introduced, the central pathways and themes of biochemical energy production can be described (Chapter 21). If the time you have available to cover biochemistry is limited, stop with Chapter 21 and your students will have an excellent preparation in the essentials of metabolism. The following chapters cover more carbohydrate chemistry (Chapter 22), then lipid chemistry (Chapters 23 and 24), followed by protein and amino acid metabolism (Chapter 25). Next, we discuss nucleic acids and protein synthesis (Chapter 26) and genomics (Chapter 27). The last two chapters cover the function of hormones and neurotransmitters and the action of drugs (Chapter 28) and provide an overview of the chemistry of body fluids (Chapter 29).

Chapter-by-Chapter Changes

Coverage of General Chemistry

The major revisions in this section involve reorganization or revision of content to strengthen the connections between concepts and to provide a more focused coverage of specific concepts. Concept Maps, included in all general chemistry chapters, reinforce the relationship between topics.

Specific changes to chapters are provided below:

Chapter 1

- Content related to elements and the periodic table was moved to Chapter 2.
- Information on shape-memory alloys was added to the Chemistry in Action "Temperature Sensitive Materials" and the clinical information in the Chemistry in Action "Aspirin" and "A Measurement Example: Obesity and Body Fat" was updated.

Chapter 2

- Content from Chapter 1 on matter and the periodic table was moved to Chapter 2 to provide a more comprehensive and concentrated focus in the chapter.
- Information on the periodic table has been updated to reflect recent discoveries.
- A new Chemistry in Action, "Essential Elements and Group Chemistry," has been added. One Chemistry in Action was eliminated and "Are Atoms Real?" and "Atoms and Light" were revised to strengthen the connections between chapter content and clinical applications.

Chapter 3

- Sections have been reorganized to provide a more logical progression from ions and ion formation to the naming of ions and ionic compounds and finishing with the properties of ionic compounds. Coverage on the octet rule was also expanded and moved to earlier in the chapter.
- The Chemistry in Action "Salt" was streamlined to enhance clarity and relevancy to the student, and clinical information added.

Chapter 4

- Additional tables and text have been added, including a new Worked Example on coordinate covalent bonds, and some figures have been modified to enhance student learning of molecular models and molecular shape.
- Both the Chemistry in Action "VERY Big Molecules" and "Damascenone by Any Other Name Would Smell as Sweet" were updated with new clinical applications and photos.

Chapter 5

- Content from Section 5.3 from the seventh edition (Classes of Chemical Reactions) has been distributed to the individual sections dealing with the types of reactions: 5.3 (Precipitation Reactions), 5.4 (Neutralization Reactions), and 5.5 (Redox Reactions).
- Both Chemistry in Action were streamlined, and the Chemistry in Action "Batteries" was updated with relevant, new clinical applications.

Chapter 6

- The limiting reactant and percent yield discussion was expanded and clarified with new, specific examples to enhance student understanding.
- One Chemistry in Action was eliminated, and others were revised to strengthen the connections between chapter content and practical applications.

Chapter 7

- The quantitative aspects of spontaneity, entropy, enthalpy discussions (including the Worked Example) were revised to enhance clarity, and the Worked Example on drawing energy diagrams was simplified.
- One Chemistry in Action was eliminated, and the Chemistry in Action "Regulation of Body Temperature" was updated with new, practical applications.

Chapter 8

- The qualitative discussions on enthalpy and entropy in Section 8.1 were significantly streamlined.
- Section 8.13 from the seventh edition (Water: A Unique Liquid) has been deleted, and the content has been distributed to other sections to provide relevant examples for key concepts.
- The title to the last section (Section 8.14) was changed to "Change of State Calculations" to more clearly identify the focus for this section and to distinguish the content from the more general discussion on the changes of state of matter in Section 8.1.
- The Chemistry in Action "CO_2 as an Environmentally Friendly Solvent" was updated with new, cutting-edge information on supercritical fluids as they relate to allied health.

Chapter 9

- Section 9.3 (Solid Hydrates) was modified and converted into a new Chemistry in Action, "Solid Hydrates—Salt + Water."
- Section 9.10 from the seventh edition (Electrolytes in Body Fluids) has been modified in the eighth edition and combined with Section 9.9 (Ions in Solution: Electrolytes). References to gram-equivalents have been removed.
- The Chemistry in Action "Time-Release Drug Delivery Systems" was updated with new, clinical content.

Chapter 10

- Sections 10.1 (Acids and Bases in Aqueous Solution) and 10.3 (The Bronsted-Lowry Definition of Acids and Bases) have been combined to highlight the relationship between the various definitions of acids and bases.
- The information in Section 10.2 (Some Common Acids and Bases) has been condensed into Table 10.1.
- Section 10.7 (Measuring Acidity in Aqueous Solution: pH) and Section 10.9 (Laboratory Determinations of Acidity) have been combined to strengthen the connection between these concepts.
- Section 10.12 (Some Common Acid-Base Reactions) has been moved forward in the chapter, and Sections 10.10 (Buffer Solutions), 10.14 (Acidity and Basicity of

Salt Solutions), and 10.13 (Titrations) have been rearranged to improve the logical progression of these concepts.
- The Chemistry in Action "Acid Rain" was updated with new statistics, maps, and bar graphs.

Chapter 11

- Section 11.6 (Radioactive Decay Series) was abbreviated and combined with Section 11.5 (Radioactive Half-Life). A new, additional Worked Example on half-lives was added as metadata indicated students struggled with this concept.
- Sections 11.8 (Detecting Radiation) and 11.9 (Measuring Radiation) were condensed and combined.

Coverage of Organic Chemistry

Since organic and biological chemistry are so tightly allied with one another, a major emphasis has been placed on the introduction of biologically significant molecules throughout the organic chapters in this edition. Emphasis on making the fundamental reactions that organic molecules undergo much clearer to the reader, with particular attention on those reactions encountered again in biochemical transformations has been retained in the Mastering Reactions feature boxes. This boxed feature discusses in relative depth the "how" behind a number of organic reactions. Mastering Reactions has been designed so that they may be integrated into an instructor's lecture or simply left out with no detriment to the material in the text itself, to accommodate those that do not wish to discuss the mechanisms of organic reactions. More emphasis on the use and evaluation of line-angle structure for organic molecules has been added, as this is incredibly important when discussing biomolecules. New to this edition is the inclusion of a more detailed examination of stereochemistry and chirality; its new placement at the end of Chapter 14 will allow students more time to grasp these concepts, but will also allow instructors who do not wish to discuss it to easily omit them. New and updated application features (Chemistry in Action) have been included in almost all the organic chapters, stressing the clinical aspects of the different classes of organic molecules and reflecting current understanding and research into the topics covered. Additionally, each chapter includes a new supplementary feature known as Integrated Worked Examples, which will provide students with tutor-like walkthroughs of topics and reactions they need to be familiar with before heading into the biological chemistry sections of this text.

Other specific changes to chapters are provided below:

Chapter 12

- Several figures were revised and/or simplified for clarity and to enhance understanding. Art was added to help students synthesize complex topics where visuals were previously lacking.
- Table 12.1 has been reworked to highlight the atoms responsible for each functional group.
- Table 12.2 (Common Abbreviations in Organic Chemistry) has been added.
- A three-step mechanism (initiation, propagation, and termination) was added to the halogenation section along with a new Worked Example on drawing halogenated isomers; this Worked Example will be useful throughout the organic chapters in learning to draw isomers of other organic molecules.
- A new Chemistry in Action discussing biological methylation, "How Important Can a Methyl Group Really Be?," has been added, and the Chemistry in Action "Surprising Uses of Petroleum" was updated with new clinical information.
- There is an expanded functional group concept map that will aid in classifying functional groups; this will be included at the end of each of the organic chapters, with coloring added as each functional group family is discussed.

Chapter 13

- Expanded use and discussion of line structures has been added throughout.
- A new Chemistry in Action discussing biologically active alkynes, "Enediyne Antibiotics: A Newly Emerging Class of Antitumor Agents," has been added.

Chapter 14

- Table 14.1 (Common Alcohols and Their Uses) has been added, replacing and expanding on what was previously Section 14.3, making it easier for students to digest.
- A new and expanded discussion of stereochemistry and chirality has been added (Section 14.10), moving the introduction of these topics from Chapter 18 to a more appropriate location in the text.
- Two new Worked Examples, one on drawing alcohols, have been added.
- A new Chemistry in Action discussing the harm ethanol has on fetuses, "Fetal Alcohol Syndrome: Ethanol as a Toxin," has been added.

Chapter 15

- Chapter 15, known previously as the amine chapter, now covers aldehydes and ketones.
- The section on common aldehydes and ketones has been shortened by the inclusion of Table15.2 (Common Aldehydes and Ketones and Their Uses) making it easier for students to read.
- The Addition of Alcohols to Aldehydes and Ketones section was revised to clarify the distinction between hemiketals and hemiacetals.
- Worked Examples and problems have been modified to include the early introduction of carbohydrates.
- A new Chemistry in Action discussing anticancer drugs, "When Is Toxicity Beneficial?," has been added.

Chapter 16

- This is now the amine chapter, which was Chapter 15 in the seventh edition.
- The section on alkaloids has been simplified by the inclusion of Table16.2 (Some Alkaloids and Their Properties) making it easier for students to digest the material.
- A new Worked Example on ammonium ions as acids has been included.
- A new Chemistry in Action discussing antidepressants, "Calming a Stormy Mind: Amines as Anti-Anxiety Medications," has been added.

Chapter 17

- The concept of pKa is discussed in Section 17.2; in addition, Table 17.2 now contains pKa values for the acids listed.
- Section 17.3 in the seventh edition has been expanded and converted into a new Chemistry in Action, "Medicinally Important Carboxylic Acids and Derivatives."
- The Worked Example on acid anhydrides has been removed and their coverage is limited in this edition.
- The Chemistry in Action "Medications, Body Fluids, and the 'Solubility Switch'" that was in Chapter 15 in the seventh edition has been updated and moved to the end of this chapter.

Coverage of Biological Chemistry

Biological chemistry, or biochemistry as professionals refer to the subject, is the chemistry of organisms and particularly chemistry at the cellular level—both inside and outside the cell. The foundations of biological chemistry are found in inorganic and organic chemistry, the first two major topics of this textbook. Biological chemistry integrates

inorganic and organic chemistry in the study of biological molecules, many of which are large organic molecules with specific cellular roles. As you will see in the following chapters, biological molecules undergo the same reactions studied in the organic chemistry part of this book, and the fundamentals of inorganic chemistry are also important in cells.

Chapter 18

- The chapter was reorganized for a smoother flow that is more pedagogically sound. We now present an overview of proteins first, then discuss amino acids, peptides and peptide bonds, followed by protein structure and chemical properties. The one letter code for each amino acid was added to Table 18.3.
- The chirality discussion is limited to amino acids (the rest of this discussion moved to Chapter 14).
- Diagrams of the specific examples of the forces involved in tertiary protein structure were added.

Chapter 19

- Two new tables and a revised discussion enhance the "Enzyme Cofactors" section.
- The enzyme classification section has a new table describing each classification.
- The vitamins, minerals, and antioxidants section was streamlined for clarity.
- A Mastering Reactions on how to read biochemical reactions has been added.
- The Chemistry in Action "Enzymes in Medical Diagnosis" was updated to reflect current blood chemistry tests used in diagnosis of a heart attack.

Chapter 20

- This is now the carbohydrates chapter.
- Two new tables, one on important monosaccharides and another on disaccharides, make this content easy for students to digest. Both polysaccharides sections were streamlined and combined into one section.

Chapter 21

- This is now the generation of biological energy chapter.
- The first two sections were streamlined by reducing much of the review material from Chapter 7 (a Concept to Review link was added in place of lengthy narrative, directing students back to where they can review the material if necessary) and combined into one section.
- The citric acid cycle is now explained equation by equation with the description of each step directly above the equation for better student understanding.
- The section on reactive oxygen species has been converted into a new Chemistry in Action, "Reactive Oxygen Species and Antioxidant Vitamins."
- The discussion of "uncouplers" has been integrated into a new Chemistry in Action, "Metabolic Poisons."

Chapter 22

- The discussion of the steps in glycolysis was improved by explicitly splitting the descriptions of the reactions into individual steps.
- Most of the discussion of glucose metabolism in diabetes has been moved to a revised and now comprehensive Chemistry in Action "Diagnosis and Monitoring of Diabetes."

Chapter 23

- The Phospholipids and Glycolipids section was reorganized to ensure a smoother, more logical presentation of concepts.
- The Chemistry in Action "Lipids in the Diet" was updated to include some information from the deleted Chemistry in Action "Butter and Its Substitutes" as well as updated dietary and obesity statistics.

- The text discussion of eicosanoids was converted into a new Chemistry in Action, "Eicosanoids: Prostaglandins and Leucotrienes."

Chapter 24

- A clearer explanation of fatty acid activation and beta-oxidation is presented step-by-step with the appropriate biochemical reaction shown with each step's description.
- The discussion of energy yields from fat metabolism was converted into two sequential Worked Examples.
- The Chemistry in Action "Lipids and Atherosclerosis" was combined with information from the deleted Chemistry in Action "Fat Storage: A Good Thing or Not?" and updated to give a new Chemistry in Action, "Fat Storage, Lipids, and Atherosclerosis."

Chapter 25

- This chapter, Protein and Amino Acid Metabolism, was Chapter 27 in the seventh edition.
- The Chemistry in Action "The Importance of Essential Amino Acids and Effects of Deficiencies" on essential amino acids has been updated with new clinical information and streamlined.

Chapter 26

- Changes were made to the figure showing DNA replication to clarify copying of the opposite strands.
- The Chemistry in Action "Influenza: Variations on a Theme" now focuses on the nature of the common influenza viruses, primarily type A, and zoonotic pools for the mutating virus.

Chapter 27

- This chapter, "Genomics," was Chapter 26 in the seventh edition.
- The Chemistry in Action on the polymerase chain reaction has been shortened and streamlined.
- The Chemistry in Action "DNA Fingerprinting" has been updated to include PCR fingerprinting.

Chapter 28

- This chapter is now focused only on the messenger aspect of these peptides, amino acid derivatives, and steroids.
- Table 28.2, "Acetylcholine Drug Family" (therapeutic or poisonous), has been added to clarify this section for students.
- The steroid-abuse section was condensed to increase relevance for the student.

Chapter 29

- A new Chemistry in Action on common blood tests, "What's in Your Blood Test?," has been added and the Chemistry in Action "Blood–Brain Barrier" was updated with new clinical information.

Acknowledgments

Although this text is now in its eighth edition, each revision has aspired to improve the quality and accuracy of the content and emphasize its relevance to the student users. Achieving this goal requires the coordinated efforts of a dedicated team of editors and media experts. Without them, this textbook would not be possible.

On behalf of all my coauthors, I would like to thank Jeanne Zalesky (Editor in Chief), Chris Hess (Senior Acquisitions Editor) and Scott Dustan (Senior Acquisitions Editor) for building an excellent team for this project. Thanks also to Andrea Stefanowicz (Production Manager), Eric Schrader (Photo Researcher), Sarah Shefveland (Program Manager), and Lindsey Pruett (Editorial Assistant) for their attention to detail as we moved forward. Coleen Morrison, our developmental editor, deserves special recognition for providing invaluable feedback—her painstaking perusal of each chapter and her eye for details have contributed greatly to the accessibility and relevance of the text. Very special thanks also to Beth Sweeten, Senior Project Manager, who patiently guided the process and worked closely with us—thank you for your flexibility and dedication to the success of this project.

The value of this text has also been enhanced by the many individuals who have worked to improve the ancillary materials. Particular thanks to Emily Halvorson for her efforts to ensure the accuracy of the answers to problems provided in the text and Susan McMurry for her revisions to the solutions manual. Thanks to Kyle Doctor, Jackie Jakob, Sara Madsen and Dario Wong for their work on the media supplements. Thanks also to Margaret Trombley, Kristin Mayo, and Jayne Sportelli for their efforts to expand and improve Pearson Mastering Chemistry.

Finally, thank you to the many instructors and students who have used the seventh edition and have provided valuable insights and feedback to improve the accuracy of the current edition. We gratefully acknowledge the following reviewers for their contributions to the eighth edition.

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Martin Wallace, *Butte College*
Erik Wasinger, *California State University, Chico*

Reviewers of the Eighth Edition

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The authors are committed to maintaining the highest quality and accuracy and look forward to comments from students and instructors regarding any aspect of this text and supporting materials. Questions or comments should be directed to the lead coauthor.

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Acknowledgments for the Global Edition

Pearson would like to thank and acknowledge the following people for their contributions to this Global Edition.

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Christel Meert, *Hogeschool Gent*
Andrew Pearson, *Griffith University*

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Increased Focus on Clinical Relevancy

Active learning, an increased focus on clinical examples, updates based on current teaching and research findings, and digital innovations designed to engage and personalize students' experiences make the eighth edition of *Fundamentals of General, Organic, and Biological Chemistry* simply the best choice for students with a future in allied health.

NEW! Chapter-opening stories and visuals throughout the text have a greater clinical focus, providing even more relevance to allied health majors. Throughout the chapters, Learning Objectives follow each section head, and each chapter ends with a summary study guide offering students targeted problems designed to help them assess their ability to understand those topics.

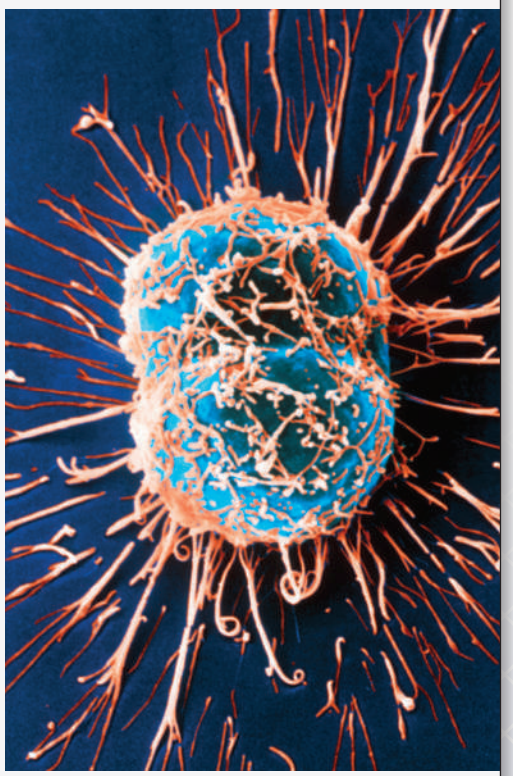
13

Alkenes, Alkynes, and Aromatic Compounds

CONTENTS

CONCEPTS TO REVIEW

A. VSEPR and Molecular Shapes (Section 4.8)
B. Families of Organic Molecules: Functional Groups (Section 12.2)
C. Drawing Organic Structures (Section 12.4)
D. The Shapes of Organic Molecules (Section 12.5)
E. Naming Alkanes (Section 12.6)



▲ In the war on cancer, potent new drugs containing carbon–carbon triple bonds are providing hope for the treatment of diseases such as cervical cancer.

Functional groups give organic molecules their characteristic physical, chemical, and biological properties. In Chapter 12, we examined the simplest hydrocarbons, alkanes, which provide the scaffolding upon which the complicated molecules responsible for life are built. Now we will look at the chemistry of molecules that contain carbon–carbon multiple bonds, or *unsaturated* hydrocarbons. While alkenes and aromatic systems are found in many naturally occurring biomolecules, alkynes are not as commonly observed. However, when

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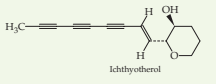
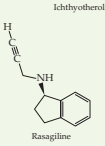
CHEMISTRY IN ACTION boxes (many with a clinical focus) extend the discussion of major chapter topics in new ways, providing students with an enhanced perspective on core concepts relevant to their future careers. The final Chemistry in Action box in each chapter ties back to the chapter-opening topic, ensuring the clinical relevancy is woven throughout the chapter from beginning to end.

CHEMISTRY IN ACTION

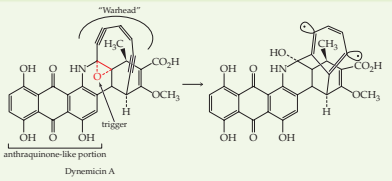
Enediyne Antibiotics: A Newly Emerging Class of Antitumor Agents

While we discuss alkynes only briefly in this chapter and this text as a whole, it is not because alkynes are not important in organic chemistry. Alkynes are not usually found in nature; however, when they are isolated from natural sources, such as plants and bacteria, they have unexpected physiological properties, including toxicity. For example, ichthyotherol, a trialkyne, isolated from the leaves of a small herb found in the Amazon and Central America, inhibits energy production in mitochondria, and while being toxic to fish, mice, and dogs, has no effect on humans. This has caused chemists to investigate what might happen if the alkyne function were introduced into other biologically active molecules, which has led to the discovery of pharmaceuticals such as Rasagiline, a monoamine oxidase inhibitor effective in treating Parkinson's disease. This compound, due to its neuroprotective nature, is also offering a novel approach to Alzheimer's drug therapy. Rasagiline seems to enhance memory and learning, while also improving mood, motivation, and age-related memory decline and provides a great lead for the discovery of new medicines to treat this debilitating disease. Due to successes such as Rasagiline, chemists and biochemists have intensified the hunt for naturally occurring alkynes. This expanding pursuit for new alkyne-containing natural products has led to the discovery of a very unlikely class of antitumor antibiotics known as the enediynes, which we first learned about at the beginning of the chapter. Initially discovered in a fermentation broth derived from the bacteria *Micromonospora*, they represent a new chemical structure class for antibiotics.





The enediyne family of compounds represents the most potent antitumor agents known. The toxic nature of these compounds arises from their ability to cause scission of DNA strands in their target. The enediyne antibiotics fall into three basic families: the calicheamicins, the dynemicins (shown next), and the most complex of the group, the chromoproteins. All members have three distinct regions within them: (1) an anthraquinone-like portion; (2) a chemical "warhead" comprised of two triple bonds, conjugated through a double bond, within a 9–10-membered ring; and (3) a "trigger." In Dynemicin A (shown above), that trigger is the three-membered epoxide ring (highlighted in red). The anthraquinone portion intercalates into the major groove of DNA; the trigger is then activated by some nucleophilic species (such as an oxygen, nitrogen, or sulfur atom) that attacks and then opens the epoxide ring. Once opened, the warhead undergoes a rearrangement reaction, producing an extremely reactive diradical aromatic species, which then induces the breakage of the DNA strands.



All of the enediynes are very toxic, as are all antitumor agents. One way to utilize them in the war on cancer would be to attach them to an antibody specifically prepared to target the tumor cells the doctor wishes to destroy. This method, known as "immunotargeting," would allow the preparation of a "magic bullet," which would attack only the tumor cells and nothing else. One of the reasons that the enediyne antibiotics are so attractive is that they have activity against drug-resistant tumors. Many cancer cells have natural resistance to a number of the drugs usually used to treat them or will develop resistance over the course of a treatment. This, coupled with a lack of selectivity to antitumor agents (antitumor drugs affect all cells, not just cancer) is one of the major causes of the ineffectiveness of anticancer therapies. Compounds such as Dynemicin A and others discovered through studies of the enediynes could represent a new weapon in our assault on an old and deadly foe: cancer.

The meaning of the wedged and dashed bonds will be clarified in Section 14.10 when we discuss stereochemistry.

CIA Problem 13.4 What beneficial properties of Rasagiline make it useful for the treatment of Alzheimer's disease?

CIA Problem 13.5 Why would attaching an enediyne-containing molecule to an antibody be an attractive way to treat cancer cells?

CIA Problem 13.6 What are the major causes of the ineffectiveness of anticancer therapies?

NEW! These boxes now include questions at the end of the narrative, designed specifically as engaging checkpoints to help students asses their understanding.

Active Learning Leads to Conceptual Understanding

Fundamentals of General, Organic, and Biological Chemistry has always provided a remarkably clear introduction to the broad subject of allied health chemistry in an appealing, applied, and precise manner. In the eighth edition, the authors make learning chemistry more active through features designed to get students doing chemistry.

HANDS-ON CHEMISTRY 3.1

Obtain a set of Lego building blocks and separate them into groups that are one, two, and three units long (if you do not have access to a physical set of blocks, visit www.buildwithchrome.com/builder). The blocks will represent anions and cations that have charges of 1, 2, and 3, respectively. If possible, try to have multiple colors within each group. Label the blocks in each group as follows:

–*One unit long:* Label as Na^+, K^+, Cl^-, and NO_3^-.
–*Two units long:* Label as Mg^{2+}, Ca^{2+}, Fe^{2+}, O^{2-}, and SO_4^{2-}.
–*Three units long:* Label as Al^{3+}, Fe^{3+}, N^{3-}, and PO_4^{3-}.

Try to have at least three blocks for each ion in a given group and, if possible, keep the colors consistent for a given ion; for example, let all Na^+ ions be black, all Cl^- ions be yellow, all O^{2-} ions be blue, and so on.

Using the blocks, assemble the following compounds by matching anion and cation blocks. Starting with the cation block, connect an anion on top of it. If the anion layer is not long enough for the two layers to match up exactly, add another anion of the same type beside it on top of the cation layer. If the anion layer extends over the end of the cation layer, add another cation to the bottom layer. When the cation and anion layers match exactly in length, count how many of the cation and anion blocks were necessary to determine the formula of the ionic compound.

Try building the compounds suggested next, or make up your own combinations. Just be sure that each compound has a cation and an anion!

a) Cation = Na^+ Anion = SO_4^{2-}
b) Cation = Fe^{2+} Anion = NO_3^-
c) Cation = Mg^{2+} Anion = PO_4^{3-}

HANDS-ON CHEMISTRY 19.1

Do food items contain active catalase? You can test this at home with samples of raw meat and vegetables. You will need clear (not colored), transparent glasses, 3% (v/v) hydrogen peroxide (from a drugstore or grocery store), and a few 1 cm cubes of raw meat such as chicken liver or a bit of hamburger. Also cube some raw potato. Drop some of the raw meat in a glass with a few centimeters of hydrogen peroxide in it. Using a different glass of hydrogen peroxide, do the same thing with potato cubes. What happened with the meat? With the potato? Does the amount of meat or potato used matter? Repeat your experiment with cooked meat and cooked potato. What happened?

Evolution of bubbles means catalase present in the sample was converting hydrogen peroxide to water and oxygen; the enzyme was active, in its native state and not denatured. If no significant amount of bubbles appeared, catalase was either absent or inactive. Based on the results of the trials with raw and cooked samples, was catalase present, absent, or inactive? If inactive, why?

NEW! **HANDS-ON CHEMISTRY** boxes offer students an opportunity to solidify their understanding of chemistry through elementary experiments that can be safely done in their home with household items. Many students strongly benefit from kinesthetic activities, and regardless of whether this is their preferred style, evidence suggests that variety in exposure to concepts is tremendously valuable.

GROUP PROBLEMS

2.95 Look up one of the experiments by the scientists discussed in the Chemistry in Action on page 78, and explain how it contributed to our understanding of atomic structure.

2.96 Do a web search to identify each of the following elements/isotopes and indicate the number of neutrons, protons, and electrons in an atom of the element/isotope:

(a) A radioactive isotope used in cancer treatments. (There may be more than one answer!)

(b) The element having the greatest density.

(c) An element with $Z < 90$ that is *not* found in nature.

2.97 Tellurium $(Z = 52)$ has a *lower* atomic number than iodine $(Z = 53)$, yet it has a *higher* atomic mass (127.60 amu for Te vs. 126.90 amu for I). How is this possible? Can you find any other instances in the periodic table where two adjacent elements exhibit a similar behavior, that is, the element with the lower atomic number has a higher atomic mass?

2.98 Look again at the trends illustrated in Figures 2.3 and 2.4.

(a) How do the peaks/valleys correlate with locations in the periodic table?

(b) Are there other chemical properties that also exhibit periodic trends? What are they?

NEW! **GROUP PROBLEMS** at the end of every chapter are ideally used in class to get students to carefully think about higher level problems, such as how concepts fit together, or to put the concepts they have learned to use in a clinical application.

Integrated Learning Pathway

Chapters now have a more integrated narrative where Learning Objectives provide a starting point and are later revisited as capstones to the chapter in summary and question form.

Measurable **LEARNING OBJECTIVES** are listed as bullet points underneath each chapter section within the text.

18.2 Proteins and Their Functions: An Overview

Learning Objective:

- Describe the different functions of proteins and give an example for each function.

The word *protein* is a familiar one. Taken from the Greek *proteios,* meaning "primary," "protein" is an apt description for the biological molecules that are of primary importance to all living organisms. Approximately 50% of your body's dry mass is protein.

What roles do proteins play in living things? No doubt you are aware that a hamburger is produced from animal muscle protein and that we depend on our own muscle proteins for every move we make. But this is only one of many essential roles of proteins. They provide *structure* (keratin) and *support* (actin filaments) to tissues and organs throughout our bodies. As *hormones* (oxytocin) and *enzymes* (catalase), they control all aspects of metabolism. In body fluids, water-soluble proteins pick up other molecules for *storage* (casein) or *transport* (transferrin, Fe^{3+}). And the proteins of the immune system provide *protection* (Immunoglobulin G) against invaders such as bacteria and viruses. To accomplish their biological functions, which are summarized in Table 18.2, some proteins must be tough and fibrous, whereas others must be globular molecule, as you will see protein in our metabolism.

SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Describe the different functions of proteins and give an example for each function.** Proteins can be grouped by function such as structural, transport, etc. See Table 18.2 *(see Problems 40 and 41).*
- **Describe and recognize the 20 alpha amino acid structures and their side chains.** Amino acids in body fluids have an ionized carboxylic acid group ($-COO^-$), an ionized amino group ($-NH_3^+$), and a side-chain R group bonded to a central carbon atom (the α-carbon). Twenty different amino acids occur in *proteins* (Table 18.3) *(see Problems 38 and 42–45).*
- **Categorize amino acids by the polarity or neutrality of the side chain and predict which are hydrophilic and which are hydrophobic.** Amino acid side chains have acidic or basic functional groups or neutral groups that are either polar or nonpolar. Side chains that form hydrogen bonds with water are hydrophilic; nonpolar side chains that do not form hydrogen bonds with water are hydrophobic *(see Problems 50–51, 110, and 111).*
- **Explain chirality and identify which amino acids are chiral.** All α-amino acids except glycine are chiral *(see Problems 39 and 42–51).*
- **Draw all ionic structures for an amino acid under acidic and basic conditions, and identify the zwitterion.** The dipolar ion in which an amino group and a carboxylic acid group are both ionized is known as a *zwitterion* and the electrical charge on the molecule is zero. For each amino acid, there is a distinctive *isoelectric point*—th which the numbers of positive and negative charges in a so equal. At a more acidic pH, all carboxylic acid groups are protonated; at a more basic pH, all NH_3^+ groups are deprotonated *(see Problems 34 and 52–59).*
- **Identify a peptide bond, and explain how it is formed.** The amide bond formed between the carboxyl group of one amino acid with the amino group of a second amino acid is called a peptide bond *(see Problems 36 and 60–65).*
- **Draw and name a simple protein structure given its amino acid sequence.** Peptides are named by combining the names of the amino acids. Amino acid sequences are often represented by using the three-letter or one-letter abbreviations for the amino acids in a left to right order *(see Problems 36 and 60–65).*
- **Identify the amino-terminal end and the carboxyl-terminal end of a simple protein (peptide) structure given its amino acid sequence.** Amino acid sequences are written with the amino group of the end amino acid on the left and the carboxyl group of the amino acid on the other end of the chain on the right *(see Problems 36 and 60–65).*
- **Define primary protein structure and explain how primary structures are represented.** Protein *primary structure* is the sequence in which the amino acids are connected by peptide bonds. Using formulas or amino acid abbreviations, the primary structures are written with the amino-terminal end on the left and

Each chapter concludes with a summary study guide section that restates the Learning Objectives for each section and lists problems students can do to practice the skills learned for each objective.

ADDITIONAL PROBLEMS

PROTEINS AND THEIR FUNCTIONS: AN OVERVIEW (SECTION 18.2)

18.40 Name four biological functions of proteins in the human body, and give an example of a protein for each function.

18.41 What kind of biological function would each of the following proteins perform?

(a) Human growth hormone **(b)** Myosin
(c) Protease **(d)** Myoglobin

AMINO ACIDS (SECTION 18.3)

18.42 What amino acids do the following abbreviations stand for? Draw the structure of each.
(a) Val **(b)** Ser **(c)** Glu

18.43 What amino acids do the following abbreviations stand for? Draw the structure of each.
(a) Ile **(b)** Thr **(c)** Gln

18.44 Name and draw the structures of the amino acids that fit the following descriptions:
(a) Contains a thiol group **(b)** Contains a phenol group

18.45 Name and draw the structures of the amino acids that fit the following descriptions:
(a) Contains an isopropyl group
(b) Contains a secondary alcohol group

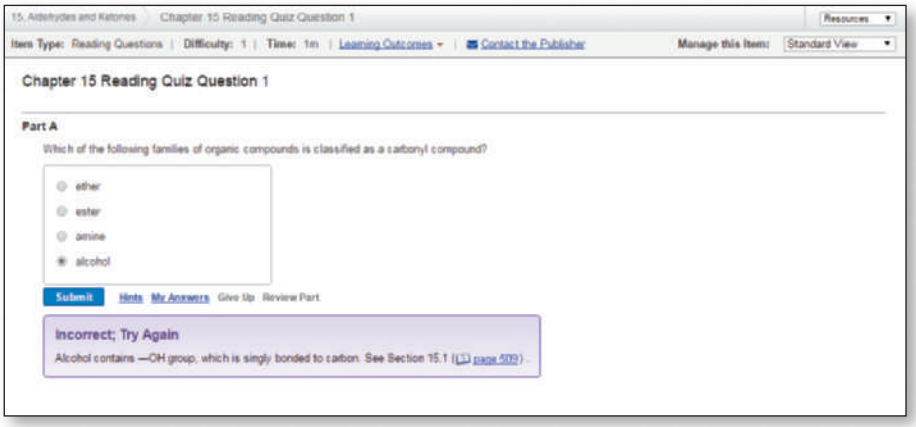
End-of-chapter problems tie back to chapter Learning Objectives, allowing students to test their knowledge of emphasized topics. Metadata, drawn from Pearson Mastering Chemistry usage, on which problems students struggled with most was used to revise both in-chapter and end-of-chapter problems. Further revisions were made to end-of-chapter problems, where applicable, to increase clinical relevancy.

Personalize Learning with Pearson Mastering Chemistry

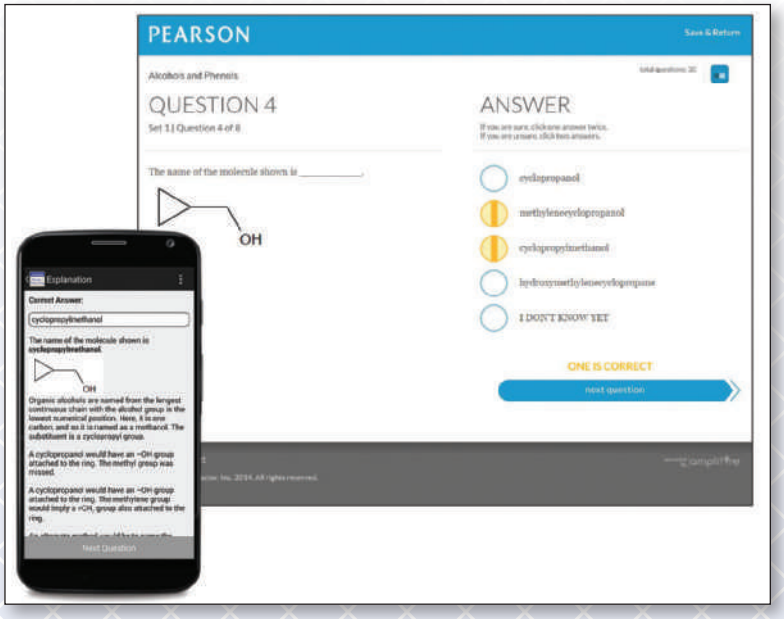
NEW! A strengthened relationship with Pearson Mastering Chemistry helps students develop conceptual understanding before, during, and after class.

BEFORE CLASS

Chapter-specific quizzes and activities focus on important, hard-to-grasp chemistry concepts.

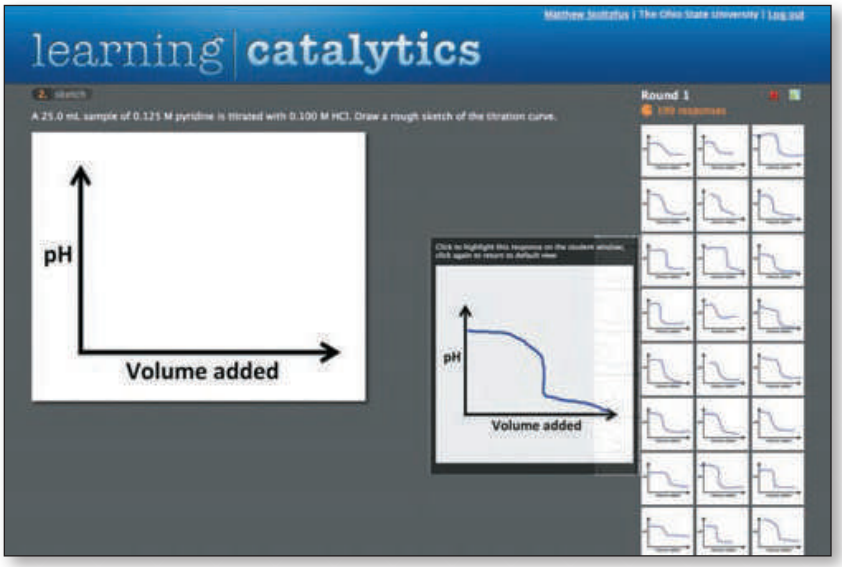


NEW! **DYNAMIC STUDY MODULES** help students study effectively on their own by continuously assessing their activity and performance in real time. Students initially answer a subset of questions, indicating their confidence level for each answer. At the end of this and each subsequent subset, students are given explanations for any problems they missed as well as coaching that moves them toward conceptual understanding. This recursive process continues until students answer all questions in the module correctly and confidently. Dynamic Study Modules are available as graded assignments for use prior to class, and are accessible on smartphones, tablets, and computers.



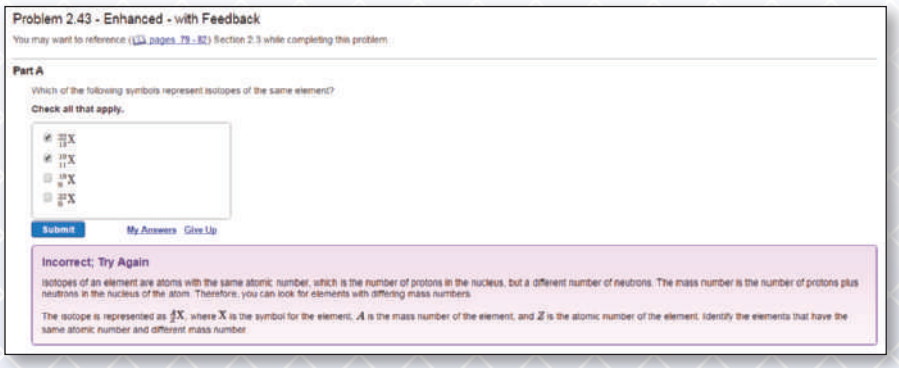
DURING CLASS

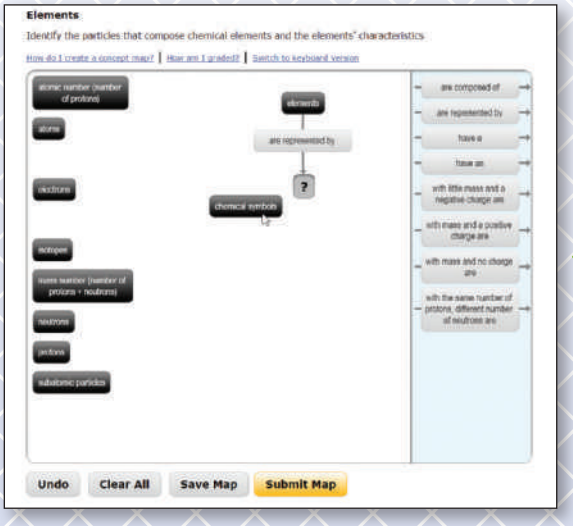
NEW! **LEARNING CATALYTICS™** generates class discussion, guides your lecture, and promotes peer-to-peer learning with real-time analytics. Pearson Mastering Chemistry with eText now provides Learning Catalytics—an interactive student response tool that uses students' smartphones, tablets, or laptops to engage them in more sophisticated tasks and thinking.



AFTER CLASS

End-of-chapter problems within the textbook are available within Pearson Mastering Chemistry and can be automatically graded and assigned for homework or practice. ***New to this edition, 300 problems contain enhanced, wrong answer feedback.***





CONCEPT MAP ACTIVITIES use interactive concept maps and related multiple-choice quiz questions to help students make connections between important concepts within each chapter.

Instructor Resources

Name of Supplement	Available Online	Description
Instructor Resource Manual	✓	The IRM features lecture outlines with presentation suggestions, teaching tips, suggested in-class demonstrations, topics for classroom discussion, and answers to group problems.
TestGen Test Bank	✓	The test bank has been updated to reflect revisions in this text, and contains more than 2,000 multiple choice, true/false, matching, and short answer questions.
Instructor's Resource Materials	✓	The Instructor Resource area provides the following downloadable resources: All illustrations, tables and photos from the text in JPEG format, and pre-built PowerPoint® Presentations (lecture–including Worked Examples, images).

1

Matter and Measurements

CONTENTS

▲ The percentage of body fat can be determined by underwater immersion, which takes advantage of the differences in density of fat as compared to muscle and bone.

According to the U.S. Centers for Disease Control and Prevention, the U.S. population is suffering from a fat epidemic, with more than one-third (34.9% or 78.6 million) of U.S. adults characterized as obese. But how do we define obesity, and how is it measured? Obesity is defined as an excessive amount of body fat. But some body fat is important for good health, so how much body fat is healthy and how much is too much? What is fat, and how do we measure it? Body fat can be estimated using a Body Mass Index (BMI) as discussed later in the chapter, or can be measured directly using underwater immersion, or buoyancy testing, as illustrated in the photo above. The immersion tank uses buoyancy—a property related to the differences in density—to determine the percentage

of body fat. Checking the observed buoyancy on a standard table then gives an estimation of body fat. Density is just one of the concepts we will explore in this chapter, as we learn about the properties of matter and the various forms that matter can take.

The ancient philosophers believed that all matter was composed of four fundamental substances—earth, air, fire, and water. We now know that matter is much more complex, made up of 91 naturally occurring fundamental substances, or elements, in millions of unique combinations. Everything you see, touch, taste, and smell is made of chemicals formed from these elements. Many chemicals occur naturally, but others are synthetic, including the plastics, fibers, and medicines that are so critical to modern life. Just as everything you see is made of chemicals, many of the natural changes you observe taking place around you are the result of *chemical reactions*—the change of one chemical into another. The crackling fire of a log burning in the fireplace, the color change of a leaf in the fall, and the changes that a human body undergoes as it grows and ages are all results of chemical reactions. To understand these and other natural processes, you must have a basic understanding of chemistry.

As you might expect, the chemistry of living organisms is complex, and it is not possible to understand all concepts without a proper foundation. Thus, we will gradually learn to connect the basic concepts, beginning in the first 11 chapters with a grounding in the scientific fundamentals that govern all of chemistry. Next, in the following six chapters, we look at the nature of the carbon-containing substances, or *organic chemicals,* that compose all living things. In the final 12 chapters, we apply what we have learned in the first part of the book to the study of biological chemistry.

We begin in Chapter 1 with an examination of the states and properties of matter. Since our knowledge of chemistry is based on observations and measurements, we include an introduction to the systems of measurement that are essential to our understanding of matter and its behavior.

1.1 Chemistry: The Central Science

Learning Objective:

- Identify properties of matter and differentiate between chemical and physical changes.

Chemistry is often referred to as "the central science" because it is essential to nearly all other sciences. In fact, as more and more is learned, the historical dividing lines between chemistry, biology, and physics are fading, and current research is more interdisciplinary. Figure 1.1 diagrams the relationship of chemistry and biological chemistry to other fields of scientific study.

Chemistry is the study of matter—its nature, properties, and transformations. **Matter,** in turn, is an all-encompassing word used to describe anything physically real—anything you can see, touch, taste, or smell. In more scientific terms, matter is anything that has mass and volume. Like all the other sciences, our knowledge of chemistry has developed by application of a process called the **scientific method.** The discovery of aspirin, for example, is a combination of serendipity and the scientific method: observation, evaluation of data, formulation of a hypothesis, and the design of experiments to test the hypothesis and further our understanding (see the Chemistry in Action on p. 41). Advances in scientific knowledge are typically the result of this systematic approach; hypotheses can be tested by carefully designed experiments, modified based on the results of those experiments, and further tested to refine our understanding.

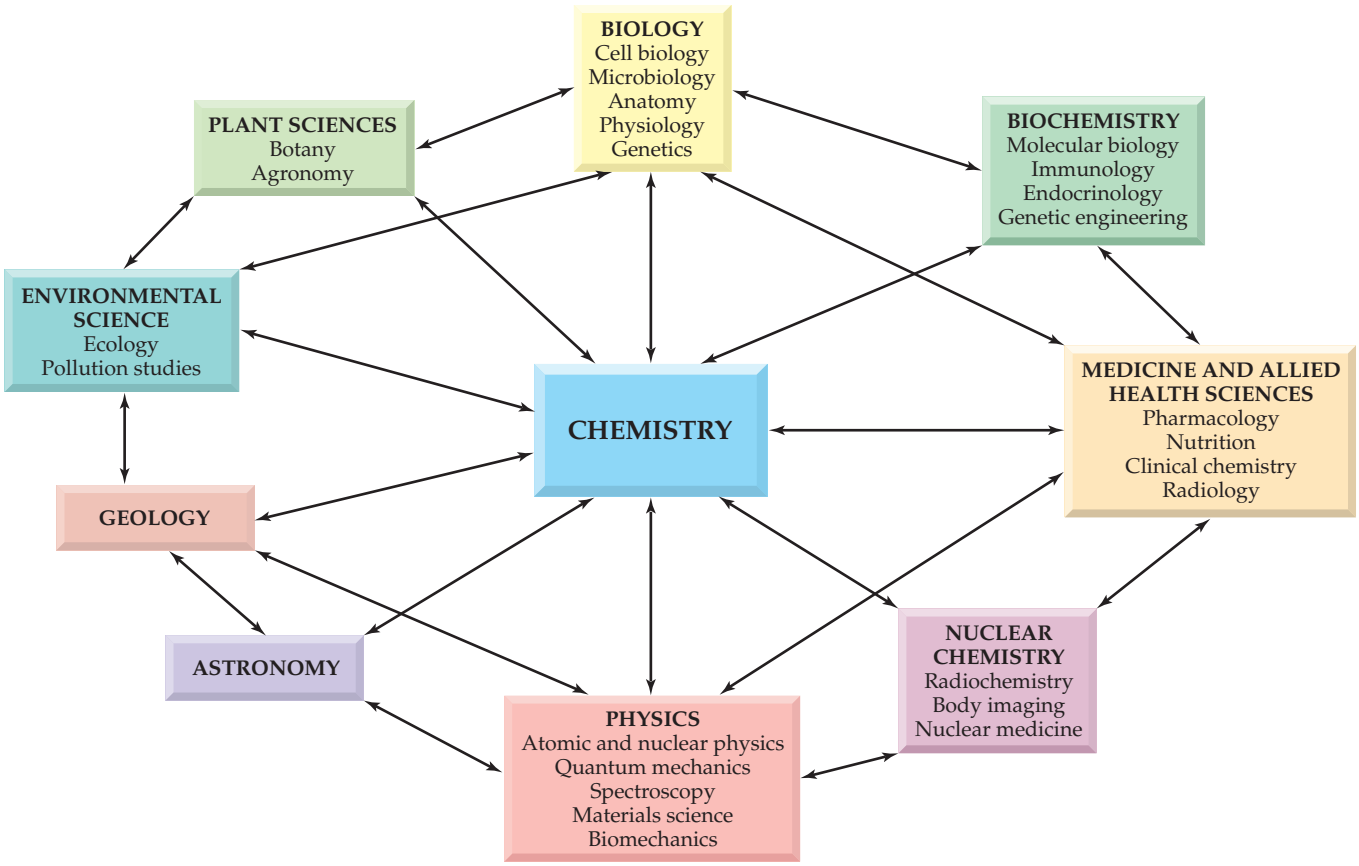
All of chemistry is based on the study of matter and the changes that matter undergoes. How might we describe different kinds of matter more specifically? Any characteristic used to describe or identify something is called a **property;** size, color,

Chemistry The study of the nature, properties, and transformations of matter.

Matter The physical material that makes up the universe; anything that has mass and occupies space.

Scientific method The systematic process of observation, hypothesis, and experimentation used to expand and refine a body of knowledge.

Property A characteristic useful for identifying a substance or object.



▲ **Figure 1.1**
Some relationships between chemistry—the central science—and other scientific and health-related disciplines.

and temperature are all familiar examples. Less familiar properties include *chemical composition,* which describes what matter is made of, and *chemical reactivity,* which describes how matter behaves. Rather than focusing on the properties themselves, it is often more useful to think about *changes* in properties. There are two types of changes: *physical* and *chemical.* A **physical change** is one that does not alter the identity of a substance, whereas a **chemical change** *does* alter a substance's identity. For example, the melting of solid ice to give liquid water is a physical change because the water changes only in form but not in chemical makeup. However, the rusting of an iron bicycle left in the rain is a chemical change because iron combines with oxygen and moisture from the air to give a new substance, rust.

Physical change A change that does not affect the chemical makeup of a substance or object.

Chemical change A change in the chemical makeup of a substance.

Table 1.1 lists some chemical and physical properties of several familiar substances—water, table sugar (sucrose, a carbohydrate), and baking soda (sodium hydrogen carbonate). Note in Table 1.1 that changes occurring when sugar and baking soda are heated are chemical changes because new substances are produced.

Worked Example 1.1 Chemical vs. Physical Change

Identify each of the following as a chemical change or a physical change:

a) Sugar dissolving in water.

b) Sugar heated in a saucepan to make caramel.

ANALYSIS A physical change does not result in a change in the identity of the substance, whereas a chemical change results in the creation of a new substance with properties that are different than the original substance.

SOLUTION

a) Physical change: When sugar dissolves in water, the sugar and the water retain their identity. The water can be removed by evaporation, and the sugar can be recovered in its original form.

b) Chemical change: When sugar is heated in a saucepan, it melts and darkens and thickens into caramel. When cooled, the caramel clearly has significantly different properties (color, consistency) than the original sugar, indicating that a chemical change has occurred and a new substance has been formed.

Table 1.1 Some Properties of Water, Sugar, and Baking Soda

Water	Sugar (Sucrose)	Baking Soda (Sodium Hydrogen Carbonate)
Physical properties		
Colorless liquid	White crystals	White powder
Odorless	Odorless	Odorless
Melting point: 0 °C	Begins to decompose at 160 °C, turning black and giving off water.	Decomposes at 270 °C, giving off water and carbon dioxide.
Boiling point: 100 °C	—	—
Chemical properties		
Composition:*	Composition:*	Composition:*
11.2% hydrogen	6.4% hydrogen	27.4% sodium
88.8% oxygen	42.1% carbon	1.2% hydrogen
	51.5% oxygen	14.3% carbon
		57.1% oxygen
Does not burn.	Burns in air.	Does not burn.

**Compositions are given by mass percent.*

HANDS-ON CHEMISTRY 1.1

Look in the refrigerator or on the counter top in your home, apartment, or work place. If there is a bowl of fruit, onions, potatoes, etc., take a look at these items and compare what they would look like in the grocery store versus in their current location. Do you see mold? Is the flesh of the food soft, etc.? If so, would this be a physical change or a chemical change? What evidence can you cite to support your answer?

▲ Burning of potassium in water is an example of a chemical change.

1.2 States of Matter

Learning Objective:

- Identify the three states of matter and describe their properties.

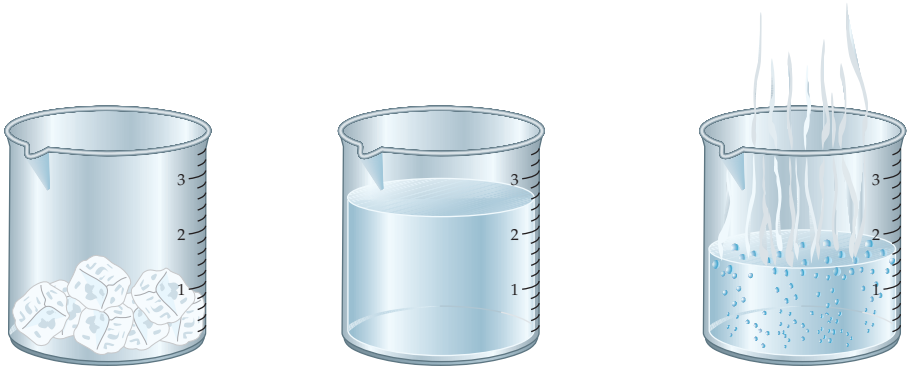
Solid *(s)* A substance that has a definite shape and volume.

Liquid *(l)* A substance that has a definite volume but assumes the shape of its container.

Gas *(g)* A substance that has neither a definite volume nor a definite shape.

Matter exists in three forms: solid, liquid, and gas. A **solid** has a definite volume and a definite shape that does not change regardless of the container in which it is placed; for example, a wooden block, marbles, or a cube of ice all keep their volume and shape whether they are placed on a table or in a box. A **liquid,** by contrast, has a definite volume but an indefinite shape. The volume of a liquid, such as water, remains the same when it is poured into a different container, but its shape changes as it takes the shape of the container. A **gas** is different still, having neither a definite volume nor a definite shape. A gas expands to fill the volume and take the shape of any container it is placed in, such as the helium in a balloon or steam formed by boiling water (Figure 1.2).

▶ Figure 1.2
The three states of matter—solid, liquid, and gas.



(a) Ice: A solid has a definite volume and a definite shape independent of its container.

(b) Water: A liquid has a definite volume but a variable shape that depends on its container.

(c) Steam: A gas has both variable volume and shape that depend on its container.

State of matter The physical state of a substance as a solid *(s),* liquid *(l),* or gas *(g).*

Change of state The conversion of a substance from one state to another—for example, from liquid *(l)* to gas *(g).*

Many substances, such as water, can exist in all three phases, or **states of matter**—the solid state *(s),* the liquid state *(l),* and the gaseous state *(g)*—depending on the temperature. In general, a substance that is a solid can be converted to the liquid state if the temperature is increased sufficiently. Likewise, many liquids can be converted to the gaseous state by increasing the temperature even further. The conversion of a substance from one state to another is known as a **change of state.** The melting of a solid, the freezing or boiling of a liquid, and the condensing of a gas to a liquid are physical changes familiar to everyone.

Worked Example 1.2 Identifying States of Matter

Formaldehyde is a disinfectant, a preservative, and a raw material for the manufacturing of plastics. Its melting point is −92 °C, and its boiling point is −19.5 °C. Is formaldehyde a gas, a liquid, or a solid at room temperature (25 °C)?

ANALYSIS The state of matter of any substance depends on its temperature. How do the melting point and boiling point of formaldehyde compare with room temperature?

SOLUTION
Room temperature (25 °C) is above the boiling point of formaldehyde (−19.5 °C), and so the formaldehyde is a gas.

PROBLEM 1.1

Pure acetic acid, which gives the sour taste to vinegar, has a melting point of 16.7 °C and a boiling point of 118 °C. Predict the physical state of acetic acid when the ambient temperature is 10 °C.

1.3 Classification of Matter

Learning Objective:

- Distinguish between mixtures and pure substances and classify pure substances as elements or compounds

The first question a chemist asks about an unknown substance is whether it is a pure substance or a mixture. Every sample of matter is one or the other. Separately, water and sugar are pure substances, but stirring some sugar into a glass of water creates a *mixture*.

What is the difference between a pure substance and a mixture? One difference is that a **pure substance** is uniform in its chemical composition and its properties all the way down to the microscopic level. Every sample of water, sugar, or baking soda, regardless of source, has the composition and properties listed in Table 1.1. A **mixture,** however, can vary in both composition and properties, depending on how it is made. A **homogeneous mixture** is a blend of two or more pure substances having a uniform composition at the microscopic level. Sugar dissolved in water is one example. You cannot always distinguish between a pure substance and a homogeneous mixture just by looking. The sugar–water mixture *looks* just like pure water but differs on a molecular level. The amount of sugar dissolved in a glass of water will determine the sweetness, boiling point, and other properties of the mixture. A **heterogeneous mixture,** by contrast, is a blend of two or more pure substances having nonuniform composition, such as a vegetable stew in which each spoonful is different. It is relatively easy to distinguish heterogeneous mixtures from pure substances.

Another difference between a pure substance and a mixture is that the components of a mixture can be separated without changing their chemical identities. For example, water can be separated from a sugar–water mixture by boiling the mixture to drive off the steam and then condensing the steam to recover the pure water. Pure sugar is left behind in the container.

Pure substances are classified into two groups: those that can undergo a chemical breakdown to yield simpler substances and those that cannot. A pure substance that cannot be broken down chemically into simpler substances is called an **element.** Examples include hydrogen, oxygen, aluminum, gold, and sulfur. At the time this book was printed, 118 elements had been identified, although only 91 of these occur naturally.

Any pure material that *can* be broken down into simpler substances by a chemical change is called a **chemical compound.** The term *compound* implies "more than one" (think "compound fracture"). A chemical compound, therefore, is formed by combining two or more elements to make a new substance. Water, for example, is a chemical compound consisting of hydrogen and oxygen; it can be chemically changed by passing an electric current through it to produce the elements hydrogen and oxygen). In Section 1.5, we will discuss chemical changes in more detail. Figure 1.3 summarizes the classification of matter into mixtures, pure compounds, and elements.

Pure substance A substance that has a uniform chemical composition throughout.

Mixture A blend of two or more substances, each of which retains its chemical identity.

Homogeneous mixture A uniform mixture that has the same composition throughout.

Heterogeneous mixture A nonuniform mixture that has regions of different composition.

LOOKING AHEAD We'll revisit the properties of mixtures in Section 9.1 when we discuss solutions. In Problem 1.2, that sour tasting vinegar is a 5% solution of acetic acid. Another state of matter that will be discussed is solutions in water, which are given the symbol *(aq)*.

Element A fundamental substance that cannot be broken down chemically into any simpler substance.

Elements make up all the millions of other substances in the universe and are explored in the next section of this chapter (Section 1.4).

Chemical compound A pure substance that can be broken down into simpler substances by chemical reactions.

Worked Example 1.3 Classifying Matter

Classify each of the following as a mixture or a pure substance. If a mixture, classify it as heterogeneous or homogeneous. If a pure substance, identify it as an element or a compound.

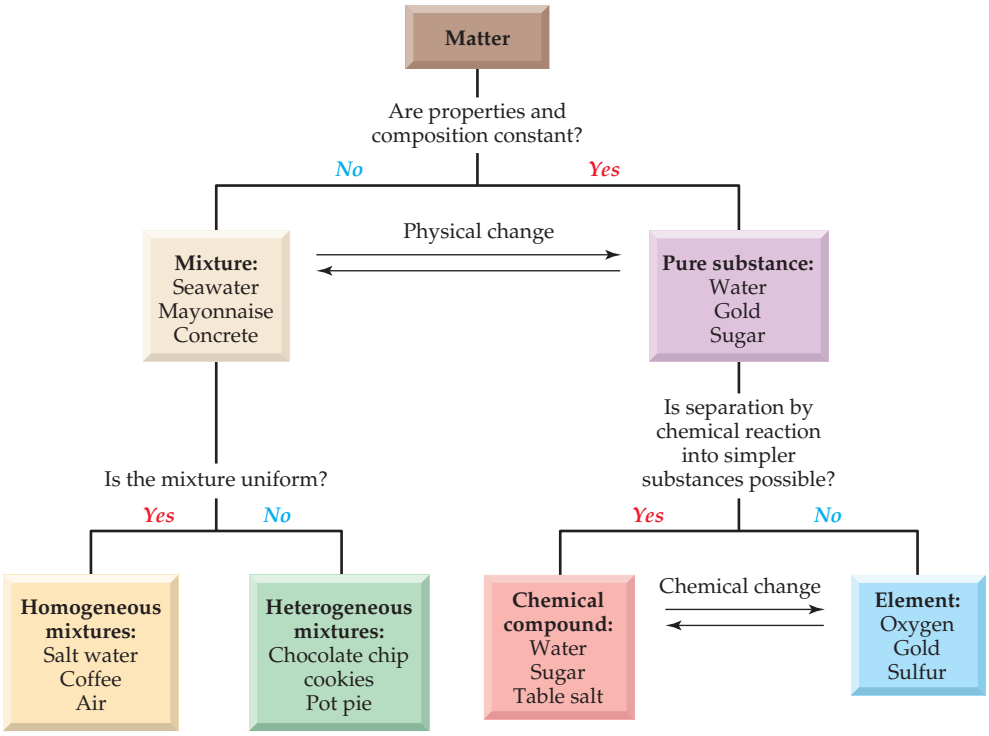
(a) Vanilla ice cream **(b)** Sugar

ANALYSIS Refer to the definitions of pure substances and mixtures. Is the substance composed of more than one kind of matter? Is the composition uniform?

SOLUTION

(a) Vanilla ice cream is composed of more than one substance—cream, sugar, and vanilla flavoring. The composition appears to be uniform throughout, so this is a homogeneous mixture.

(b) Sugar is composed of only one kind of matter—pure sugar. This is a pure substance. It can be converted to some other substance by a chemical change (see Table 1.1), so it is not an element. It must be a compound.



▶ Figure 1.3
A map for the classification of matter.

In fact, in Chapter 20, we will see that common table sugar is called sucrose; two other sugars, glucose and fructose, are chemically bonded to make one compound.

PROBLEM 1.2

Classify each of the following as a mixture or a pure substance. If a mixture, classify it as heterogeneous or homogeneous. If a pure substance, identify it as an element or a compound.

(a) Concrete
(b) The helium in a balloon
(c) A lead weight
(d) Wood

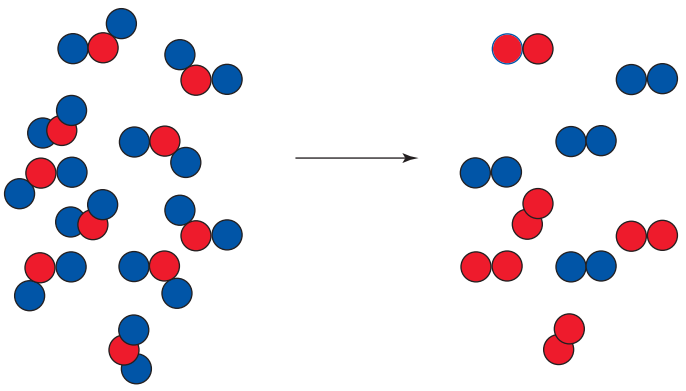
PROBLEM 1.3

Classify each of the following as a physical change or a chemical change:

(a) Dissolving sugar in water
(b) Producing carbon dioxide gas and solid lime by heating limestone
(c) Frying an egg
(d) The conversion of salicylic acid to acetylsalicylic acid (see the Chemistry in Action feature on the next page)

KEY CONCEPT PROBLEM 1.4

In the next image, red spheres represent element A and blue spheres represent element B. Identify the process illustrated in the image as a chemical change or a physical change. Also, identify the substance(s) on the left and the substance(s) on the right as pure substances or mixtures. Explain your answer.



CHEMISTRY IN ACTION

Aspirin—A Case Study

Acetylsalicylic acid (ASA), more commonly known as aspirin, is perhaps the first true wonder drug. It is a common staple in today's medicine chest, but its discovery can be traced back to 400 B.C. The ancient Greek physician Hippocrates prescribed the bark and leaves of the willow tree to relieve pain and fever. His knowledge of the therapeutic properties of these substances was derived through trial and error. In 1828, scientists isolated a bitter-tasting yellow extract, called salicin, from willow bark and identified salicin as the active ingredient responsible for the observed medical effects. Salicin could be easily converted to salicylic acid (SA). SA, however, had an unpleasant taste and often caused stomach irritation and indigestion. Further experiments were performed to convert SA to a substance that retained the therapeutic activity of SA but without the unpleasant side effects. Bayer marketed the new drug, now called aspirin, in water-soluble tablets.

But how does aspirin work? Once again, experimental data provided insights into the therapeutic activity of aspirin. In 1971, the British pharmacologist John Vane discovered that aspirin suppresses the body's production of prostaglandins, which are responsible for the pain and swelling that accompany inflammation. The discovery of this mechanism led to the development of new analgesic drugs.

Aspirin is classified as a *n*on-*s*teroidal *a*nti-*i*nflammatory *d*rug (NSAID), but its therapeutic value goes well beyond relieving aches and pains. Because aspirin also has anticoagulant activity, a daily, low-dose aspirin regimen (~100 mg) is recommended by many physicians to reduce the risks associated with cardiovascular disease—heart attacks and strokes. Its anti-inflammatory activity is also believed to reduce the risk of developing certain types of cancer, especially in patients who suffer from chronic or persistent inflammation. For example, in a study of almost 20,000 women, the risk of ovarian cancer decreased by over 20% for women who followed a daily low-dose aspirin regimen, and that these benefits increased with long-term use. Individuals who followed the low-dose regimen for 5 years or more experienced lower incidence of colorectal cancers, and the 20-year risk of cancer death remained lower for a wide variety of other cancers, including stomach and esophageal cancers and adenocarcinomas—common malignant cancers that develop in the lungs, colon, and prostate.

▲ Hippocrates, the ancient Greek physician, prescribed a precursor of aspirin extracted from willow bark (above) to relieve pain.

CIA Problem 1.1 The active ingredient in aspirin, ASA, melts at 140 °C. Is it a solid or a liquid at room temperature?

CIA Problem 1.2 Do you think the conversion of SA to aspirin is a chemical change or a physical change? Give evidence to support your answer.

1.4 Chemical Elements and Symbols

Learning Objective:

- Identify the symbols and names of the common elements.

As of the date this book was printed, 118 chemical elements have been identified. Some are certainly familiar to you—for example, oxygen, helium, iron, aluminum, copper, and gold—but many others are probably unfamiliar—rhenium, niobium, thulium, and promethium. Rather than writing out the full names of elements, chemists use a shorthand notation in which elements are referred to by one- or two-letter symbols. The names and symbols of some common elements are listed in Table 1.2, and a complete alphabetical list is given inside the front cover of this book.

Note that all two-letter symbols have only their first letter capitalized, whereas the second letter is always lowercase. The symbols of most common elements are the first one or two letters of the elements' commonly used names, such as H (hydrogen) and Al (aluminum). Pay special attention, however, to the elements grouped in the last column to the right in Table 1.2. The symbols for these elements are derived from their original Latin names, such as Na for sodium, once known as *natrium*. The only way to learn these symbols is to memorize them; fortunately, they are few in number.

Prostaglandins can be synthesized from arachidonic acid and have many biological effects, which are discussed in the Chemistry in Action feature in Chapter 23, p. 769. Aspirin can inhibit the formation of prostaglandins.

We will discuss the creation of new elements by nuclear bombardment in Chapter 11. Many of these new substances are used as medical diagnostic tracers or therapeutic agents.

Table 1.2 Names and Symbols for Some Common Elements

Elements with Symbols Based on Modern Names						Elements with Symbols Based on Latin Names	
Al	Aluminum	**Co**	Cobalt	**N**	Nitrogen	**Cu**	Copper *(cuprum)*
Ar	Argon	**F**	Fluorine	**O**	Oxygen	**Au**	Gold *(aurum)*
Ba	Barium	**He**	Helium	**P**	Phosphorus	**Fe**	Iron *(ferrum)*
Bi	Bismuth	**H**	Hydrogen	**Pt**	Platinum	**Pb**	Lead *(plumbum)*
B	Boron	**I**	Iodine	**Rn**	Radon	**Hg**	Mercury *(hydrargyrum)*
Br	Bromine	**Li**	Lithium	**Si**	Silicon	**K**	Potassium *(kalium)*
Ca	Calcium	**Mg**	Magnesium	**S**	Sulfur	**Ag**	Silver *(argentum)*
C	Carbon	**Mn**	Manganese	**Ti**	Titanium	**Na**	Sodium *(natrium)*
Cl	Chlorine	**Ni**	Nickel	**Zn**	Zinc	**Sn**	Tin *(stannum)*

Only 91 elements occur naturally; the remaining elements have been produced artificially by chemists and physicists. Each element has its own distinctive properties, and just about all of the first 95 elements have been put to use in some way that takes advantage of those properties. As indicated in Table 1.3, which shows the approximate elemental composition of the earth's crust and the human body, the naturally occurring elements are not equally abundant. Oxygen and silicon together account for nearly 75% of the mass in the earth's crust; oxygen, carbon, and hydrogen account for nearly all the mass of a human body.

In Chapter 29, elements found in the human body will be discussed in greater detail along with body fluids.

Table 1.3 Elemental Composition of the Earth's Crust and the Human Body*

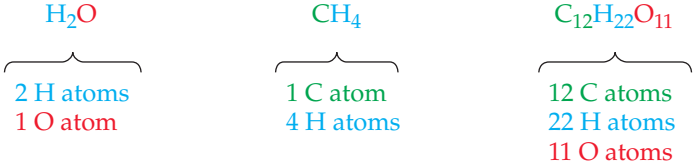
Earth's Crust		Human Body	
Oxygen	46.1%	Oxygen	61%
Silicon	28.2%	Carbon	23%
Aluminum	8.2%	Hydrogen	10%
Iron	5.6%	Nitrogen	2.6%
Calcium	4.1%	Calcium	1.4%
Sodium	2.4%	Phosphorus	1.1%
Magnesium	2.3%	Sulfur	0.20%
Potassium	2.1%	Potassium	0.20%
Titanium	0.57%	Sodium	0.14%
Hydrogen	0.14%	Chlorine	0.12%

**Mass percent values are given.*

Chemical formula A notation for a chemical compound using element symbols and subscripts to show how many atoms of each element are present.

We'll learn more about the structure of atoms and how they form compounds in Chapter 2.

Just as elements combine to form chemical compounds, symbols are combined to produce **chemical formulas,** which use subscripts to identify how many *atoms* (the smallest fundamental units) of each element are in a given chemical compound. For example, the formula H_2O represents water, which contains two hydrogen atoms combined with one oxygen atom. Similarly, the formula CH_4 represents methane (natural gas), and the formula $C_{12}H_{22}O_{11}$ represents table sugar (sucrose). When no subscript is given for an element, as for carbon in the formula CH_4, a subscript of "1" is understood.



Those elements essential for human life are listed in Table 1.4. In addition to the well-known elements such as carbon, hydrogen, oxygen, and nitrogen, less familiar elements such as molybdenum and selenium are also important.

Table 1.4 Elements Essential for Human Life*

Element	Symbol	Function
Carbon Hydrogen Oxygen Nitrogen	C H O N	These four elements are present in all living organisms (Ch. 12–29).
Boron	B	Aids in the use of Ca, P, and Mg.
Calcium*	Ca	Necessary for growth of teeth and bones.
Chlorine*	Cl	Necessary for maintaining salt balance in body fluids (Ch. 29).
Chromium	Cr	Aids in carbohydrate metabolism (Ch. 22).
Cobalt	Co	Component of vitamin B_{12} (Ch. 19).
Copper	Cu	Necessary to maintain blood chemistry (Ch. 29).
Iodine	I	Necessary for thyroid function (Ch. 28).
Iron	Fe	Necessary for oxygen-carrying ability of blood (Ch. 29).
Magnesium*	Mg	Necessary for bones, teeth, and muscle and nerve action (Ch. 28).
Manganese	Mn	Necessary for carbohydrate metabolism and bone formation (Ch. 22).
Molybdenum	Mo	Component of enzymes necessary for metabolism (Ch. 19).
Phosphorus*	P	Necessary for growth of bones and teeth; present in DNA/RNA (Ch. 26).
Potassium*	K	Component of body fluids; necessary for nerve action (Ch. 28–29).
Selenium	Se	Aids vitamin E action and fat metabolism (Ch. 24).
Sodium*	Na	Component of body fluids; necessary for nerve and muscle action (Ch. 28–29).
Sulfur*	S	Component of proteins; necessary for blood clotting (Ch. 25 and 29).
Zinc	Zn	Necessary for growth, healing, and overall health.

C, H, O, and N are present in most foods. Other elements listed vary in their distribution in different foods. Those marked with an asterisk are macronutrients, essential in the diet at more than 100 mg/day; the rest, other than C, H, O, and N, are micronutrients, essential at 15 mg or less per day.

The elements listed in Table 1.4 are not present in our bodies in their free forms. Instead, they are combined into many thousands of different chemical compounds. We will talk about some compounds formed by metals in Chapter 3 and compounds formed by nonmetals in Chapter 4. The role that many of these elements play in biochemical functions will also be discussed in Chapters 19, 21, 25, 28, and 29.

PROBLEM 1.5

Match the names of the elements described below (a–f) with their elemental symbols (1–6).

(a) Sodium, a major component in table salt
(b) Tungsten, a metal used in light bulb filaments
(c) Strontium, used to produce brilliant red colors in fireworks
(d) Titanium, used in artificial hips and knee-replacement joints
(e) Fluorine, added to municipal water supplies to strengthen tooth enamel
(f) Tin, a metal used in solder

(1) W **(2)** Na **(3)** Sn **(4)** F **(5)** Ti **(6)** Sr

PROBLEM 1.6

Identify the elements represented in each of the following chemical formulas and tell the number of atoms of each element:

(a) NH_3 (ammonia)
(b) $NaHCO_3$ (sodium hydrogen carbonate)
(c) C_8H_{18} (octane, a component of gasoline)
(d) $C_6H_8O_6$ (vitamin C)

1.5 Chemical Reactions: Examples of Chemical Change

Learning Objective:

- Identify a chemical change as a chemical reaction.

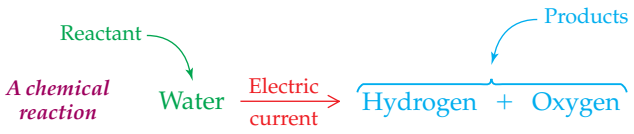
Chemical reaction A process in which the identity and composition of one or more substances are changed.

Reactant A starting substance that undergoes change during a chemical reaction.

Product A substance formed as the result of a chemical reaction.

We will discuss how reactions are classified in Chapter 5.

Chemists represent chemical changes using a symbolic shorthand notation called a **chemical reaction.** In writing this chemical change, the initial substances, or **reactants,** are written on the left; the new substances, or **products,** are written on the right. An arrow connects the two parts to indicate the chemical change or the chemical reaction. The conditions necessary to bring about the reaction are written above and below the arrow. Consider again the example of a chemical change discussed previously, in which electric current was passed through the reactant water (H_2O) to break it down into the products, the elements hydrogen (H_2) and oxygen (O_2). This chemical reaction can be expressed in words as shown next.



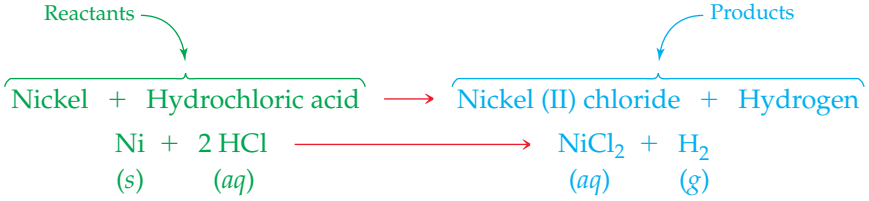
Chemists, however, find it more convenient to use chemical symbols to represent the elements and compounds involved in the reaction. This chemical reaction would more commonly be expressed as

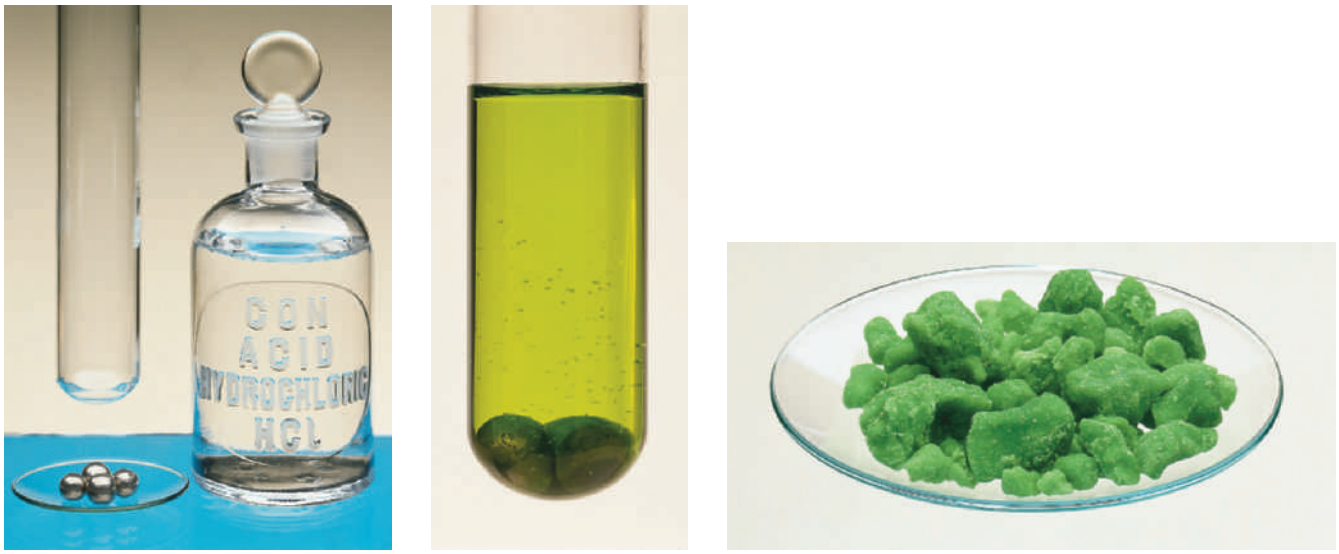
$$H_2O(l) \xrightarrow[\text{current}]{\text{Electric}} H_2(g) + O_2(g)$$

Note that the reactants and products are represented using their chemical formulas, but that the physical states of the reactants and products are also indicated as a liquid *(l)* or gas *(g).* The formation of gas bubbles is an indication that a chemical reaction has occurred.

If we take a quick look at another example of a chemical reaction in Figure 1.4, we can reinforce these ideas. The element *nickel* is a hard, shiny metal, and the compound *hydrogen chloride* is a colorless gas that dissolves in water to give a solution called *hydrochloric acid.* When pieces of nickel are added to hydrochloric acid in a test tube, the nickel slowly dissolves, the colorless solution turns green, and a gas bubbles out of the test tube. The change in color, the dissolving of the nickel, and the appearance of gas bubbles are indications that a chemical reaction is taking place.

Again, the overall reaction of nickel with hydrochloric acid can be written in words or represented in a shorthand notation using symbols to represent the elements or compounds involved as reactants and products, as shown below. The physical states of the reactants are indicated as solid *(s)* for Ni and the HCl as *(aq),* which means "aqueous," or "dissolved in water." The physical states of the products are *(aq)* for the nickel(II) chloride dissolved in water and *(g)* for the H_2 gas. If the water is evaporated away, the nickel(II) chloride product can be collected as a solid, also shown in Figure 1.4.





(a) (b) (c)

▲ **Figure 1.4**
Reactants and products of a chemical reaction.
(a) The reactants: Nickel (shown on the flat dish), an element that is a typical lustrous metal, and hydrochloric acid (in the bottle), a solution of the chemical compound hydrogen chloride in water. (b) The reaction: As the chemical reaction occurs, the colorless solution turns green when water-insoluble nickel metal slowly changes into the water-soluble chemical compound nickel(II) chloride. Hydrogen gas bubbles are produced and rise slowly through the green solution. (c) The product: Hydrogen gas can be collected as it bubbles from the solution and removal of water from the solution leaves behind the other product, a solid, green chemical compound known as nickel(II) chloride.

1.6 Physical Quantities: Units and Scientific Notation

Learning Objective:

- Write very large and very small numbers using scientific notation or units with appropriate numerical prefixes.

Our understanding of matter depends on our ability to measure the changes in physical properties associated with physical and chemical change. Mass, volume, temperature, density, and other physical properties that can be measured are called **physical quantities** and are described by both a number and a **unit** that defines the nature and magnitude of the number.

Physical quantity A physical property that can be measured.

Unit A defined quantity used as a standard of measurement.

Number Unit
61.2 kilograms

Units of Measurement

The number alone is not much good without a unit. If you ask how much blood an accident victim has lost, the answer "three" would not tell you much. Three drops? Three milliliters? Three pints? Three liters? By the way, an adult human has only 5–6 liters of blood.

Any physical quantity can be measured in many different units. For example, a person's height might be measured in inches, feet, yards, centimeters, or many other units. To avoid confusion, scientists from around the world have agreed on a system of standard units, called by the French name *Système International d'Unites* (International System of Units), abbreviated *SI*. **SI units** for some common physical quantities

SI units Units of measurement defined by the International System of Units. Examples include kilograms, meters, and kelvins.

CHEMISTRY IN ACTION

Mercury and Mercury Poisoning

Mercury, the only metallic element that is liquid at room temperature, has fascinated people for millennia. Much of the recent interest in mercury has concerned its toxicity, but mercury, in nontoxic forms, has a wide array of clinical uses. For example, the mercury compound Hg_2Cl_2 (called *calomel*) has a long history of medical use as a laxative, yet it is also used as a fungicide and rat poison. Dental amalgam, a solid alloy of elemental mercury, silver, tin, copper, and zinc, was used by dentists for many years to fill tooth cavities, with little or no adverse effects except in individuals with a hypersensitivity to mercury. Yet, exposure to elemental mercury *vapor* for long periods leads to mood swings, headaches, tremors, and loss of hair and teeth. The widespread use of mercuric nitrate, a mercury compound used to make the felt used in hats, exposed many hatters of the eighteenth and nineteenth centuries to toxic levels of mercury. The eccentric behavior displayed by hatters suffering from mercury poisoning led to the phrase "mad as a hatter."

Why is mercury more toxic in some forms than in others? It turns out that the toxicity of mercury and its compounds is related to solubility. Only soluble mercury compounds are highly toxic because they can be transported through the bloodstream to all parts of the body, where they react with different enzymes and interfere with various biological processes. Elemental mercury and insoluble mercury compounds become toxic only when converted into soluble compounds, reactions that are extremely slow in the body. Calomel, for example, is an insoluble mercury compound that passes through the body long before it is converted into any soluble compounds. Mercury alloys were considered safe for dental use because mercury does not evaporate readily from the alloys and it neither reacts with nor dissolves in saliva. Mercury vapor, however, remains in the lungs when breathed, until it is slowly converted into soluble compounds. Soluble organic forms of mercury can be particularly toxic. Trace amounts are found in nearly all seafood, but some larger species such as king mackerel and swordfish contain higher levels of mercury. Because mercury can affect the developing brain and nervous system of a fetus, pregnant women are often advised to avoid consuming them.

▲ Cinnabar, the dark red crystals in this photo, is a mineral comprised of mercury (Hg) and sulfur (S), and is one of the major commercial sources of elemental mercury.

Recent events have raised new concerns regarding the safe use of mercury in some other applications. Perhaps the most controversial example is the use of thimerosal, an organic mercury compound, as a preservative in flu vaccines. Concerns about possible links between thimerosal and autism in children resulted in elimination of its use in 1999, although most scientific data seem to refute any connection. In response to these concerns, preservative-free versions of the influenza vaccine are available for use in infants, children, and pregnant women.

CIA Problem 1.3 Calomel (Hg_2Cl_2) is not toxic but methyl mercury chloride (CH_3HgCl) is highly toxic. What physical property explains this difference in toxicity?

are given in Table 1.5. Mass is measured in *kilograms* (kg), length is measured in *meters* (m), volume is measured in *cubic meters* (m^3), temperature is measured in *kelvins* (K), and time is measured in *seconds* (s).

SI units are closely related to the more familiar *metric units* used in all industrialized nations of the world except the United States, which uses the English system of units (inches, feet, ounces, pounds, etc.). One advantage of the SI system is that units are related by powers of 10. If you compare the SI and metric units shown in Table 1.5, you will find that the basic metric unit of mass is the *gram* (g) rather than the kilogram ($1\ g = 1/1000\ kg$), the metric unit of volume is the *liter* (L) rather than the cubic meter ($1\ L = 1/1000\ m^3$), and the metric unit of temperature is the *Celsius degree* (°C) rather than the kelvin. The meter is the unit of length, and the second is the unit of time in both systems. Although SI units are now preferred in scientific research, metric units are still used in some fields. You will probably find yourself working with both.

In addition to the units listed in Table 1.5, many other widely used units are derived from them. For instance, units of *meters per second* (m/s) are often used for *speed*—the distance covered in a given time. Similarly, units of *grams per cubic centimeter* (g/cm^3)

The symbol °C means degrees Celsius, one of three temperature scales in common use, and will be discussed in Section 1.11.

Table 1.5 Some SI and Metric Units and Their Equivalents

Quantity	SI Unit (Symbol)	Metric Unit (Symbol)	Equivalents
Mass	Kilogram (kg)	Gram (g)	1 kg = 1000 g
Length	Meter (m)	Meter (m)	—
Volume	Cubic meter (m^3)	Liter (L)	1 m^3 = 1000 L
Temperature	Kelvin (K)	Celsius degree (°C)	See Section 1.11
Time	Second (s)	Second (s)	—

are often used for *density*—the mass of substance in a given volume. We will see other such derived units in future chapters.

One problem with any system of measurement is that the sizes of the units often turn out to be inconveniently large or small for the problem at hand. A biologist describing the diameter of a red blood cell (0.000 006 m) would find the meter to be an inconveniently large unit, but an astronomer measuring the average distance from the earth to the sun (150,000,000,000 m) would find the meter to be inconveniently small. For this reason, metric and SI units can be modified by prefixes to refer to either smaller or larger quantities. For instance, the SI unit for mass—the kilogram—differs by the prefix *kilo-* from the metric unit gram. *Kilo-* indicates that a kilogram is 1000 times as large as a gram:

$$1\text{ kg} = (1000)(1\text{ g}) = 1000\text{ g}$$

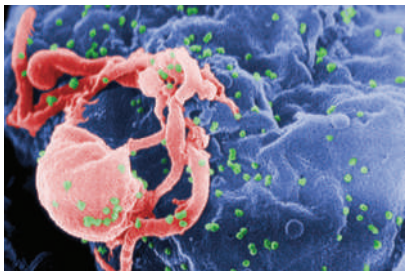
Small quantities of active ingredients in medications are often reported in *milligrams* (mg). The prefix *milli-* shows that the unit gram has been divided by 1000, which is the same as multiplying by 0.001:

$$1\text{ mg} = \left(\frac{1}{1000}\right)(1\text{ g}) = (0.001)(1\text{ g}) = 0.001\text{ g}$$

A list of prefixes is given in Table 1.6, with the most common ones displayed in color. *Centi-* is seen most often in the length unit *centimeter* (1 cm = 0.01 m), and *deci-* is used most often in clinical chemistry, where the concentrations of blood components are given in milligrams per deciliter (1 dL = 0.1 L). These prefixes allow us to compare the magnitudes of different numbers by noting how the prefixes modify a common unit.

Table 1.6 Some Prefixes for Multiples of Metric and SI Units

Prefix	Symbol	Base Unit Multiplied By	Example
mega	M	1,000,000 = 10^6	1 megameter (Mm) = 10^6 m
kilo	k	1000 = 10^3	1 kilogram (kg) = 10^3 g
hecto	h	100 = 10^2	1 hectogram (hg) = 100 g
deka	da	10 = 10^1	1 dekaliter (daL) = 10 L
deci	d	0.1 = 10^{-1}	1 deciliter (dL) = 0.1 L
centi	c	0.01 = 10^{-2}	1 centimeter (cm) = 0.01 m
milli	m	0.001 = 10^{-3}	1 milligram (mg) = 0.001 g
micro	μ	0.000 001 = 10^{-6}	1 micrometer (μm) = 10^{-6} m
nano	n	0.000 000 001 = 10^{-9}	1 nanogram (ng) = 10^{-9} g
pico	p	0.000 000 000 001 = 10^{-12}	1 picogram (pg) = 10^{-12} g
femto	f	0.000 000 000 000 001 = 10^{-15}	1 femtogram (fg) = 10^{-15} g



▲ The HIV-1 virus particles (in green) budding from the surface of a lymphocyte have an approximate diameter of 0.000 000 120 m.

One approach for deactivating the HIV-1 virus is called *inhibition* and will be discussed in Chapter 19. How small would the inhibition agent have to be to fit in a specific location on the surface of the virus particle?

Scientific notation A number expressed as the product of a number between 1 and 10, times the number 10 raised to a power.

For example,

$$1 \text{ meter} = 10 \text{ dm} = 100 \text{ cm} = 1000 \text{ mm} = 1{,}000{,}000\ \mu\text{m}$$

Such comparisons will be useful when we start performing calculations involving units. It is worth noting that, as mentioned before, all the metric units displayed above are related by factors of 10. Note also in Table 1.6 that numbers having five or more digits to the right of the decimal point are shown with thin spaces every three digits for convenience—0.000 001, for example. This manner of writing numbers is becoming more common and will be used throughout this book.

Scientific Notation

Another way to solve the problem of representing very large or very small numbers is to use **scientific notation.** Rather than write very large or very small numbers in their entirety, it is more convenient to express them using *scientific notation.* A number is written in scientific notation as the product of a number between 1 and 10, times the number 10 raised to a power. Thus, 215 is written in scientific notation as 2.15×10^2:

$$215 = 2.15 \times 100 = 2.15(10 \times 10) = 2.15 \times 10^2$$

Notice that in this case, where the number is *larger* than 1, the decimal point has been moved *to the left* until it follows the first digit. The exponent on the 10 is positive and tells how many places we had to move the decimal point to position it just after the first digit:

$$215. = 2.15 \times 10^2$$

Decimal point is moved two places to the left, so exponent is 2.

To express a number *smaller* than one in scientific notation, we have to move the decimal point *to the right* until it follows the first digit. The number of places moved is the negative exponent of 10. For example, the number 0.002 15 can be rewritten as 2.15×10^{-3}:

$$0.002\,15 = 2.15 \times \frac{1}{1000} = 2.15 \times \frac{1}{10 \times 10 \times 10} = 2.15 \times \frac{1}{10^3} = 2.15 \times 10^{-3}$$

$$0.002\,15 = 2.15 \times 10^{-3}$$

Decimal point is moved three places to the right, so exponent is −3.

To convert a number written in scientific notation to standard notation, the process is reversed. For a number with a *positive* exponent, the decimal point is moved to the *right* a number of places equal to the exponent:

$$3.7962 \times 10^4 = 37{,}962$$

Positive exponent of 4, so decimal point is moved to the right four places.

For a number with a *negative* exponent, the decimal point is moved to the *left* a number of places equal to the exponent:

$$1.56 \times 10^{-8} = 0.000\,000\,015\,6$$

Negative exponent of −8, so decimal point is moved to the left eight places.

Worked Example 1.4 Units and Scientific Notation

The HIV-1 virus particles seen in the margin photo on p. 48 are very small, on the order of 0.000 000 120 m in diameter. Express this value using scientific notation and using an appropriate numerical prefix to modify the basic unit.

ANALYSIS The number is significantly less than one, so when we convert to scientific notation we should have a number with a negative exponent. We can use the value of that exponent to identify the appropriate numerical prefix.

SOLUTION

To convert to scientific notation we have to move the decimal place to the right by seven places, so $0.000\,000\,120\ \text{m} = 1.20 \times 10^{-7}$ m. From Table 1.6, the closest numerical prefixes are *micro* (10^{-6}) or *nano* (10^{-9}). If we moved the decimal place six places to the right we would obtain:

$$0.000\,000\,120\ \text{m} = 0.120 \times 10^{-6}\ \text{m} = 0.120\ \text{micrometers}\ (\mu\text{m})$$

If we move the decimal place nine places to the right we obtain:

$$0.000\,000\,120\ \text{m} = 120 \times 10^{-9}\ \text{m} = 120\ \text{nanometers (nm)}.$$

PROBLEM 1.7

Give the full name of the following units and express the quantities in terms of the basic unit (e.g., 1 mL = 1 milliliter = 0.001 L):

(a) 1 cm **(b)** 1 dg **(c)** 1 km **(d)** 1 μs **(e)** 1 ng

1.7 Measuring Mass, Length, and Volume

Learning Objective:

- Name and correctly use the metric and SI units of measurement for mass, length, volume, and temperature and convert units appropriately.

The terms *mass* and *weight,* though often used interchangeably, really have quite different meanings. **Mass** is a measure of the amount of matter in an object, whereas **weight** is a measure of the gravitational pull that the earth, moon, or other large body exerts on an object. Clearly, the amount of matter in an object does not depend on location. Whether you are standing on the earth or standing on the moon, the mass of your body is the same. On the other hand, the weight of an object *does* depend on location. Your weight on earth might be 64 kg, but it would only be 10 kg on the moon because the pull of gravity there is only about one-sixth as great.

Mass A measure of the amount of matter in an object.

Weight A measure of the gravitational force that the earth or other large body exerts on an object.

At the same location, two objects with identical masses have identical weights; that is, gravity pulls equally on both. Thus, the *mass* of an object can be determined by comparing the *weight* of the object to the weight of a known reference standard. Much of the confusion between mass and weight is simply due to a language problem: We speak of "weighing" when we really mean that we are measuring mass by comparing two weights. Figure 1.5 shows a two-pan balance in which the mass of objects are measured by comparison with the known masses of standard materials, such as brass weights.

One kilogram, the SI unit for mass, is too large a quantity for many purposes in chemistry and medicine. Thus, smaller units of mass such as the gram, milligram (mg), and microgram (μg), are more commonly used. Table 1.7 shows the relationships between metric and common units for mass.

The meter is the standard measure of length, or distance, in both the SI and metric systems. One meter is much too large for most measurements in chemistry and medicine. Other, more commonly used measures of length are the *centimeter* (cm; $1/100\ m$) and the *millimeter* (mm; $1/1000$ m). Table 1.8 lists the relationships of these units.

Volume is the amount of space occupied by an object. The SI unit for volume—the cubic meter, m^3—is so large that the liter ($1\ \text{L} = 0.001\ \text{m}^3 = 1\ \text{dm}^3$) is much more

▲ **Figure 1.5**
The two-pan balance is used to measure the mass of objects, such as the coins on the left pan, by comparing them with the mass of standard objects, such as the brass weights on the right pan.

Table 1.7 Units of Mass

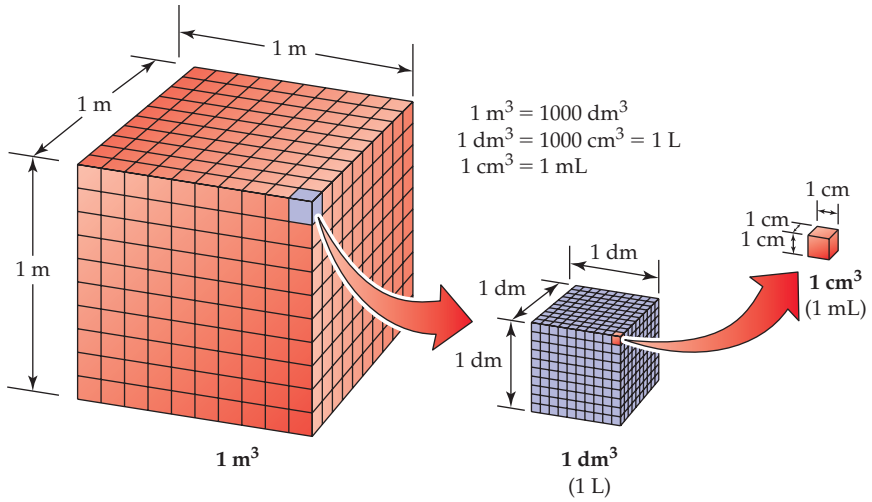
Unit	Equivalent	Unit	Equivalent
1 kilogram (kg)	= 1000 grams = 2.205 pounds*	1 ton	= 1000 kilograms
1 gram (g)	= 0.001 kilogram = 1000 milligrams = 0.035 27 ounce*	1 pound (lb)*	= 16 ounces* = 0.454 kilogram = 454 grams
1 milligram (mg)	= 0.001 gram = 1000 micrograms	1 ounce (oz)*	= 0.028 35 kilogram = 28.35 grams = 28,350 milligrams
1 microgram (μg)	= 0.000 001 gram = 0.001 milligram		

Table 1.8 Units of Length

Unit	Equivalent
1 kilometer (km)	= 1000 meters = 0.6214 mile*
1 meter (m)	= 100 centimeters = 1000 millimeters = 1.0936 yards* = 39.37 inches*
1 centimeter (cm)	= 0.01 meter = 10 millimeters = 0.3937 inch*
1 millimeter (mm)	= 0.001 meter = 0.1 centimeter
1 mile (mi)*	= 1.609 kilometers = 1609 meters
1 yard (yd)*	= 0.9144 meter = 91.44 centimeters
1 foot (ft)*	= 0.3048 meter = 30.48 centimeters
1 inch (in)*	= 2.54 centimeters = 25.4 millimeters

** indicates non-SI units that are used in non-scientific contexts and in everyday life (especially in the U.S.).*

commonly used in chemistry and medicine. One liter has the volume of a cube 10 cm (1 dm) on edge. Each liter is further divided into 1000 *milliliters* (mL), with 1 mL being the size of a cube 1 cm on edge, or 1 cm^3. In fact, the milliliter is often called a *cubic centimeter* (cm^3 or cc) in medical work. Figure 1.6 shows the divisions of a cubic meter, and Table 1.9 shows the relationships among units of volume.



◄ Figure 1.6
A cubic meter is the volume of a cube 1 m on edge. Each cubic meter contains 1000 cubic decimeters (liters), and each cubic decimeter contains 1000 cubic centimeters (milliliters). Thus, there are 1000 mL in a liter and 1000 L in a cubic meter.

Table 1.9 Units of Volume

Unit	Equivalent
1 cubic meter (m^3)	= 1000 liters
1 liter (L)	= 0.001 cubic meter = 1000 milliliters
1 deciliter (dL)	= 0.1 liter = 100 milliliters
1 milliliter (mL)	= 0.001 liter = 1000 microliters
1 microliter (μL)	= 0.001 milliliter

HANDS-ON CHEMISTRY 1.2

The mass of an object provides us with important information about its composition, that is, what elements it contains. But mass is not the only property that can be used to distinguish between objects. Consider the U.S. penny—its composition has changed significantly over time. For example, the penny was pure copper from 1793 to 1837, and then incorporated varying amounts of other metals (mainly zinc, nickel, and tin) from 1837 to 1982. Interestingly, in 1943, the penny was made mainly of zinc-coated steel because copper and zinc were needed for the war effort. From 1962 to 1982, the penny contained 95% copper and 5% zinc; after 1982, the composition changed to 2.5% copper and 97.5% zinc. The significant difference in composition can be seen in the different properties of pre-and post-1982 pennies.

Similarly, to explore such differences, sort through your spare change jar and collect 10 pre-2007 and 10 post-2007 coins and perform the following activities:

a. Collect two identical glasses or jars. Take the 10 pre-2007 coins and drop them in the glass jar and listen to them as they hit the glass sides. Then, take the 10 post-2007 coins and drop them in the glass jar and listen to them as they hit the glass sides. Do they sound different? (Note: If glasses or jars are not readily available, you can use a hard surface, like the kitchen counter.)

b. If a food scale is available, weigh 10 pre-2007 coins and weigh 10 post-2007 coins. Are their masses different? Which has more mass?

c. Find a pair of heavy duty metal shears. Carefully cut a coin from each group in half. Is one coin easier to cut than the other? Which one is easier? Now look at the inside of the coins. How are they different?

1.8 Measurement and Significant Figures

Learning Objective:

- Use significant figures and scientific notation to represent the precision of a measurement.

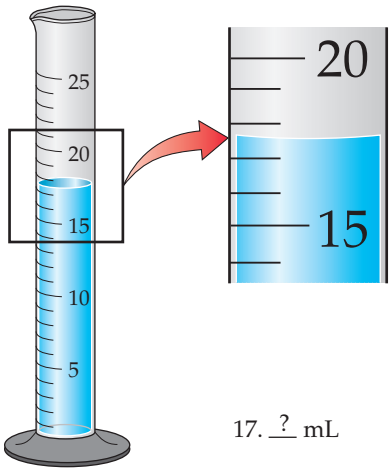
▲ The tennis ball weighs 54.07 g on this common laboratory balance, which is capable of determining mass to about 0.01 g.

How much does a tennis ball weigh? If you put a tennis ball on an ordinary bathroom scale, the scale would probably register 0 kg. If you placed the same tennis ball on a common laboratory balance, however, you might get a reading of 54.07 g. On an expensive analytical balance like those found in clinical and research laboratories, you might find the ball has a mass of 54.071 38 g. Clearly, the precision of your answer depends on the equipment used for the measurement.

Every experimental measurement, no matter how precise, has a degree of uncertainty to it because there is always a limit to the number of digits that can be determined. An analytical balance, for example, might reach its limit in measuring mass to the fifth decimal place, and weighing the tennis ball several times might produce slightly different readings, such as 54.071 39 g, 54.071 38 g, and 54.071 37 g. Also, different people making the same measurement might come up with slightly different answers. How, for instance, would you record the volume of the liquid shown in Figure 1.7? It is clear that the volume of liquid lies between 17.0 and 18.0 mL, but the exact value of the last digit must be estimated.

To indicate the precision of a measurement, the value recorded should use all the digits known with certainty, plus one additional estimated digit that is usually considered uncertain by plus or minus 1 (written as ± 1). The total number of digits used to express such a measurement is called the number of **significant figures.** Thus, the quantity 54.07 g has four significant figures (5, 4, 0, and 7), and the quantity 54.071 38 g has seven significant figures. *Remember:* All but one of the significant figures are known with certainty; the last significant figure is only an estimate accurate to ± 1.

Significant figures The number of meaningful digits used to express a value.



▲ **Figure 1.7**
What is the volume of liquid in this graduated cylinder?

Uncertain digit
54.07 g — A mass between 54.06 g and 54.08 g (±0.01 g)

Uncertain digit
54.071 38 g — A mass between 54.071 37 g and 54.071 39 g (±0.000 01 g)

Deciding the number of significant figures in a given measurement is usually simple, but it can be troublesome when zeroes are involved. Depending on the circumstances, a zero might be significant or might be just a space filler to locate the decimal point. For example, how many significant figures does each of the following measurements have?

94.072 g	Five significant figures (9, 4, 0, 7, 2)
0.0834 cm	Three significant figures (8, 3, 4)
0.029 07 mL	Four significant figures (2, 9, 0, 7)
138.200 m	Six significant figures (1, 3, 8, 2, 0, 0)
23,000 kg	*Anywhere* from two (2, 3) to five (2, 3, 0, 0, 0) significant figures

The following rules are helpful for determining the number of significant figures when zeroes are present:

RULE 1: Zeroes in the middle of a number are like any other digit; they are always significant. Thus, 94.072 g has five significant figures.

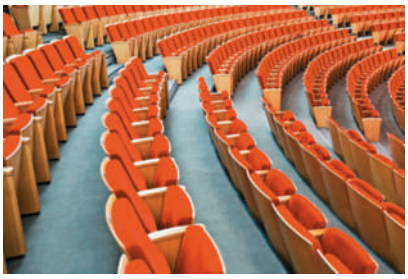
RULE 2: Zeroes at the beginning of a number are not significant; they act only to locate the decimal point. Thus, 0.0834 cm has three significant figures, and 0.029 07 mL has four.

RULE 3: Zeroes at the end of a number and *after* the decimal point are significant. It is assumed that these zeroes would not be shown unless they were significant. Thus, 138.200 m has six significant figures. If the value were known to only four significant figures, we would write 138.2 m.

RULE 4: Zeroes at the end of a number and *before* an implied decimal point may or may not be significant. We cannot tell whether they are part of the measurement or whether they act only to locate the unwritten but implied decimal point. Thus, 23,000 kg may have two, three, four, or five significant figures. Adding a decimal point at the end would indicate that all five numbers are significant.

Often, however, a little common sense is useful. A temperature reading of 20 °C probably has two significant figures rather than one, because one significant figure would imply a temperature anywhere from 10 °C to 30 °C and would be of little use. Similarly, a volume given as 300 mL probably has three significant figures. On the other hand, a figure of 150,000,000 km for the distance between the earth and the sun has only two or three significant figures because the distance is variable. We will see a better way to deal with this problem in the next section.

One final point about significant figures: some numbers, such as those obtained when counting objects and those that are part of a definition, are *exact* and effectively have an unlimited number of significant figures. Exact numbers are not measured and do not affect the number of significant figures in a calculated answer. Thus, a class might have *exactly* 32 students (not 31.9, 32.0, or 32.1), and 1 kilometer is defined to have exactly 1000 meters.



▲ The number of seats in this auditorium is an exact number with an unlimited number of significant figures.

Worked Example 1.5 Significant Figures of Measurements

How many significant figures do the following measurements have?

(a) 2730.78 m **(b)** 0.0076 mL **(c)** 3400 kg **(d)** 3400.0 m^2

ANALYSIS All nonzero numbers are significant; the number of significant figures will then depend on the status of the zeroes in each case. (Hint: Which rule applies in each case?)

SOLUTION

(a) Six (rule 1; Zeroes in the middle of a number are significant.)

(b) Two (rule 2; Leading zeroes after a decimal point are not significant.)

(c) Two, three, or four (rule 4; Trailing zeroes with no decimal point may or may not be significant.)

(d) Five (rule 3; Trailing zeroes are significant if a decimal point is included.)

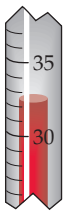
PROBLEM 1.8

How many significant figures do the following measurements have?

(a) 3.45 m **(b)** 0.1400 kg **(c)** 10.003 L **(d)** 35 cents

KEY CONCEPT PROBLEM 1.9

How would you record the temperature reading on the following Celsius thermometer? How many significant figures do you have in your answer?



Scientific Notation and Significant Figures

Rules for doing arithmetic with numbers written in scientific notation are reviewed in Appendix A.

Scientific notation is particularly helpful for indicating how many significant figures are present in a number that has zeroes at the end but to the left of a decimal point. If we read, for instance, that the distance from the earth to the sun is 150,000,000 km, we do not really know how many significant figures are indicated. Some of the zeroes might be significant, or they might merely act to locate the decimal point. Using scientific notation, however, we can indicate how many of the zeroes are significant. Rewriting 150,000,000 as 1.5×10^8 indicates two significant figures, whereas writing it as 1.500×10^8 indicates four significant figures. Scientific notation is not ordinarily used for numbers that are easily written, such as 10 or 175, although it is sometimes helpful in doing arithmetic.

Worked Example 1.6 Significant Figures and Scientific Notation

There are 1,760,000,000,000,000,000,000 molecules of sucrose (table sugar) in 1 g. Use scientific notation to express this number with four significant figures.

ANALYSIS Because the number is larger than 1, the exponent will be positive. You will have to move the decimal point 21 places to the left.

SOLUTION
The first four digits—1, 7, 6, and 0—are significant, meaning that only the first of the 19 zeroes is significant. Because we have to move the decimal point 21 places to the left to put it after the first significant digit, the answer is 1.760×10^{21}.

▲ How many molecules are in this 1 g pile of table sugar?

Worked Example 1.7 Scientific Notation

The rhinovirus responsible for the common cold has a diameter of 20 nm or 0.000 000 020 m. Express this number in scientific notation.

ANALYSIS The number is smaller than 1, and so the exponent will be negative. You will have to move the decimal point eight places to the right.

SOLUTION
There are only two significant figures because zeroes at the beginning of a number are not significant. We have to move the decimal point eight places to the right to place it after the first digit, so the answer is 2.0×10^{-8} m.

Worked Example 1.8 Scientific Notation and Unit Conversions

A clinical laboratory found that a blood sample contained 0.0026 g of phosphorus and 0.000 101 g of iron.

(a) Give these quantities in scientific notation.

(b) Give these quantities in the units normally used to report them—milligrams for phosphorus and micrograms for iron.

ANALYSIS Is the number larger or smaller than 1? How many places do you have to move the decimal point?

SOLUTION

(a) 0.0026 g phosphorus $= 2.6 \times 10^{-3}$ g phosphorus

$0.000\,101$ g iron $= 1.01 \times 10^{-4}$ g iron

(b) We know from Table 1.6 that 1 mg $= 1 \times 10^{-3}$ g, where the exponent is -3. Expressing the amount of phosphorus in milligrams is straightforward because the amount in grams $(2.6 \times 10^{-3}\ \text{g})$ already has an exponent of -3. Thus, 2.6×10^{-3} g $= 2.6$ mg of phosphorus.

$$(2.6 \times 10^{-3}\ \text{g})\left(\frac{1\ \text{mg}}{1 \times 10^{-3}\ \text{g}}\right) = 2.6\ \text{mg}$$

We know from Table 1.6 that 1 μg $= 1 \times 10^{-6}$ g where the exponent is -6. Expressing the amount of iron in micrograms thus requires that we restate the amount in grams so that the exponent is -6. We can do this by moving the decimal point six places to the right:

$$0.000\,101\ \text{g iron} = 101 \times 10^{-6}\ \text{g iron} = 101\ \mu\text{g iron}$$

PROBLEM 1.10

Convert the following values to scientific notation:

(a) 0.058 g **(b)** 46,792 m **(c)** 0.006 072 cm **(d)** 345.3 kg

PROBLEM 1.11

Convert the following values from scientific notation to standard notation:

(a) 4.885×10^{4} mg **(b)** 8.3×10^{-6} m **(c)** 4.00×10^{-2} m

PROBLEM 1.12

Rewrite the following numbers in scientific notation as indicated:

(a) 630,000 with five significant figures

(b) 1300 with three significant figures

(c) 794,200,000,000 with four significant figures

1.9 Rounding Off Numbers

Learning Objective:

- Determine the appropriate number of significant figures in a calculated result and round off numbers in calculations involving measurements.

It often happens, particularly when doing arithmetic on a pocket calculator, that a quantity appears to have more significant figures than are really justified. For example, you might calculate the fuel consumption of your motorcycle by finding that it takes 11.70 liters of gasoline to ride 278 kilometers:

$$\text{Fuel consumption} = \frac{\text{Kilometers}}{\text{Liters}} = \frac{278\ \text{km}}{11.70\ \text{L}} = 23.760\,684\ \text{km/L (kmpl)}$$

Although the answer on a calculator has eight digits, your calculated result is really not as precise as it appears. In fact, as we will see next, your answer is good to only three significant figures and should be **rounded off** to 23.8 km/L.

Rounding off A procedure used for deleting nonsignificant figures.

How do you decide how many digits to keep? The full answer to this question is a bit complex and involves a mathematical treatment called *error analysis,* but for our purposes, a simplified procedure using just two rules is sufficient:

RULE 1: In carrying out a multiplication or division, the answer cannot have more significant figures than either of the original numbers. After all, if you do not know the number of kilometers you drove better than to three significant figures

(278 could mean 277, 278, or 279), you certainly cannot calculate your fuel consumption to more than the same number of significant figures.

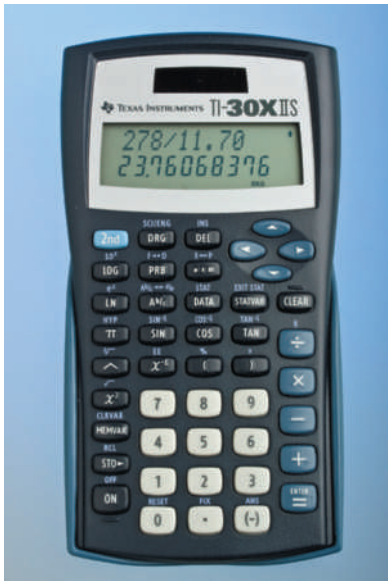
Three significant figures

Three significant figures

$$\frac{278\ \text{km}}{11.70\ \text{L}} = 23.8\ \text{km/L}$$

Four significant figures

RULE 2: In carrying out an addition or subtraction, the answer cannot have more digits after the decimal point than either of the original numbers. For example, if you have 3.18 L of water and you add 0.013 15 L more, you now have 3.19 L.



▲ Calculators often display more digits than are justified by the precision of the data.

If you do not know the volume you started with past the second decimal place (it could be 3.17, 3.18, or 3.19), you cannot know the total of the combined volumes past the same decimal place.

Volume of water at start →	3.18? ?? L	← Two digits after decimal point
Volume of water added →	+ 0.013 15 L	← Five digits after decimal point
Total volume of water →	3.19? ?? L	← Two digits after decimal point

If a calculation has several steps, it is generally best to round off at the end after all the steps have been carried out, keeping the number of significant figures determined by the least precise number in your calculations. Once you decide how many digits to retain for your answer, the rules for rounding off numbers are straightforward:

RULE 1: If the first digit you remove is four or less, drop it and all following digits. Thus, 2.4271 becomes 2.4 when rounded off to two significant figures because the first of the dropped digits (2) is four or less.

RULE 2: If the first digit you remove is five or greater, round the number up by adding a 1 to the digit to the left of the one you drop. Thus, 4.5832 becomes 4.6 when rounded off to two significant figures because the first of the dropped digits (8) is five or greater.

Worked Example 1.9 Significant Figures and Calculations: Addition/Subtraction

Suppose that you weigh 55.8 kg before dinner. How much will you weigh after dinner if you eat 0.850 kg of food?

ANALYSIS When performing addition or subtraction, the number of significant figures you report in the final answer is determined by the number of digits in the least precise number in the calculation.

SOLUTION

Your after-dinner weight is found by adding your original weight to the weight of the food consumed:

$$\begin{array}{r} 55.8\ \text{kg} \\ +\ 0.850\ \text{kg} \\ \hline 56.650\ \text{kg (Unrounded)} \end{array}$$

Because the value of your original weight has no significant figures after the decimal point, your after-dinner weight also must have no significant figures after the decimal point. Thus, 56.650 kg must be rounded off to 56.7 kg.

Worked Example 1.10 Significant Figures and Calculations: Multiplication / Division

To make currant jelly, 13.75 cups of sugar was added to 18 cups of currant juice. How much sugar was added per cup of juice?

ANALYSIS For calculations involving multiplication or division, the final answer cannot have more significant figures than either of the original numbers.

SOLUTION

The quantity of sugar must be divided by the quantity of juice:

$$\frac{13.75 \text{ cups sugar}}{18 \text{ cups juice}} = 0.763\,888\,89 \frac{\text{cup sugar}}{\text{cup juice}} \text{ (Unrounded)}$$

The number of significant figures in the answer is limited to two by the quantity 18 cups in the calculation and must be rounded to 0.76 cup of sugar per cup of juice.

PROBLEM 1.13

Round off the following quantities to the indicated number of significant figures:

(a) 2.304 g (three significant figures)
(b) 188.3784 mL (five significant figures)
(c) 0.008 87 L (one significant figure)
(d) 1.000 39 kg (four significant figures)

PROBLEM 1.14

Carry out the following calculations, rounding each result to the correct number of significant figures:

(a) 4.87 mL + 46.0 mL
(b) 3.4 × 0.023 g
(c) 19.333 m − 7.4 m
(d) 55 mg − 4.671 mg + 0.894 mg
(e) 62,911 ÷ 611

1.10 Problem Solving: Unit Conversions and Estimating Answers

Learning Objective:

- Use the factor-label method (conversion factors) to solve a problem and check the result to ensure that it makes sense chemically and physically.

Many activities in the laboratory and in medicine—measuring, weighing, preparing solutions, and so forth—require converting a quantity from one unit to another. For example: "These pills contain 1.3 grains of aspirin, but I need 200 mg. Is one pill enough?" Converting between units is not mysterious; we all do it every day. If you run nine laps around a 400 m track, for instance, you have to convert between the distance unit "lap" and the distance unit "meter" to find that you have run 3600 m (9 laps times 400 m / lap).

The simplest way to carry out calculations involving different units is to use the **factor-label method.** In this method, a quantity in one unit is converted into an equivalent quantity in a different unit by using a **conversion factor** that expresses the relationship between units:

$$\text{Starting quantity} \times \text{Conversion factor} = \text{Equivalent quantity}$$

▲ Currency exchange between the US$ and euros is another activity that requires a unit conversion.

Factor-label method A problem-solving procedure in which equations are set up so that unwanted units cancel and only the desired units remain.

Conversion factor An expression of the numerical relationship between two units.

As an example, we know that 1 km = 0.6214 mi. Writing this relationship as a fraction restates it in the form of a conversion factor, either kilometers per mile or miles per kilometer.

Since 1 km = 0.6214 mi, then:

Conversion factors between kilometers and miles

$$\frac{1\text{ km}}{0.6214\text{ mi}} = 1 \quad \text{or} \quad \frac{0.6214\text{ mi}}{1\text{ km}} = 1$$

Note that this and all other conversion factors are numerically equal to 1 because the value of the quantity above the division line (the numerator) is equal in value to the quantity below the division line (the denominator). Thus, multiplying by a conversion factor is equivalent to multiplying by 1 and so does not change the value of the quantity being multiplied.

These two quantities are the same.

$$\frac{1\text{ km}}{0.6214\text{ mi}} \quad \text{or} \quad \frac{0.6214\text{ mi}}{1\text{ km}}$$

These two quantities are the same.

The key to the factor-label method of problem solving is that units are treated like numbers and can thus be multiplied and divided (though not added or subtracted) just as numbers can. When solving a problem, the idea is to set up an equation so that all unwanted units cancel, leaving only the desired units. Usually, it is best to start by writing what you know and then manipulating that known quantity. For example, if you know there are 26.22 mi in a marathon and want to find how many kilometers that is, you could write the distance in miles and multiply by the conversion factor in kilometers per mile. The unit "mi" cancels because it appears both above and below the division line, leaving "km" as the only remaining unit.

$$26.22\ \cancel{\text{mi}} \times \frac{1\text{ km}}{0.6214\ \cancel{\text{mi}}} = 42.20\text{ km}$$

Starting quantity | Conversion factor | Equivalent quantity

The factor-label method gives the right answer only if the equation is set up so that the unwanted unit (or units) cancels. If the equation is set up in any other way, the units will not cancel and you will not get the right answer. Thus, if you selected the incorrect conversion factor (miles per kilometer) for the above problem, you would end up with an incorrect answer expressed in meaningless units:

$$\text{Incorrect } 26.22\text{ mi} \times \frac{0.6214\text{ mi}}{1\text{ km}} = 16.29\,\frac{\text{mi}^2}{\text{km}}\ \text{Incorrect}$$

The main drawback to using the factor-label method is that it is possible to get an answer without really understanding what you are doing. It is therefore best when solving a problem to first think through a rough estimate, or *ballpark estimate,* as a check on your work. If your ballpark estimate is not close to the final calculated solution, there is a misunderstanding somewhere and you should think the problem through again. If, for example, you came up with the answer 5.3 cm^3 when calculating the volume of a human cell, you should realize that such an answer could not possibly be right. Cells are too tiny to be distinguished with the naked eye, but a volume of 5.3 cm^3 is about the size of a walnut. The Worked Examples 1.11, 1.12, and 1.13 at the end of this section show how to estimate the answers to simple unit-conversion problems.

The factor-label method and the use of ballpark estimates are techniques that will help you solve problems of many kinds, not just unit conversions. Problems sometimes seem complicated, but you can usually sort out the complications by analyzing the problem properly:

STEP 1: Identify the information given, including units.

STEP 2: Identify the information needed in the answer, including units.

STEP 3: Find the relationships between the known information and unknown answer, and plan a series of steps, including conversion factors, for getting from one to the other.

STEP 4: Solve the problem.

BALLPARK CHECK Make a ballpark estimate at the beginning and check it against your final answer to be sure the value and the units of your calculated answer are reasonable.

Worked Example 1.11 Factor Labels: Unit Conversions

Write conversion factors for the following pairs of units (use Tables 1.7–1.9):

(a) Deciliters and milliliters

(b) Pounds and grams

ANALYSIS Start with the appropriate equivalency relationship and rearrange to form conversion factors.

SOLUTION

(a) Since $1\text{ dL} = 0.1\text{ L}$ and $1\text{ mL} = 0.001\text{ L}$, then $1\text{ dL} = (0.1\text{ L})\left(\dfrac{1\text{ mL}}{0.001\text{ L}}\right) = 100\text{ mL}$. The conversion factors are

$$\frac{1\text{ dL}}{100\text{ mL}} \quad \text{and} \quad \frac{100\text{ mL}}{1\text{ dL}}$$

(b) $\dfrac{1\text{ lb}}{454\text{ g}}$ and $\dfrac{454\text{ g}}{1\text{ lb}}$

Worked Example 1.12 Factor Labels: Unit Conversions

(a) Convert 0.75 lb to grams.

(b) Convert 0.50 qt to deciliters.

ANALYSIS Start with conversion factors and set up equations so that units cancel appropriately.

SOLUTION

(a) Select the conversion factor from Worked Example 1.9(b) so that the "lb" units cancel and "g" remains:

$$0.75\ \cancel{\text{lb}} \times \frac{454\text{ g}}{1\ \cancel{\text{lb}}} = 340\text{ g}$$

(b) In this, as in many problems, it is convenient to use more than one conversion factor. As long as the unwanted units cancel correctly, two or more conversion factors can be strung together in the same calculation. In this case, we can convert first between quarts and milliliters and then between milliliters and deciliters:

$$0.50\ \cancel{\text{qt}} \times \frac{946.4\ \cancel{\text{mL}}}{1\ \cancel{\text{qt}}} \times \frac{1\text{ dL}}{100\ \cancel{\text{mL}}} = 4.7\text{ dL}$$

Worked Example 1.13 Factor Labels: Unit Conversions

A child is 21.5 inches long at birth. How long is this in centimeters?

ANALYSIS This problem calls for converting from inches to centimeters, so we will need to know how many centimeters are in an inch and how to use this information as a conversion factor.

—continued on next page

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BALLPARK ESTIMATE It takes about 2.5 cm to make 1 in., and so it should take two and a half times as many centimeters to make a distance equal to approximately 20 in., or about 20 in. $\times$ 2.5 $=$ 50 cm.

SOLUTION

STEP 1: Identify given information.

$$\text{Length} = 21.5 \text{ in.}$$

STEP 2: Identify answer and units.

$$\text{Length} = ?? \text{ cm}$$

STEP 3: Identify conversion factor.

$$1 \text{ in.} = 2.54 \text{ cm} \rightarrow \frac{2.54 \text{ cm}}{1 \text{ in.}}$$

STEP 4: Solve. Multiply the known length (in inches) by the conversion factor so that units cancel, providing the answer (in centimeters)

$$21.5 \cancel{\text{in.}} \times \frac{2.54 \text{ cm}}{1 \cancel{\text{in.}}} = 54.6 \text{ cm} \quad (\text{Rounded off from } 54.61)$$

BALLPARK CHECK How does this value compare with the ballpark estimate we made at the beginning? Are the final units correct? 54.6 cm is close to our original estimate of 50 cm.

Worked Example 1.14 Factor Labels: Concentration to Mass

A patient requires an injection of 0.012 g of a pain killer available as a 15 mg/mL solution. How many milliliters of solution should be administered?

▲ How many milliliters should be injected?

ANALYSIS Knowing the amount of pain killer in 1 mL allows us to use the concentration as a conversion factor to determine the volume of solution that would contain the desired amount.

BALLPARK ESTIMATE One milliliter contains 15 mg of the pain killer, or 0.015 g. Since only 0.012 g is needed, a little less than 1.0 mL should be administered.

SOLUTION

STEP 1: Identify known information.

$$\text{Dosage} = 0.012 \text{ g}$$
$$\text{Concentration} = 15 \text{ mg/mL}$$

STEP 2: Identify answer and units.

$$\text{Volume to administer} = ?? \text{ mL}$$

STEP 3: Identify conversion factors. Two conversion factors are needed. First, g must be converted to mg. Once we have the mass in mg, we can calculate mL using the conversion factor of mL/mg.

$$1 \text{ mg} = .001 \text{ g} \Rightarrow \frac{1 \text{ mg}}{0.001 \text{ g}}$$
$$15 \text{ mg/mL} \Rightarrow \frac{1 \text{ mL}}{15 \text{ mg}}$$

STEP 4: Solve. Starting from the desired dosage, we use the conversion factors to cancel units, obtaining the final answer in mL.

$$(0.012 \cancel{\text{g}})\left(\frac{1 \cancel{\text{mg}}}{0.001 \cancel{\text{g}}}\right)\left(\frac{1 \text{ mL}}{15 \cancel{\text{mg}}}\right) = 0.80 \text{ mL}$$

BALLPARK CHECK Consistent with our initial estimate of a little less than 1 mL.

Worked Example 1.15 Factor Labels: Multiple Conversion Calculations

Administration of digitalis to control atrial fibrillation in heart patients must be carefully regulated because even a modest overdose can be fatal. To take differences between patients into account, dosages are sometimes prescribed in micrograms per kilogram of body weight (μg/kg). Thus, two people may differ greatly in weight, but both will receive the proper dosage. At a dosage of 20 μg/kg body weight, how many milligrams of digitalis should a 72.6 kg patient receive?

ANALYSIS Knowing the patient's body weight (in kg) and the recommended dosage (in μg/kg), we can calculate the appropriate amount of digitalis.

BALLPARK ESTIMATE At a dosage of 20 μg/kg, an 80 kg patient should receive 80 $\times$ 20 μg, or about 1600 μg of digitalis, or 1.6 mg.

SOLUTION

STEP 1: Identify known information.

STEP 2: Identify answer and units.

STEP 3: Identify conversion factors. The correct dose can be determined based on μg digitalis / kg of body weight. Then, the dosage in μg is converted to mg.

STEP 4: Solve. Use the known information and the conversion factors so that units cancel, obtaining the answer in mg.

Patient weight $= 72.6$ kg

Prescribed dosage $= 20\ \mu$g digitalis/kg body weight

Delivered dosage $=$?? mg digitalis

$$1\text{ mg} = (0.001\ \cancel{\text{g}})\left(\frac{1\ \mu\text{g}}{10^{-6}\ \cancel{\text{g}}}\right) = 1000\ \mu\text{g}$$

$$72.6\ \cancel{\text{kg}} \times \frac{20\ \cancel{\mu\text{g}}\text{ digitalis}}{1\ \cancel{\text{kg}}} \times \frac{1\text{ mg}}{1000\ \cancel{\mu\text{g}}}$$

$$= 1.5\text{ mg digitalis (Rounded off)}$$

BALLPARK CHECK Close to our estimate of 1.6 mg.

PROBLEM 1.15

Write appropriate conversion factors and carry out the following conversions:

(a) 16.0 oz $=$? g **(b)** 2500 mL $=$? L **(c)** 99.0 L $=$? qt

PROBLEM 1.16

Convert 0.840 qt to milliliters in a single calculation using more than one conversion factor.

PROBLEM 1.17

A patient is to receive 20 mg of methimazole, a drug used to treat hyperthyroid conditions. The drug is dissolved in solution containing 8 mg/mL. What volume of solution should be administered?

PROBLEM 1.18

Calculate the dosage in milligrams per kilogram body weight for a 61 kg adult who takes two aspirin tablets containing 0.324 g of aspirin each. Calculate the dosage for a 18 kg child who also takes two aspirin tablets.

1.11 Temperature, Heat, and Energy

Learning Objectives:

- Define the relationship between temperature and heat energy and convert temperatures between various temperature scales.
- Use temperature and specific heat to evaluate the flow of heat / energy in matter.

All chemical reactions are accompanied by a change in **energy,** which is defined in scientific terms as *the capacity to do work or supply heat* (Figure 1.8). Detailed discussion of the various kinds of energy will be included in Chapter 7, but for now we will look at the various units used to describe energy and heat, and how heat energy can be gained or lost by matter.

Temperature, the measure of the amount of heat energy in an object, is commonly reported either in Fahrenheit (°F) or Celsius (°C) units. The SI unit for reporting temperature, however, is the *kelvin* (K). (Note that we say only "kelvin," not "degrees kelvin.")

▲ **Figure 1.8**
The reaction of aluminum with bromine releases energy in the form of heat.
When the reaction is complete, the products undergo no further change.

Energy The capacity to do work or supply heat.

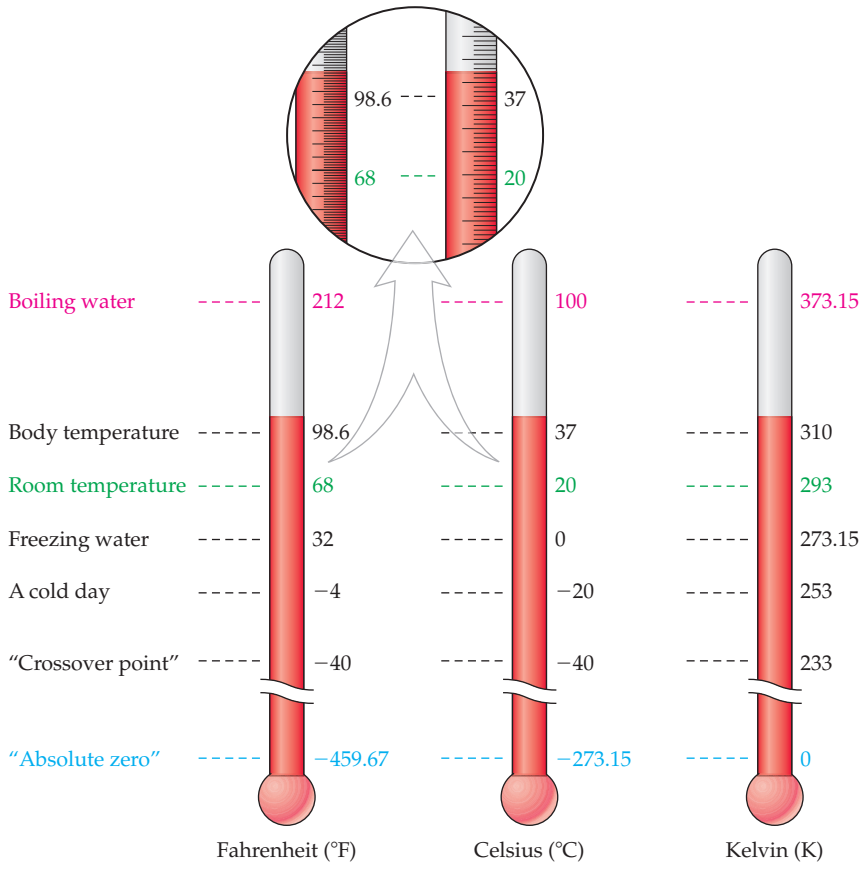
Temperature The measure of the amount of heat energy in an object.

The kelvin and the Celsius degree are the same size—both are 1/100 of the interval between the freezing point of water and the boiling point of water at atmospheric pressure. Thus, a change in temperature of 1 °C is equal to a change of 1 K. The only difference between the Kelvin and Celsius temperature scales is that they have different zero points. The Celsius scale assigns a value of 0 °C to the freezing point of water, but the Kelvin scale assigns a value of 0 K to the coldest possible temperature, sometimes called *absolute zero,* which is equal to −273.15 °C. Thus, 0 K = −273.15 °C, and +273.15 K = 0 °C. For example, a warm spring day with a temperature of 25 °C has a Kelvin temperature of 298 K (for most purposes, rounding off to 273 is sufficient).

$$\text{Temperature in K} = \text{Temperature in °C} + 273.15$$
$$\text{Temperature in °C} = \text{Temperature in K} - 273.15$$

For practical applications in medicine and clinical chemistry, the Fahrenheit and Celsius scales are used almost exclusively. The Fahrenheit scale defines the freezing point of water as 32 °F and the boiling point of water as 212 °F, whereas 0 °C and 100 °C are the freezing and boiling points of water on the Celsius scale. Thus, it takes 180 °F to cover the same range encompassed by only 100 °C, and a Celsius degree is therefore exactly 180/100 = 9/5 = 1.8 times as large as a Fahrenheit degree. In other words, a change in temperature of 1.0 °C is equal to a change of 1.8 °F. Figure 1.9 gives a comparison of all three scales.

Converting between the Fahrenheit and Celsius scales is similar to converting between different units of length or volume, but is a bit more complex because two corrections need to be made—one to adjust for the difference in degree size and one to adjust for the different zero points. The degree-size correction is made by using the relationship 1 °C = 1.8 °F and 1 °F = (1/1.8) °C. The zero-point correction is made by



▲ **Figure 1.9**
A comparison of the Fahrenheit, Celsius, and Kelvin temperature scales.
One Celsius degree is 1.8 times the size of one Fahrenheit degree.

CHEMISTRY IN ACTION

Temperature-Sensitive Materials

The physical properties of many materials change with the ambient temperature. Substances known as thermochromic materials change color as their temperature increases, and they change from the liquid phase to a semicrystalline-ordered state. These "liquid crystals" can be incorporated into plastics or paints and can be used to monitor temperature. For example, some meat packaging now includes a temperature strip that darkens when the meat is stored above a certain temperature, which makes the meat unsafe to eat. Hospitals and other medical facilities now routinely use strips that, when placed under the tongue or applied to the forehead, change color to indicate the patient's body temperature.

Other temperature-sensitive materials, called *shape-memory alloys* (SMAs), can be bent out of shape and will recover their original shape when heated above a certain temperature. These materials have many practical and clinical applications, including orthodontic wires that do not need to be tightened. The SMA is bent to fit into the orthodontic form, but once in the mouth its temperature increases and it contracts back to its original shape, applying constant force to align the teeth. SMAs are also used in stents. A collapsed stent can be inserted into an artery or vein; at body temperature the stent expands to its original shape and provides support for the artery or vein, improving blood flow.

▲ This stent, made from shape memory alloy, can be collapsed for insertion into an artery. Once in position, it is expanded by application of heat to maintain the arterial opening.

CIA Problem 1.4 A thermochromic plastic chip included in a shipping container for beef undergoes an irreversible color change if the storage temperature exceeds 28 °F. What is this temperature on the Celsius and Kelvin scales?

CIA Problem 1.5 A temperature-sensitive bath toy undergoes several color changes in the temperature range from 37 °C to 47 °C. What is the corresponding temperature range on the Kelvin scale?

remembering that the freezing point is higher by 32 on the Fahrenheit scale than on the Celsius scale. These corrections are incorporated into the following formulas, which show the conversion methods:

$$\textit{Celsius to Fahrenheit}: \quad ^\circ\text{F} = \left(\frac{1.8\ ^\circ\text{F}}{^\circ\text{C}} \times ^\circ\text{C}\right) + 32\ ^\circ\text{F}$$

$$\textit{Fahrenheit to Celsius}: \quad ^\circ\text{C} = \left(\frac{^\circ\text{C}}{1.8\ ^\circ\text{F}}\right) \times (^\circ\text{F} - 32\ ^\circ\text{F})$$

Energy is represented in SI units by the unit *joule* (J; pronounced "jool"), but the metric unit *calorie* (cal) is still widely used in medicine. In this text we will present energy values in both units. One calorie is the amount of heat necessary to raise the temperature of 1 g of water by 1 °C. A *kilocalorie* (kcal), often called a *large calorie* (Cal) or *food calorie* by nutritionists, equals 1000 cal:

$$1000\ \text{cal} = 1\ \text{kcal} \qquad 1000\ \text{J} = 1\ \text{kJ}$$
$$1\ \text{cal} = 4.184\ \text{J} \qquad 1\ \text{kcal} = 4.184\ \text{kJ}$$

Not all substances have their temperatures raised to the same extent when equal amounts of heat energy are added. One calorie raises the temperature of 1 g of water by 1 °C but raises the temperature of 1 g of iron by 10 °C. The amount of heat needed

Specific heat The amount of heat that will raise the temperature of 1 g of a substance by 1 °C.

to raise the temperature of 1 g of a substance by 1 °C is called the **specific heat** of the substance. It is measured in units of cal/(g·°C).

$$\text{Specific heat} = \frac{\text{calories}}{\text{grams} \times \text{°C}}$$

Specific heats vary greatly from one substance to another, as shown in Table 1.10. The specific heat of water, 1.00 cal/(g·°C) or 4.184 J/g °C, is higher than that of most other substances, which means that a large transfer of heat is required to change the temperature of a given amount of water by a given number of degrees. One consequence is that the human body, which is about 60% water, is able to withstand changing outside conditions.

Table 1.10 Specific Heats of Some Common Substances

Substance	Specific Heat [cal/g °C]; [J/g °C]	
Ethanol	0.59	2.5
Gold	0.031	0.13
Iron	0.106	0.444
Mercury	0.033	0.14
Sodium	0.293	1.23
Water	1.00	4.18

Knowing the mass and specific heat of a substance makes it possible to calculate how much heat must be added or removed to accomplish a given temperature change, as shown in Worked Example 1.17.

$$\text{Heat (cal)} = \text{Mass (g)} \times \text{Temperature change } (\Delta\,\text{°C}) \times \text{Specific heat}\left(\frac{\text{cal}}{\text{g}\cdot\text{°C}}\right)$$

Worked Example 1.16 Temperature Conversions: Fahrenheit to Celsius

A body temperature above 107 °F can be fatal. What does 107 °F correspond to on the Celsius scale?

ANALYSIS Using the temperature (in °F) and the appropriate temperature conversion equation, we can convert from the Fahrenheit scale to the Celsius scale.

BALLPARK ESTIMATE Note that in Figure 1.9 the normal body temperature is 98.6 °F or 37 °C. A temperature of 107 °F is approximately 8 °F above normal; since 1 °C is nearly 2 °F then 8 °F is about 4 °C. Thus, the 107 °F body temperature is 41 °C.

SOLUTION

STEP 1: Identify known information.

STEP 2: Identify answer and units.

STEP 3: Identify conversion factors. We can convert from °F to °C using this equation.

STEP 4: Solve. Substitute the known temperature (in °F) into the equation.

$$\text{Temperature} = 107\ \text{°F}$$

$$\text{Temperature} = ??\ \text{°C}$$

$$\text{°C} = \left(\frac{\text{°C}}{1.8\ \text{°F}}\right)(\text{°F} - 32\ \text{°F})$$

$$\text{°C} = \left(\frac{\text{°C}}{1.8\ \text{°F}}\right)(107\ \text{°F} - 32\ \text{°F}) = 42\ \text{°C}^*$$

(Rounded off from 41.666 667 °C)

BALLPARK CHECK Close to our estimate of 41 °C.

*It is worth noting that the 1.8 conversion factor in the equation is an exact conversion, and so it does not impact the number of significant figures in the final answer.

Worked Example 1.17 Specific Heat: Mass, Temperature, and Energy

Taking a bath might use about 95 kg of water. How much energy (in calories and Joules) is needed to heat the water from a cold 15 °C to a warm 40 °C?

ANALYSIS From the amount of water being heated (95 kg) and the amount of the temperature change (40 °C − 15 °C = 25 °C), the total amount of energy needed can be calculated by using specific heat [1.00 cal/(g·°C)] as a conversion factor.

BALLPARK ESTIMATE The water is being heated by 25 °C (from 15 °C to 40 °C), and it therefore takes 25 cal to heat each gram. The tub contains nearly 100,000 g (95 kg is 95,000 g), and so it takes about 25 × 100,000 cal, or 2,500,000 cal, to heat all the water in the tub.

SOLUTION

STEP 1: Identify known information.

STEP 2: Identify answer and units.

STEP 3: Identify conversion factors. The amount of energy (in cal) can be calculated using the specific heat of water (cal/g · °C), and it will depend on both the mass of water (in g) to be heated and the total temperature change (in °C). In order for the units in specific heat to cancel correctly, the mass of water must first be converted from kg to g.

STEP 4: Solve. Starting with the known information, use the conversion factors to cancel unwanted units.

Mass of water = 95 kg

Temperature change = 40 °C − 15 °C = 25 °C

Heat = ?? cal

$$\text{Specific heat} = \frac{1.0\ \text{cal}}{\text{g} \cdot {}^\circ\text{C}}$$

$$1\ \text{kg} = 1000\ \text{g} \rightarrow \frac{1000\ \text{g}}{1\ \text{kg}}$$

$$95\ \cancel{\text{kg}} \times \frac{1000\ \cancel{\text{g}}}{\cancel{\text{kg}}} \times \frac{1.00\ \text{cal}}{\cancel{\text{g}} \cdot \cancel{{}^\circ\text{C}}} \times 25\ \cancel{{}^\circ\text{C}} = 2{,}400{,}000\ \text{cal}$$

$$= 2.4 \times 10^6\ \text{cal (or } 1.0 \times 10^7\ \text{J)}$$

BALLPARK CHECK Close to our estimate of 2.5×10^6 cal.

PROBLEM 1.19

The highest land temperature ever recorded was 136 °F in Al Aziziyah, Libya, on September 13, 1922. What is this temperature on the Kelvin scale?

PROBLEM 1.20

A patient exhibits a temperature of 39 °C. What is the body temperature of the patient in K?

PROBLEM 1.21

Assuming that Coca-Cola has the same specific heat as water, how much energy in calories is removed when 350 g of Coca-Cola (about the contents of one 33 cL can) is cooled from room temperature (25 °C) to refrigerator temperature (3 °C)?

PROBLEM 1.22

What is the specific heat of aluminum if it takes 674 J (161 cal) to raise the temperature of a 75 g aluminum bar by 10.0 °C? Express this specific heat in J/(K · mol).

1.12 Density and Specific Gravity

Learning Objective:

- Define density and specific gravity and use these quantities in mass / volume calculations.

Density The physical property that relates the mass of an object to its volume; mass per unit volume.

One further physical quantity that we will take up in this chapter is **density,** which relates the mass of an object to its volume. Density is usually expressed in units of grams per cubic centimeter (g/cm^3) for solids and grams per milliliter (g/mL) for liquids. Thus, if we know the density of a substance, we know both the mass of a given volume and the volume of a given mass. The densities of some common materials are listed in Table 1.11.

$$\text{Density} = \frac{\text{Mass (g)}}{\text{Volume (mL or cm}^3\text{)}}$$

Although most substances contract when cooled and expand when heated, water behaves differently. Water contracts when cooled from 100 °C to 3.98 °C but below this temperature it begins to *expand* again. The density of liquid water is at its maximum of 1.0000 g/mL at 3.98 °C but decreases to 0.999 87 g/mL at 0 °C. When freezing occurs, the density drops still further to a value of 0.917 g/cm^3 for ice at 0 °C. Since a

▲ The Galileo thermometer contains several weighted bulbs that rise or fall as the density of the liquid changes with temperature.

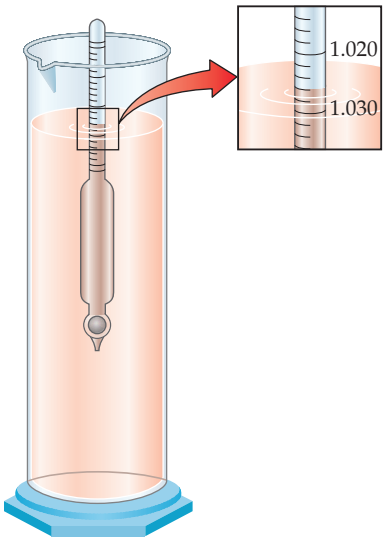
less dense substance will float on top of a more dense fluid, ice and any other substance with a density less than that of water will float in water. Conversely, any substance with a density greater than that of water will sink in water.

Table 1.11 Densities of Some Common Materials at 25 °C

Substance	Density*	Substance	Density*
Gases		Solids	
Helium	0.000 194	Ice (0 °C)	0.917
Air	0.001 185	Gold	19.3
		Human fat	0.94
Liquids		Cork	0.22–0.26
Water (3.98 °C)	1.0000	Table sugar	1.59
Urine	1.003–1.030	Balsa wood	0.12
Blood plasma	1.027		

**Densities are in g/cm³ for solids and g/mL for liquids and gases. As noted in Section 1.7, 1 mL = 1 cm³.*

Specific gravity The density of a substance divided by the density of water at the same temperature.



▲ **Figure 1.10**
A hydrometer for measuring specific gravity.
The instrument has a weighted bulb at the end of a calibrated glass tube. The depth to which the hydrometer sinks in a liquid indicates the liquid's specific gravity.

Knowing the density of a liquid is useful because it is often easier to measure a liquid's volume rather than its mass. Suppose, for example, that you need 1.50 g of ethanol. Rather than use a dropper to weigh out exactly the right amount, it would be much easier to look up the density of ethanol (0.7893 g/mL at 20 °C) and measure the correct volume (1.90 mL) with a syringe or graduated cylinder. Thus, density acts as a conversion factor between mass (g) and volume (mL).

$$1.50 \text{ g ethanol} \times \frac{1 \text{ mL ethanol}}{0.7893 \text{ g ethanol}} = 1.90 \text{ mL ethanol}$$

For many purposes, ranging from winemaking to medicine, it is more convenient to use *specific gravity* than density. The **specific gravity** (sp gr) of a substance (usually a liquid) is simply the density of the substance divided by the density of water at the same temperature. Because all units cancel, specific gravity is unitless:

$$\text{Specific gravity} = \frac{\text{Density of substance } (\text{g/mL})}{\text{Density of water at the same temperature } (\text{g/mL})}$$

At typical temperatures, the density of water is very close to 1 g/mL. Thus, the specific gravity of a substance is numerically equal to its density and is used in the same way.

The specific gravity of a liquid can be measured using an instrument called a *hydrometer,* which consists of a weighted bulb on the end of a calibrated glass tube, as shown in Figure 1.10. The depth to which the hydrometer sinks when placed in a fluid indicates the fluid's specific gravity: the lower the bulb sinks, the lower the specific gravity of the fluid.

In medicine, a hydrometer called a *urinometer* is used to indicate the amount of solids dissolved in urine. Although the specific gravity of normal urine is about 1.003–1.030, conditions such as diabetes mellitus or a high fever cause an abnormally high urine specific gravity, indicating either excessive elimination of solids or decreased elimination of water. Abnormally low specific gravity is found in individuals using diuretics—drugs that increase water elimination.

Worked Example 1.18 Density: Mass-to-Volume Conversion

What volume of isopropanol (rubbing alcohol) would you use if you needed 25.0 g? The density of isopropanol is 0.7855 g/mL at 20 °C.

ANALYSIS The known information is the mass of isopropanol needed (25.0 g). The density (0.7855 g/mL) acts as a conversion factor between mass and the unknown volume of isopropanol.

BALLPARK ESTIMATE Because 1 mL of isopropanol contains only 0.7885 g of the alcohol, obtaining 1 g of alcohol requires almost 20% more than 1 mL, or about 1.2 mL. Therefore, a volume of about $25 \times 1.2\ \text{mL} = 30\ \text{mL}$ is needed to obtain 25 g of alcohol.

SOLUTION

STEP 1: Identify known information.

STEP 2: Identify answer and units.

STEP 3: Identify conversion factors. Starting with the mass of isopropanol (in g), the corresponding volume (in mL) can be calculated using density (g/mL) as the conversion factor.

STEP 4: Solve. Starting with the known information, set up the equation with conversion factors so that unwanted units cancel.

Mass of rubbing alcohol = 25.0 g
Density of rubbing alcohol = 0.7855 g/mL
Volume of rubbing alcohol = ?? mL
Density = g/mL → 1/density = mL/g

$$25.0\ \cancel{\text{g alcohol}} \times \frac{1\ \text{mL alcohol}}{0.7855\ \cancel{\text{g alcohol}}} = 31.8\ \text{mL alcohol}$$

BALLPARK CHECK Our estimate was 30 mL.

PROBLEM 1.23

A sample of pumice, a porous volcanic rock, weighs 17.4 grams and has a volume of 27.3 cm^3. If this sample is placed in a container of water, will it sink or will it float? Explain.

PROBLEM 1.24

Chloroform, once used as an anesthetic agent, has a density of 1.474 g/mL. What volume would you use if you needed 12.37 g?

PROBLEM 1.25

The sulfuric acid solution in an automobile battery typically has a specific gravity of about 1.27. Is battery acid more dense or less dense than pure water?

▲ The specific gravity of urine, measured by a urinometer, is used to diagnose conditions such as diabetes.

CHEMISTRY IN ACTION

A Measurement Example: Obesity and Body Fat

At the beginning of the chapter, we mentioned that some fat is good, but how much is too much and what are the health risks of too much body fat? The impacts of obesity include significant adverse health effects like heart disease, stroke, type 2 diabetes, and certain types of cancer. Worldwide obesity has more than doubled since 1980. In 2014, more than 1.9 billion adults, 18 years and older, were overweight. Among them, over 600 million were obese and 41 million children under the age of 5 were overweight or obese. Most of the world's population live in countries where obesity kills more than being underweight does.

At the beginning of the chapter, we learned that obesity is an excessive amount of body fat and one way to measure body fat is

▲ A person's percentage body fat can be estimated by measuring the thickness of the fat layer under the skin.

through buoyancy testing. But obesity is also defined by reference to *body mass index* (BMI), which is equal to a person's mass in kilograms divided by the square of his or her height in meters. BMI can also be calculated by dividing a person's weight in pounds by the square of her or his height in inches multiplied by 703. For instance, someone 1.70 m tall weighing 66.7 kg has a BMI of 23:

$$\text{BMI} = \frac{\text{weight (kg)}}{[\text{height (m)}]^2}$$

A BMI of 25 or above is considered overweight, and a BMI of 30 or above is obese. By these standards, approximately 61% of the U.S. population is overweight. Health professionals are concerned by the rapid rise in obesity in the United States because of the link between BMI and health problems. Many reports have documented the correlation between health and BMI, including a recent study on more than 1 million adults. The lowest death risk from any cause, including cancer and heart disease, is associated with a BMI between 22 and 24. Risk increases steadily as BMI increases, more than doubling for a BMI above 29.

An individual's percentage of body fat is most easily measured by the skinfold-thickness method. The skin at several locations on the arm, shoulder, and waist is pinched, and the thickness of the fat layer beneath the skin is measured with calipers. Comparing the measured results to those in a standard table gives an estimation of percentage body fat. As an alternative to skinfold measurement, a more accurate assessment of body fat can be made by underwater immersion, or buoyancy testing as we learned at the beginning of the chapter.

There is good news—obesity can be prevented by making healthier food choices and ensuring regular physical activity (60 minutes a day for children and 150 minutes spread through the week for adults).

Weight (kg)

Height (cm)	50.0	52.3	54.5	56.8	59.1	61.4	63.6	65.9	68.2	70.5	72.7	75.0	77.3	79.5	81.8	84.1	86.4	88.6	90.9
152.4	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
157.4	20	21	22	22	23	24	25	26	27	28	29	30	31	32	33	33	34	35	36
162.5	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	31	32	33	34
167.6	17	18	19	20	21	21	22	23	24	25	25	26	27	28	29	29	30	31	32
172.7	16	17	18	19	19	20	21	22	22	23	24	25	25	26	27	28	28	29	30
177.8	15	16	17	18	18	19	20	20	21	22	23	23	24	25	25	26	27	28	28
182.8	15	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27
187.9	14	14	15	16	16	17	18	18	19	19	20	21	21	22	23	23	24	25	25
193.0	13	14	14	15	15	16	17	17	18	18	19	20	20	21	22	22	23	23	24

Body Mass Index (numbers in boxes)

CIA Problem 1.6 Calculate the BMI for an individual who is

(a) 155 cm tall and weighs 70 kg
(b) 180 cm tall and weighs 77 kg
(c) 190 cm tall and weighs 88 kg

Which of these individuals is likely to have increased health risks?

CIA Problem 1.7 Liposuction is a technique for removing fat deposits from various areas of the body. How many liters of fat would have to be removed to result in a 2.3 kg weight loss? The density of human fat is 0.94 g/mL

SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Identify properties of matter and differentiate between chemical and physical changes.** *Matter* is anything that has mass and occupies volume—that is, anything physically real. A *property* is any characteristic that can be used to describe or identify something: *physical* properties can be seen or measured without changing the chemical identity of the substance (i.e., color, melting point), while *chemical* properties can only be seen or measured when the substance undergoes a *chemical change,* such as a chemical reaction *(see Problems 33–35).*
- **Identify the three states of matter and describe their properties.** Matter can be classified by its physical state as *solid, liquid,* or *gas.* A solid has a definite volume and shape, a liquid has a definite volume but indefinite shape, and a gas has neither a definite volume nor a definite shape *(see Problems 26, 36–39, and 41).*
- **Distinguish between mixtures and pure substances and classify pure substances as elements or compounds.** Matter can also be classified by composition as being either *pure* or a *mixture.* Every pure substance is either an *element* or a *chemical compound.* Elements are fundamental substances that cannot be chemically changed into anything simpler. A chemical compound, by contrast, can be broken down by chemical change into simpler substances. Mixtures are composed of two or more pure substances and can be separated into component parts by physical means *(see Problems 40–43, 53, and 92).*
- **Identify the symbols and names of the common elements.** Elements are represented by one- or two-letter symbols, such as H for hydrogen, Ca for calcium, Al for aluminum, and so on. Most symbols are the first one or two letters of the element name, but some symbols are

derived from Latin names—Na (sodium), for example *(see Problems 26, 27, 44–52, and 114).*

- **Identify a chemical change as a chemical reaction.** A chemical reaction is a symbolic representation of a chemical change. The starting materials (reactants) are on the left, the final materials (products) are on the right. An arrow is used to indicate a chemical change as reactants are converted to products, with reaction conditions written above/ below the arrow. The reactants and products are identified using chemical symbols to represent the elements or compounds, and their physical states are indicated using appropriate abbreviations *(s, l, g, aq) (see Problems 34, 35, 42, 43, and 92).*
- **Write very large or very small numbers using scientific notation or units with appropriate numerical prefixes.** Measurements of small and large quantities are usually written in *scientific notation* as the product of a number between 1 and 10, times a power of 10. Numbers greater than 10 have a positive exponent, and numbers less than 1 have a negative exponent. For example, $3562 = 3.562 \times 10^3$, and $0.003\,91 = 3.91 \times 10^{-3}$ *(see Problems 55–58 and 67).*
- **Name and correctly use the metric and SI units of measurement for mass, length, volume, and temperature, and convert units appropriately.** A property that can be measured is called a *physical quantity* and is described by both a number and a label, or *unit.* The preferred units are either those of the International System of Units (*SI units*) or the *metric system.* Mass, the amount of matter an object contains, is measured in *kilograms* (kg) or *grams* (g). Length is measured in *meters* (m). Volume is measured in *cubic meters* (m^3) in the SI system and in *liters* (L) or *milliliters* (mL) in the metric system. Temperature is measured in *kelvins* (K) in the SI system and in *degrees Celsius* (°C) in the metric system. A measurement in one unit can be converted to another unit by multiplying by a *conversion factor* that expresses the exact relationship between the units. The conversion factor should be arranged so that the starting unit is canceled and the desired unit is carried over to the answer *(see Problems 54–56, 58, 67–77, 93, 94, 96–98, 103, 106, 110, and 115).*
- **Use significant figures and scientific notation to represent the precision of a measurement.** When measuring physical quantities or using them in calculations, it is important to indicate the exactness of the measurement by using significant figures or numbers to represent those decimal places that are known with certainty, plus one additional decimal place indicating the point at which the measured value is uncertain. For example, a mass that was recorded as 15.34 g has an uncertainty in the last decimal place of ±0.01 g *(see Problems 29–31, 59, 60, and 97).*
- **Determine the appropriate number of significant figures in a calculated result and round off numbers in calculations involving measurements.** For multiplication and division, the number of significant figures in the calculated result is the same as the number with the fewest significant figures involved in the calculation. For addition and subtraction, the number of significant figures in the calculated result is determined by the least precise decimal place for the numbers involved in the calculation. If necessary, the calculated result is *rounded off* to obtain the final answer to the correct number of *significant figures (see Problems 42, 43, 59–66, 101, and 105).*
- **Use the factor-label method (conversion factors) to solve a problem and check the result to ensure that it makes sense chemically and physically.** Problems are best solved by applying the *factor-label method* in which units can be multiplied and divided just as numbers can. The idea is to set up an equation so that all unwanted units cancel, leaving only the desired units. Usually it is best to start by identifying the known and needed information, then decide how to convert the known information to the answer, and finally check to make sure the answer is reasonable both chemically and physically *(see Problems 67–77, 96–101, 103–107, 112, and 113).*
- **Define the relationship between temperature and heat energy and be able to convert temperatures between various temperature scales.** *Temperature* is a measure of the amount of heat energy in an object. The SI unit of temperature is Kelvin and non-SI units such as Celsius and Fahrenheit are also very common, with conversions between scales as shown on pages 62–63 *(see Problems 78, 91, 102, and 111).*
- **Use temperature and specific heat to evaluate the flow of heat / energy in matter.** Heat flows from a hot object to a cold object. The *specific heat* of a substance is the amount of heat necessary to raise the temperature of 1 g of the substance by 1 °C (1 cal/ g °C or 4.184 J/ g °C). Water has an unusually high specific heat, which helps our bodies to maintain an even temperature *(see Problems 79–84, 95, 104, 107, and 108).*
- **Define density and specific gravity and to use these quantities in mass / volume calculations.** *Density*, the physical property that relates mass to volume, is expressed in units of grams per milliliter (g/ mL) for a liquid or grams per cubic centimeter (g/ cm^3) for a solid. The *specific gravity* of a liquid is the density of the liquid divided by the density of water at the same temperature. Because the density of water is approximately 1 g/ mL, specific gravity and density have the same numerical value *(see Problems 28, 32, 85–90, 102, 107, 109, 110, 115, and 116).*

KEY WORDS

Change of state, *p. 38*
Chemical change, *p. 36*
Chemical compound, *p. 39*
Chemical formula, *p. 42*
Chemical reaction, *p. 44*
Chemistry, *p. 35*
Conversion factor, *p. 57*
Density, *p. 65*
Element, *p. 39*
Energy, *p. 61*
Factor-label method, *p. 57*
Gas *(g),* *p. 38*
Heterogeneous mixture, *p. 39*
Homogeneous mixture, *p. 39*
Liquid *(l),* *p. 38*
Mass, *p. 49*
Matter, *p. 35*
Mixture, *p. 39*
Physical change, *p. 36*
Physical quantity, *p. 45*
Product, *p. 44*
Property, *p. 35*
Pure substance, *p. 39*
Reactant, *p. 44*
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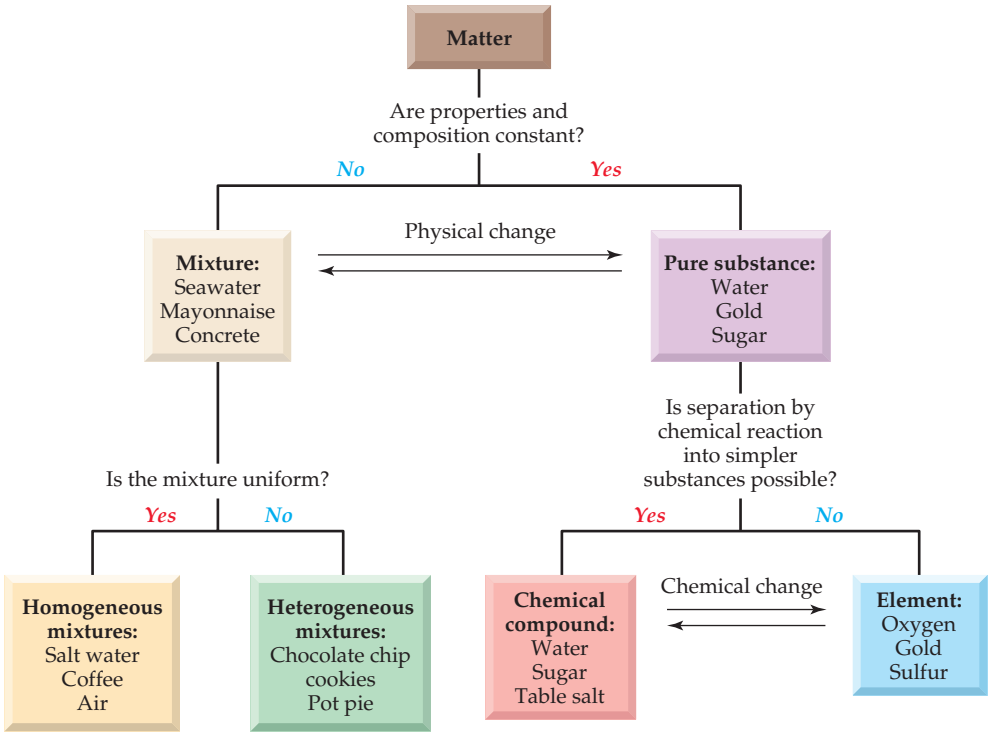
Temperature, *p. 61*
Unit, *p. 45*
Weight, *p. 49*

CONCEPT MAP: MATTER

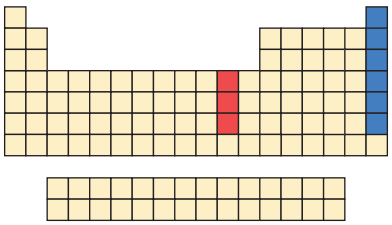


▲ **Figure 1.11 Concept Map.** Chemistry, like most subjects, makes more sense when presented in context. When we understand the connections between concepts, or how one idea leads to another, it becomes easier to see the "big picture" and to appreciate why a certain concept is important. A concept map is one way of illustrating those connections and providing a context for what we have learned and what we will be learning in later chapters. This concept map illustrates how we distinguish between the different types of matter and the types of changes that matter can undergo. As we continue exploring new topics, we will expand certain areas of this concept map or add new branches as needed.

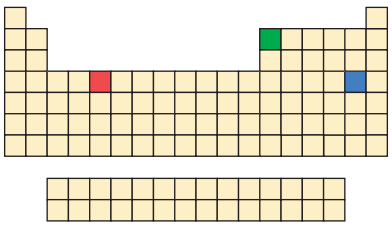
UNDERSTANDING KEY CONCEPTS

The problems in this section are intended as a bridge between the Chapter Summary and the Additional Problems that follow. Primarily visual in nature, they are designed to help you test your grasp of the chapter's most important principles before attempting to solve quantitative problems. Answers to all Key Concept Problems are at the end of the book following the appendixes.

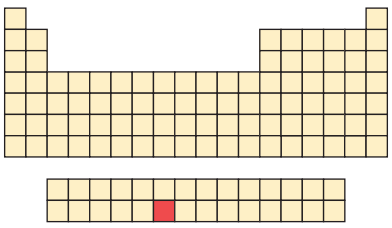
1.26 The six elements in blue at the far right of the periodic table are gases at room temperature. The red elements in the middle of the table are the so-called coinage metals. Identify each of these elements using the periodic table inside the front cover of this book.



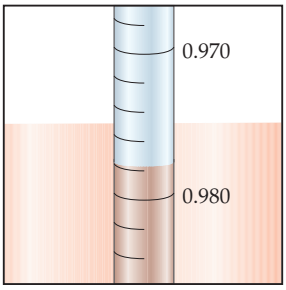
1.27 Identify the three elements indicated on the following periodic table. Do an Internet search to identify the common sources of these elements and some of their common uses or applications.



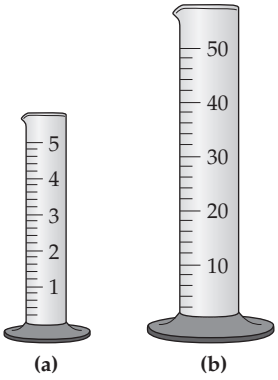
1.28 The radioactive element indicated on the following periodic table is used in smoke detectors. Identify it.



1.29 **(a)** What is the specific gravity of the following solution? **(b)** How many significant figures does your answer have? **(c)** Is the solution more dense or less dense than water?

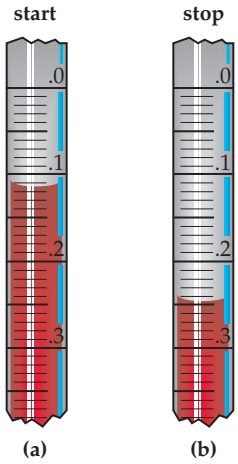


1.30 Assume that you have two graduated cylinders, one with a capacity of 5 mL (a) and the other with a capacity of 50 mL (b). Draw a line in each showing how much liquid you would add if you needed to measure 2.64 mL of water. Which cylinder do you think is more precise? Explain.



1.31 State the length of the pencil depicted in the accompanying figure in both inches and centimeters using appropriate numbers of significant figures.

1.32 Assume that you are delivering a solution sample from a pipette. Figures (a) and (b) show the volume level before and after dispensing the sample, respectively. State the liquid level (in mL) before and after dispensing the sample, and calculate the volume of the sample.



1.33 Assume that identical hydrometers are placed in ethanol (sp gr 0.7893) and in chloroform (sp gr 1.4832). In which liquid will the hydrometer float higher? Explain.

ADDITIONAL SECTION PROBLEMS

These exercises are divided into sections by topic. Each section begins with review and conceptual questions, followed by numerical problems of varying levels of difficulty. Many of the problems dealing with more difficult concepts or skills are presented in pairs, with each even-numbered problem followed by an odd-numbered one requiring similar skills. The final section consists of unpaired Conceptual Problems that draw on various parts of the chapter and, in future chapters, may even require the use of concepts from previous chapters. An additional feature in this edition is the incorporation of Group Questions that may sometimes require using resources other than the textbook and are suitable as small group activities. Answers to all even-numbered problems are given at the end of the book following the appendixes.

CHEMISTRY AND THE PROPERTIES OF MATTER (SECTION 1.1)

1.34 What is the difference between a physical change and a chemical change?

1.35 Which of the following is a physical change and which is a chemical change?

(a) Boiling water

(b) Decomposing water by passing an electric current through it

(c) Exploding of potassium metal when placed in water

(d) Breaking of glass

1.36 Which of the following is a physical change and which is a chemical change?

(a) Making lemonade (lemons + water + sugar)

(b) Frying eggs

(c) Burning a candle

(d) Whipping cream

(e) Leaves changing color

STATES AND CLASSIFICATION OF MATTER (SECTIONS 1.2, 1.3, AND 1.5)

1.37 Name and describe the three states of matter.

1.38 Name two changes of state and describe what causes each to occur.

1.39 Sulfur dioxide is a compound produced when sulfur burns in air. It has a melting point of −72.7 °C and a boiling point of −10 °C. In what state does it exist at room temperature (298 K)? (Refer to Figure 1.9.)

1.40 Butane (C_4H_8) is an easily compressible gas used in cigarette lighters. It has a melting point of −138.4 °C and a boiling point of −0.5 °C. Would you expect a butane lighter to work in winter when the temperature outdoors is 269 K? Why or why not? (Refer to Figure 1.9.)

1.41 Classify each of the following as a mixture or a pure substance:

(a) Pea soup **(b)** Seawater

(c) The contents of a propane tank

(d) Urine **(e)** Lead

(f) A multivitamin tablet

1.42 Which of these terms, (i) mixture, (ii) solid, (iii) liquid, (iv) gas, (v) chemical element, (vi) chemical compound, applies to the following substances at room temperature?

(a) Gasoline **(b)** Iodine

(c) Water **(d)** Air

(e) Blood **(f)** Sodium hydrogen carbonate

(g) Gaseous ammonia **(h)** Silicon

1.43 Hydrogen peroxide, often used in solutions to cleanse cuts and scrapes, breaks down to yield water and oxygen:

$$\text{Hydrogen peroxide, } H_2O_2(aq) \rightarrow \text{Hydrogen, } H_2(g) + \text{Oxygen, } O_2(g)$$

(a) Identify the reactants and products.

(b) Which of the substances are chemical compounds, and which are elements?

1.44 When sodium metal is placed in water, the following change occurs:

$$\text{Sodium, } Na(s) + \text{Water, } H_2O(l) \rightarrow \text{Hydrogen, } H_2(g) + \text{Sodium hydroxide, } NaOH(aq)$$

(a) Identify the reactants and products and their physical states

(b) Which of the substances are elements, and which are chemical compounds?

ELEMENTS AND THEIR SYMBOLS (SECTION 1.4)

1.45 What is the most abundant element in the earth's crust? In the human body? List the name and symbol for each.

1.46 What are the symbols for the following elements? Perform a web search to identify some of the common uses of the elements listed.

(a) Iodine **(b)** Chromium

(c) Technetium **(d)** Arsenic

(e) Barium

1.47 Supply the missing names or symbols for the elements in the spaces provided:

(a) N _____ **(b)** K _____

(c) Cl _____ **(d)** _____ Calcium

(e) _____ Phosphorus **(f)** _____ Manganese

1.48 Correct the following statements.

(a) The symbol for bromine is BR.

(b) The symbol for manganese is Mg.

(c) The symbol for carbon is Ca.

(d) The symbol for potassium is Po.

1.49 Correct the following statements.

(a) Carbon dioxide has the formula CO2.

(b) Carbon dioxide has the formula Co_2.

(c) Table salt, NaCl, is composed of nitrogen and chlorine.

1.50 The amino acid, glycine, has the formula $C_2H_5NO_2$. Which elements are present in glycine? What is the total number of atoms represented by the formula?

1.51 Glucose, a form of sugar, has the formula $C_6H_{12}O_6$. Which elements are included in this compound, and how many atoms of each are present?

1.52 Write the formula for ibuprofen: 13 carbons, 18 hydrogens, and 2 oxygens. What are the common uses of ibuprofen?

1.53 The atmosphere consists of a number of permanent gases: oxygen (O_2), nitrogen (N_2), carbon dioxide (CO_2), water vapor (H_2O), and argon (Ar). Identify each substance as an element or a compound. Would you consider the atmosphere to be a heterogeneous or a homogeneous mixture?

PHYSICAL QUANTITIES: DEFINITIONS AND UNITS (SECTIONS 1.6 AND 1.7)

1.54 What is the difference between a physical quantity and a number?

1.55 What are the units used in the SI system to measure mass, volume, length, and temperature? In the metric system?

1.56 Give the full name of the following units:

(a) cc **(b)** dm **(c)** mm

(d) nL **(e)** mg **(f)** m^3

1.57 Write the symbol for the following units:

(a) nanogram **(b)** centimeter

(c) microliter **(d)** micrometer

(e) milligram

1.58 How many picograms are in 1 mg? In 35 ng?

1.59 How many microliters are in 1 L? In 20 mL?

SCIENTIFIC NOTATION, SIGNIFICANT FIGURES, AND ROUNDING OFF (SECTIONS 1.6, 1.8, AND 1.9)

1.60 Express the following numbers in scientific notation with the correct number of significant figures:

(a) 9457 **(b)** 0.000 07

(c) 20,000,000,000 (four significant figures)

(d) 0.012 345 **(e)** 652.38

1.61 Convert the following numbers from scientific notation to standard notation:

(a) 5.28×10^{3} **(b)** 8.205×10^{-2}

(c) 1.84×10^{-5} **(d)** 6.37×10^{4}

1.62 How many significant figures does each of the following numbers have?

(a) 237,401 **(b)** 0.300

(c) 3.01 **(d)** 244.4

(e) 50,000 **(f)** 660

1.63 How many significant figures are there in each of the following quantities?

(a) Distance from New York City to Wellington, New Zealand, 14,397 km

(b) Average body temperature of a crocodile, 299 K

(c) Melting point of gold, 1337 K

(d) Diameter of an influenza virus, 0.000 01 mm

(e) Radius of a phosphorus atom, 0.110 nm

1.64 The diameter of the earth at the equator is 12,756.27 km.

(a) Round off the earth's diameter to four significant figures, to two significant figures, and to six significant figures.

(b) Express the earth's diameter in scientific notation.

1.65 Round off each of the numbers in Problem 1.63 to two significant figures and express them in scientific notation.

1.66 Carry out the following calculations, express each answer to the correct number of significant figures, and include units in the answers.

(a) 9.02 g + 3.1 g

(b) 88.80 cm + 7.391 cm

(c) 362 mL − 99.5 mL

(d) 12.4 mg + 6.378 mg + 2.089 mg

1.67 Carry out the following calculations, express the answers to the correct numbers of significant figures, and include units in the answers.

(a) $5280 \dfrac{\text{m}}{\text{km}} \times 6.2 \text{ km}$

(b) $4.5 \text{ m} \times 3.25 \text{ m}$

(c) $2.50 \text{ g} \div 8.3 \dfrac{\text{g}}{\text{cm}^3}$

(d) $4.70 \text{ cm} \times 6.8 \text{ cm} \times 2.54 \text{ cm}$

UNIT CONVERSIONS AND PROBLEM SOLVING (SECTION 1.10)

1.68 Carry out the following conversions:

(a) 3.614 mg to centigrams

(b) 12.0 kL to megaliters

(c) 14.4 μm to millimeters

(d) 6.03×10^{-6} cg to nanograms

(e) 174.5 mL to deciliters

(f) 1.5×10^{-2} km to centimeters

1.69 Carry out the following conversions. Consult Tables 1.7–1.9 as needed.

(a) 56.4 mi to kilometers and to megameters

(b) 2.0 L to quarts and to fluid ounces

(c) 7 ft 2.0 in. to centimeters and to meters

(d) 1.35 lb to kilograms and to decigrams

1.70 Express the following quantities in more convenient units by using SI unit prefixes:

(a) 9.78×10^{4} g **(b)** 1.33×10^{-4} L

(c) 0.000 000 000 46 g **(d)** 2.99×10^{8} cm

1.71 Fill in the blanks to complete the equivalencies either with appropriate unit prefixes or with the appropriate scientific notation. The first blank is filled in as an example.

(a) 125 km = 1.25×10^{5} m

(b) 6.285×10^{3} mg = _____? _____ kg

(c) 47.35 dL = 4.735 × _____? _____ mL

(d) 67.4 cm = 6.7×10^{-4} _____? _____

1.72 The speed limit in Canada is 100 km/h.

(a) How many miles per hour is this?

(b) How many meters per second?

1.73 The muzzle velocity of a projectile fired from a 9 mm handgun is 1200 ft/s.

(a) How many miles per hour is this?

(b) How many meters per second?

1.74 The diameter of a red blood cell is 6×10^{-6} m.

(a) How many centimeters is this?

(b) How many red blood cells are needed to make a line 1 cm long? 1 in. long?

1.75 The Willis Tower in Chicago has an approximate floor area of 418,000 m^2. How many square feet of floor space is this?

1.76 A normal value for blood cholesterol is 200 mg/dL of blood. If a normal adult has a total blood volume of 5 L, how much total cholesterol is present?

1.77 The recommended daily dose of calcium for an 18-year-old male is 1200 mg. If 1.0 cup of whole milk contains 290 mg of calcium and milk is his only calcium source, how much milk should an 18-year-old male drink each day?

1.78 The white blood cell concentration in normal blood is approximately 12,000 cells/mm^3 of blood. How many white blood cells does a normal adult with 5 L of blood have? Express the answer in scientific notation.

ENERGY, HEAT, AND TEMPERATURE (SECTION 1.11)

1.79 The boiling point of liquid nitrogen, used in the removal of warts and in other surgical applications, is −195.8 °C. What is this temperature in kelvins and in degrees Fahrenheit?

1.80 Diethyl ether, a substance once used as a general anesthetic, has a specific heat of 3.74 J/(g °C). How many joules and how many kilojoules of heat are needed to raise the temperature of 30.0 g of diethyl ether from 283 K to 303 K? How many calories and kilocalories?

1.81 Aluminum has a specific heat of 0.898 J/(g °C). When 108.5 J of heat is added to 18.4 g of aluminum at 20.0 °C, what is the final temperature of the aluminum?

1.82 Calculate the specific heat of copper if it takes 96 J to heat a 5.0 g sample from 25 °C to 75 °C.

1.83 The specific heat of fat is 1.9 J/g °C and the density of fat is 0.94 g/cm^3. How much energy (in joules) is needed to heat 10 cm^3 of fat from room temperature (25 °C) to its melting point (35 °C)?

1.84 A 150 g sample of mercury and a 150 g sample of iron are at an initial temperature of 25.0 °C. If 1050 J of heat is applied to each sample, what is the final temperature of each? (See Table 1.10.)

1.85 When 418 J of heat is applied to a 125 g sample, the temperature increases by 28 °C. Calculate the specific heat of the sample and compare your answer to the values in Table 1.10. What is the identity of the sample?

DENSITY AND SPECIFIC GRAVITY (SECTION 1.12)

1.86 Aspirin has a density of 1.40 g/cm^3. What is the volume in cubic centimeters of a tablet weighing 250 mg?

1.87 Gaseous hydrogen has a density of 0.0899 g/L at 0 °C. How many liters would you need if you wanted 1.0078 g of hydrogen?

1.88 What is the density of lead (in g/cm^3) if a rectangular bar measuring 0.500 cm in height, 1.55 cm in width, and 25.00 cm in length has a mass of 220.9 g?

1.89 What is the density of lithium metal (in g/cm^3) if a cube measuring 0.82 cm × 1.45 cm × 1.25 cm has a mass of 0.794 g?

1.90 Ethanol produced by fermentation has a specific gravity of 0.787 at 25 °C. What is the volume of 125 g of ethanol at this temperature? (The density of water at 25 °C is 0.997 g/mL.)

1.91 Ethane-1,2-diol, commonly used as automobile antifreeze, has a specific gravity of 1.1088 at room temperature (25 °C). What is the mass of 1.00 L of ethane-1,2-diol at this temperature?

CONCEPTUAL PROBLEMS

1.92 Another temperature scale is the Rankine scale. It represents an absolute temperature scale similar to the Kelvin scale, with a common absolute zero (i.e., 0.0 K = 0.0 °R). However, whereas a change of 1.0 K is the same as a change of 1.0 °C, a change of 1.0 °R is the same as 1.0 °F. Absolute zero on the Rankine scale equals −459.67 °F. Water freezes at 32 °F (or 0.0 °C) and boils at 212 °F (100.0 °C). Convert these temperatures to their equivalent temperatures on the Rankine scale.

1.93 A white solid with a melting point of 730 °C is melted. When electricity is passed through the resultant liquid, a brown gas and a molten metal are produced. Neither the metal nor the gas can be broken down into anything simpler by chemical means. Classify each—the white solid, the molten metal, and the brown gas—as a mixture, a compound, or an element.

1.94 Refer to the pencil in Problem 1.31. Using the equivalent values in Table 1.8 as conversion factors, convert the length measured in inches to centimeters. Compare the calculated length in centimeters to the length in centimeters measured using the metric ruler. How do the two values compare? Explain any differences.

1.95 Gemstones are weighed in carats, where 1 carat = 200 mg exactly. What is the mass in grams of the Hope diamond, the world's largest blue diamond, at 44.4 carats?

1.96 The relationship between the nutritional unit for energy and the metric unit is 1 Calorie = 1 kcal.

(a) One donut contains 350 Calories. Convert this to calories and joules.

(b) If the energy in one donut was used to heat 35.5 kg of water, calculate the increase in temperature of the water (in °C).

1.97 Drug dosages are typically prescribed in units of milligrams per kilogram of body weight. A new drug has a recommended dosage of 9 mg/kg.

(a) How many milligrams would a 55 kg woman have to take to obtain this dosage?

(b) How many 125 mg tablets should a 18 kg child take to receive the recommended dosage?

1.98 A clinical report gave the following data from a blood analysis: iron, 39 mg/dL; calcium, 8.3 mg/dL; cholesterol, 224 mg/dL. Express each of these quantities in grams per deciliter, writing the answers in scientific notation.

1.99 A weather balloon has a volume of 2.027 × 10^5 ft^3.

(a) Convert this volume to L.

(b) When in operation it is filled with helium gas. If the density of helium at room temperature is 0.179 g/L, calculate the mass of helium in the blimp.

(c) What is the mass of air occupying the same volume? The density of air at room temperature is 1.20 g/L.

1.100 Approximately 75 mL of blood is pumped by a normal human heart at each beat. Assuming an average pulse of 72 beats per minute, how many milliliters of blood are pumped in one day?

1.101 A doctor has ordered that a patient be given 15 g of glucose, which is available in a concentration of 50.00 g glucose/1000.0 mL of solution. What volume of solution should be given to the patient?

1.102 Reconsider the volume of the sample dispensed by pipette in Problem 1.32. Assuming that the solution in the pipette has a density of 0.963 g/mL, calculate the mass of solution dispensed in the problem to the correct number of significant figures.

1.103 Today, thermometers containing mercury are used less frequently than in the past because of concerns regarding the toxicity of mercury and because of its relatively high melting point (−39 °C). This means that mercury thermometers cannot be used in very cold environments because the mercury is a solid under such conditions. Alcohol

thermometers, however, can be used over a temperature range from −115 °C (the melting point of alcohol) to 78.5 °C (the boiling point of alcohol).

(a) What is the effective temperature range of the alcohol thermometer in Kelvin?

(b) The densities of alcohol and mercury are 0.79 g/mL and 13.6 g/mL, respectively. If the volume of liquid in a typical laboratory thermometer is 1.0 mL, what mass of alcohol is contained in the thermometer? What mass of mercury?

1.104 In a typical person, the level of blood glucose (also known as blood sugar) is about 85 mg/100 mL of blood. If an average body contains about 11 U.S. pints of blood, how many grams and how many pounds of glucose are present in the blood?

1.105 A patient is receiving 3000 mL/day of a solution that contains 5 g of dextrose (glucose) per 100 mL of solution. If glucose provides 16 kJ/g of energy, how many kilojoules per day is the patient receiving from the glucose?

1.106 A rough guide to fluid requirements based on body weight is 100 mL/kg for the first 10 kg of body weight, 50 mL/kg for the next 10 kg, and 20 mL/kg for weight over 20 kg. What volume of fluid per day is needed by a 55 kg woman? Give the answer with two significant figures.

1.107 Chloral hydrate, a sedative and sleep-inducing drug, is available as a solution labeled 10.0 gr/fluidram. What volume in milliliters should be administered to a patient who is meant to receive 7.5 gr per dose? (1 gr = 64.8 mg; 1 fluidram = 3.72 mL)

1.108 When 1.0 tablespoon of butter is burned or used by our body, it releases 418. 4 kJ of energy. If we could use all the energy provided, how many tablespoons of butter would have to be burned to raise the temperature of 3.00 L of water from 18.0 °C to 90.0 °C?

1.109 An archeologist finds a 1.62 kg goblet that she believes to be made of pure gold. When 5650 J of heat is added to the goblet, its temperature increases by 7.8 °C. Calculate the specific heat of the goblet. Is it made of gold? Explain.

1.110 In another test, the archeologist in Problem 1.109 determines that the volume of the goblet is 205 mL. Calculate the density of the goblet and compare it with the density of gold (19.3 g/mL), lead (11.4 g/mL), and iron (7.86 g/mL). What is the goblet probably made of?

1.111 Imagine that you place a piece of cork measuring 1.30 cm × 5.50 cm × 3.00 cm in a pan of water and that on top of the cork you place a small cube of lead measuring 1.15 cm on each edge. The density of cork is 0.235 g/cm^3 and the density of lead is 11.35 g/cm^3. Will the combination of cork plus lead float or sink?

1.112 At a certain point, the Celsius and Fahrenheit scales "cross" and the numerical value of the Celsius temperature is the same as the numerical value of the Fahrenheit temperature. At what temperature does this crossover occur?

GROUP PROBLEMS

1.113 In the chapter, the conversion of currency was used as an example for unit conversion. Find out what the current monetary conversion rates are and convert US$500 into (a) euros, (b) British pounds, (c) rupees, and (d) Canadian dollars.

1.114 Look up the chemical formula for chloral hydrate mentioned in Problem 1.107. How many different elements are included in the compound, and how many atoms of each element?

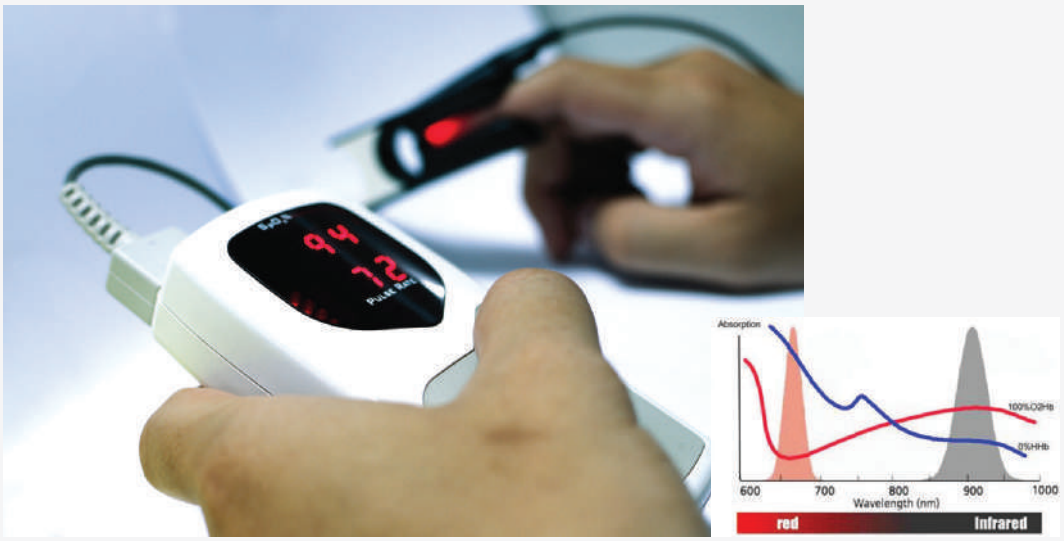
1.115 The specific gravity of ethanol is 0.787, while the specific gravity of water is 1.0. Alcoholic beverages are a mixture of water and alcohol and have a specific gravity somewhere between 0.787 and 1.0 density of ethanol, Look up the average alcohol content, typically reported as % by volume, and the specific gravity of each of the following: 80 proof whiskey; red table wine; domestic beer.

1.116 Sulfuric acid (H_2SO_4, density 1.83 g/mL) is produced in larger amounts than any other chemical: Global production exceeded 230 million metric tonnes in 2012 and is projected to exceed 267 million tonnes by 2016. What volume (in liters) of sulphuric acid was produced in 2012? What are the most common applications of sulfuric acid?

2

Atoms and the Periodic Table

CONTENTS



▲ The portable blood oximeter uses infrared light to measure the amount of oxygen dissolved in blood that is bound to hemoglobin, Hb (red line = oxygenated Hb; blue line = unoxygenated Hb), as indicated in the inserted graph. Results are reported as percent of saturation. This and related instruments, called spectrometers, take advantage of the ability of elements and compounds to interact with light of different wavelengths.

A patient visits his or her local clinic complaining of headaches and lethargy. A blood sample is taken and analyzed to determine the relative amounts of certain elements, including many metals identified as micronutrients or trace nutrients. Not enough iron, for example, could indicate anemia, while elevated levels of heavy metals, such as lead or cadmium, could be indicators of toxicity effects, such as headache or a feeling of fatigue. Knowing atomic structure and how elemental properties are related to the arrangement of electrons in a given atom allow us to identify and detect substances in the blood, including oxygen and essential nutrients, even at very low levels. Spectrometers, such as the portable blood oximeter featured above, measure the interaction of atoms or molecules with energy (such as a flame or light source) to determine the identity and concentrations of these substances, which should be in a certain range to ensure good health. As we will see in more detail in the Chemistry in Action feature on page 100, atoms will absorb or emit light of a specific wavelength based on the electron configuration and excitation in the atom. The color of the light can be used to determine the identity of certain elements, which can be used to determine the cause of the patient's symptoms.

Chemistry is studied on two levels. In the previous chapter, we learned about chemistry on the large-scale, or *macroscopic,* level, looking at the properties and transformations of matter that we can see and measure. We also introduced the elements that make up all matter and how we can use symbols to represent the many different elements and compounds of which matter is made. But what makes one element different from another? To answer that question, we need to look at the submicroscopic or atomic level, studying the behavior and properties of individual *atoms.* Although scientists have long been convinced of their existence, only within the past 20 years have powerful new instruments made it possible to see individual atoms. In this chapter, we will learn about modern atomic theory and how the structure of atoms influences macroscopic properties.

2.1 Atomic Theory and the Structure of Atoms

Learning Objective:

- Explain the major assumptions of atomic theory, and name and identify the properties of the subatomic particles that make up an atom.

Take a piece of aluminum foil, and cut it in two. Then, take one of the pieces and cut *it* in two, and so on. Assuming that you have extremely small scissors and extraordinary dexterity, how long can you keep dividing the foil? Is there a limit, or is matter infinitely divisible into ever smaller and smaller pieces? Historically, this argument dates as far back as the ancient Greek philosophers. Aristotle believed that matter could be divided infinitely, while Democritus argued (correctly) that there is a limit. The smallest and simplest bit that aluminum (or any other element) can be divided and still be identifiable as aluminum is called an **atom,** a word derived from the Greek *atomos,* meaning "indivisible."

Atom The smallest and simplest particle of an element.

Chemistry is built on four fundamental assumptions about atoms and matter, proposed by English scientist John Dalton in 1808, which together make up modern **atomic theory:**

Atomic theory A set of assumptions proposed by the English scientist John Dalton to explain the chemical behavior of matter.

- All matter is composed of atoms.
- Atoms of any given element share the same chemical properties while atoms of different elements have different properties.
- Chemical compounds consist of atoms combined in specific ratios. That is, only whole atoms can combine—one A atom with one B atom, or one A atom with two B atoms, and so on. The vast number of ways that atoms can combine with one another results in the enormous diversity in the substances around us.
- Chemical reactions change only the way that atoms are combined in compounds. The atoms themselves are unchanged and do not disappear.

LOOKING AHEAD We will further explore the topics of chemical compounds in Chapters 3 and 4 and chemical reactions in Chapters 5 and 6.

Atoms are extremely small, ranging from about 7.4×10^{-11} m in diameter for a hydrogen atom to 5.24×10^{-10} m for a cesium atom. In mass, atoms vary from 1.67×10^{-24} g for hydrogen to 3.95×10^{-22} g for uranium, one of the heaviest naturally occurring atoms. It is difficult to appreciate just how small atoms are, although it might help if you realize that a fine pencil line is about 3 million atoms across and that even the smallest speck of dust contains about 10^{16} atoms. Our current understanding of atomic structure is the result of many experiments performed in the late 1800s and early 1900s (see Chemistry in Action on p. 78).

Atoms are composed of tiny **subatomic particles** called *protons, neutrons,* and *electrons*. A **proton** has a mass of $1.672\,622 \times 10^{-24}$ g and carries a positive $(+)$ electrical charge, a **neutron** has a mass similar to that of a proton $(1.674\,927 \times 10^{-24}\ \text{g})$ but is electrically neutral, and an **electron** has a mass that is only $1/1836$ that of a proton $(9.109\,328 \times 10^{-28}\ \text{g})$ and carries a negative $(-)$ electrical charge. In fact, electrons are so much lighter than protons and neutrons that their mass is usually ignored. Table 2.1 compares the properties of the three fundamental subatomic particles.

Subatomic particles Three kinds of fundamental particles from which atoms are made—protons, neutrons, and electrons.

Proton A positively charged subatomic particle.

Neutron An electrically neutral subatomic particle.

Electron A negatively charged subatomic particle.

Table 2.1 A Comparison of Subatomic Particles

		Mass		
Name	Symbol	(Grams)	(amu)	Charge (Charge Units)
Proton	p	$1.672\,622 \times 10^{-24}$	1.007 276	+1
Neutron	n	$1.674\,927 \times 10^{-24}$	1.008 665	0
Electron	e^-	$9.109\,328 \times 10^{-28}$	$5.485\,799 \times 10^{-4}$	−1

The masses of atoms and their constituent subatomic particles are so small when measured in grams that it is more convenient to express them on a *relative* mass scale. The basis for the relative atomic mass scale is an atom of carbon that contains six protons and six neutrons. Such an atom is assigned a mass of exactly 12 **atomic mass units (amu;** also called a *dalton* in honor of John Dalton), where 1 amu $= 1.660\,539 \times 10^{-24}$ g.

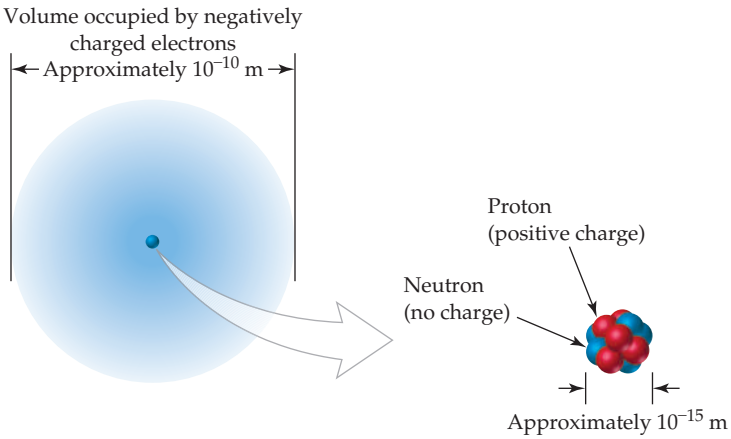
Atomic mass unit (amu) The unit for describing the mass of an atom; 1 amu $= \frac{1}{12}$ the mass of a carbon-12 atom.

▲ The relative size of a nucleus in an atom is the same as that of a pea in the middle of this stadium.

Nucleus The dense, central core of an atom that contains protons and neutrons.

Thus, for all practical purposes, both a proton and a neutron have a mass of 1 amu (Table 2.1). Hydrogen atoms are only about one-twelfth as heavy as carbon atoms and have a mass close to 1 amu, magnesium atoms are about twice as heavy as carbon atoms and have a mass close to 24 amu, and so forth.

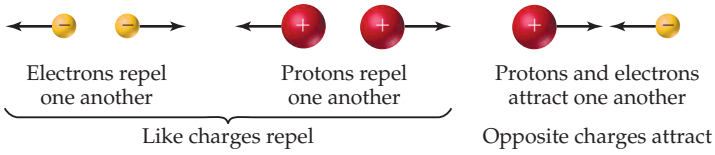
Subatomic particles are not distributed at random throughout an atom. Rather, the protons and neutrons are packed closely together in a dense core called the **nucleus.** Surrounding the nucleus, the electrons move about rapidly through a large, mostly empty volume of space (Figure 2.1). Measurements show that the diameter of a nucleus is only about 10^{-15} m, whereas that of the atom itself is about 10^{-10} m. For comparison, if an atom were the size of a large domed stadium, the nucleus would be approximately the size of a small pea in the center of the playing field.



▲ **Figure 2.1**
The structure of an atom.
Protons and neutrons are packed together in the nucleus, whereas electrons move about in the large surrounding volume. Virtually all the mass of an atom is concentrated in the nucleus.

The structure of the atom is determined by an interplay of different attractive and repulsive forces. Because unlike charges attract one another, the negatively charged electrons are held near the positively charged nucleus. But because like charges repel one another, the electrons also try to get as far away from one another as possible, accounting for the relatively large volume they occupy.

The positively charged protons in the nucleus also repel one another but are nevertheless held together by a unique attraction called the *nuclear strong force,* which we will discuss further in Chapter 11.

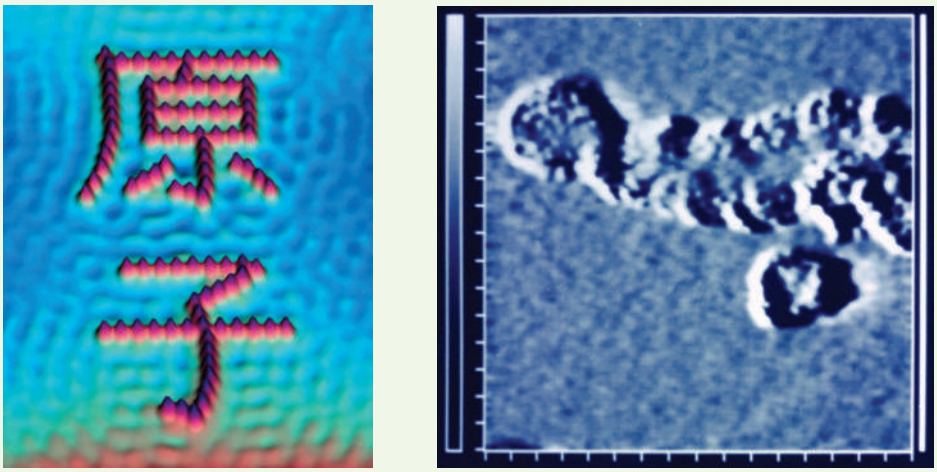


CHEMISTRY IN ACTION

Are Atoms Real?

Chemistry rests on the premise that matter is composed of the tiny particles we call atoms. Every chemical reaction and every physical law that governs the behavior of matter is explained by chemists in terms of atomic theory. But how do we know that atoms are real and not just an imaginary concept? And how do we know the structure of the atom?

The development of our understanding of atomic structure is another example of the scientific method at work, with several scientists contributing to our understanding of atomic structure. J. J. Thomson demonstrated that matter contained negatively charged particles that were 1000 times lighter than H^+, the lightest positively charged particles found in aqueous solution, and that the mass-to-charge ratio of these particles was the same regardless of the material used to produce the particles (Section 5.5 and Chapter 10). Ernest Rutherford deduced that an atom consists mostly of empty space (occupied by the negatively charged electrons) and that most of the mass and all of the positive charges are contained in a relatively small, dense region that he called the "nucleus."



(a) (b)

▲ (a) STM image of the Kanji characters for "atom" formed by iron atoms (radius = 126 pm) deposited on a copper metal surface. (b) STM image of DNA strand deposited on a graphite surface.

We can now actually "see" and manipulate individual atoms through the use of a device called a *scanning tunneling microscope,* or STM. With the STM, invented in 1981 by a research team at the IBM Corporation, magnifications of up to 10 million have been achieved, allowing chemists to look directly at atoms. The accompanying photograph shows a computer-enhanced representation of iron atoms that have been deposited on a copper surface.

Most early uses of the STM involved studies of surface chemistry, such as the events accompanying the corrosion of metals and the ordering of large molecules in polymers. More recently, however, the STM has been used to determine the structures of complex biological molecules, such as immunoglobulin G, streptavidin, proteins and enzymes, and DNA, providing vital information about the structures and functions of these biomolecules. Modifications to the STM instrumentation have allowed imaging of these materials *in situ* (i.e., in their natural state) and also allowed scientists to manipulate individual molecules.

CIA Problem 2.1 What is the advantage of using an STM rather than a normal light microscope?

CIA Problem 2.2 For the Kanji character in the lower portion of figure (a):

(1) How wide is the character in terms of iron atoms?

(2) Given the radius of an iron atom is 126 pm, calculate the width of this character in centimeters.

2.2 Elements and Atomic Number

Learning Objective:

- Identify atoms of an element based on the number of protons in the nucleus.

All atoms contain proton, neutrons, and electrons, but how do we distinguish an atom of carbon from an atom of oxygen, or sodium? Each atom has a specific number of protons, neutrons, and electrons, and the identity of the element is determined by the number of protons within the nucleus, also called the element's **atomic number *(Z)*.** Every element has a different number of protons within its nucleus, thus every element has a different atomic number. If we know the number of protons in an atom, we can identify the element. Any atom with six protons, for example, is a carbon atom because the atomic number for carbon is 6 $(Z = 6)$.

Atomic number *(Z)* The number of protons in the nucleus of an atom of a given element.

Atoms are neutral and have no net charge because the number of positively charged protons in an atom is the same as the number of negatively charged electrons. Thus, the atomic number also equals the number of electrons in every atom of a given element. Hydrogen, $Z = 1$, has only 1 proton and 1 electron; carbon, $Z = 6$, has 6 protons and 6 electrons; sodium, $Z = 11$, has 11 protons and 11 electrons; and so on, up

LOOKING AHEAD In a neutral atom, the number of electrons is equal to the number of protons. However, most elements can gain or lose electrons to form charged particles, called *ions,* which will be discussed in Chapter 3.

to the element with the largest known atomic number ($Z = 118$). In a periodic table, elements are listed in order of increasing atomic number, beginning at the upper left and ending at the lower right.

Mass number *(A)* The total number of protons and neutrons in an atom.

The sum of the protons and neutrons in an atom is called the atom's **mass number *(A).*** For example, hydrogen atoms with 1 proton and no neutrons have mass number 1, carbon atoms with 6 protons and 6 neutrons have mass number 12, sodium atoms with 11 protons and 12 neutrons have mass number 23. Atomic number and mass number can be written using chemical symbols by showing the element's mass number *(A)* as a superscript and its atomic number *(Z)* as a subscript in front of the atomic symbol. For example, ${}^{A}_{Z}X$, where *X* represents the symbol for the element, *A* represents the mass number, and *Z* represents the atomic number.

Worked Example 2.1 Atomic Structure: Protons, Neutrons, and Electrons

Phosphorus has the atomic number $Z = 15$. How many protons, electrons, and neutrons are there in phosphorus atoms, which have mass number $A = 31$?

ANALYSIS The atomic number gives the number of protons, which is the same as the number of electrons, and the mass number gives the total number of protons plus neutrons.

SOLUTION

Phosphorus atoms, with $Z = 15$, have 15 protons and 15 electrons. To find the number of neutrons, subtract the atomic number from the mass number.

Mass number (sum of protons and neutrons) — Atomic number (number of protons)

$$31 - 15 = 16 \text{ neutrons}$$

Worked Example 2.2 Atomic Structure: Atomic Number and Atomic Mass

An atom contains 28 protons and has $A = 60$. Give the number of electrons and neutrons in the atom, and identify the element.

ANALYSIS The number of protons and the number of electrons are the same and are equal to the atomic number *Z,* 28 in this case. Subtracting the number of protons (28) from the total number of protons plus neutrons (60) gives the number of neutrons.

SOLUTION

The atom has 28 electrons and $60 - 28 = 32$ neutrons. The list of elements inside the front cover shows that the element with atomic number 28 is nickel (Ni).

PROBLEM 2.1

Use the list inside the front cover to identify the following elements:

(a) $A = 186$, with 111 neutrons
(b) $A = 59$, with 21 neutrons
(c) $A = 127$, with 75 neutrons

2.3 Isotopes and Atomic Mass

Learning Objective:

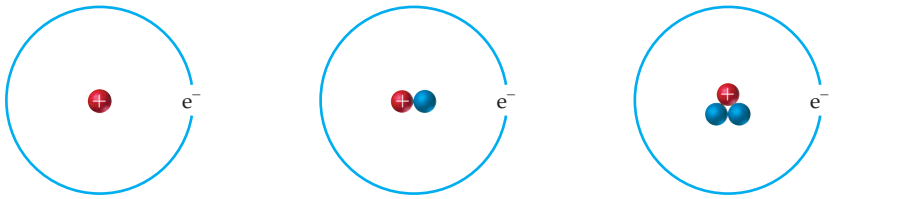
- Write the symbols for different isotopes of an element, and use relative abundances and atomic masses of isotopes to calculate the average atomic mass of an element.

Isotopes Atoms with identical atomic numbers but different mass numbers.

All atoms of a given element have the same number of protons, equal to the atomic number *(Z)* of that element; however, different atoms of an element can have different numbers of neutrons and, therefore, different mass numbers. Atoms with identical atomic numbers but different mass numbers are called **isotopes.** Hydrogen, for example, has three isotopes. The most abundant hydrogen isotope, called *protium,* has

one proton but no neutrons and thus has a mass number of 1. A second hydrogen isotope, called *deuterium,* also has one proton, but has one neutron and a mass number of 2; and a third isotope, called *tritium,* has two neutrons and a mass number of 3.

We will see that isotopes of the same element have the same *chemical* behavior (Chapter 5) but very different *nuclear behavior* (Chapter 11). Tritium, for example, is unstable and does not occur naturally in significant amounts, although it can be made in nuclear reactors.

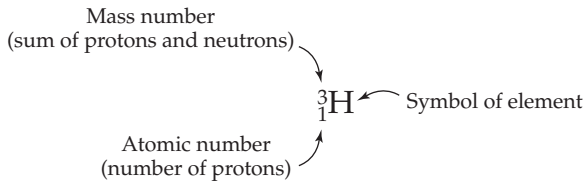


Protium—one proton (●) and no neutrons; mass number = 1

Deuterium—one proton (●) and one neutron (●); mass number = 2

Tritium—one proton (●) and two neutrons (●); mass number = 3

A specific isotope is represented by showing its mass number *(A)* as a superscript and its atomic number *(Z)* as a subscript in front of the atomic symbol, for example, ${}^{A}_{Z}X$. Thus, protium is ${}^{1}_{1}\mathrm{H}$, deuterium is ${}^{2}_{1}\mathrm{H}$, and tritium is ${}^{3}_{1}\mathrm{H}$.



Unlike the three isotopes of hydrogen, the isotopes of most elements do not have distinctive names. Instead, the mass number of the isotope is given after the name of the element. The ${}^{235}_{92}\mathrm{U}$ isotope used in nuclear reactors, for example, is usually referred to as uranium-235, or U-235.

We will discuss nuclear reactors in Section 11.9.

Most naturally occurring elements are mixtures of isotopes. In a large sample of naturally occurring hydrogen atoms, for example, 99.985% have mass number $A = 1$ (protium) and 0.015% have mass number $A = 2$ (deuterium). Therefore, it is useful to know the *average* mass of the atoms in a large sample, a value called the element's **atomic mass.** For hydrogen, the atomic mass is 1.008 amu. Atomic masses for all elements are given on the inside of the front cover of this book.

Atomic mass The weighted average mass of an element's atoms.

To calculate the atomic mass of an element, the individual masses of the naturally occurring isotopes and the percent abundance of each must be known. The atomic mass can then be calculated as the sum of the masses of the individual isotopes for that element, or

$$\text{Atomic mass} = \sum[(\text{isotopic abundance}) \times (\text{isotopic mass})]$$

where the Greek symbol $\sum$ indicates the mathematical summing of terms.

Chlorine, for example, occurs on earth as a mixture of 75.77% Cl-35 atoms (mass = 34.97 amu) and 24.23% Cl-37 atoms (mass = 36.97 amu). This can also be expressed in terms of fractional composition (i.e., 75.77% of all chlorine atoms is the same as a fraction of 0.7577). The atomic mass is found by calculating the percentage of the mass contributed by each isotope. For chlorine, the calculation is done in the following way (to four significant figures), giving an atomic mass of 35.45 amu:

$$\begin{aligned}
\text{Contribution from } {}^{35}\text{Cl: } (0.7577)(34.97\ \text{amu}) &= 26.4968\ \text{amu} \\
\text{Contribution from } {}^{37}\text{Cl: } (0.2423)(36.97\ \text{amu}) &= \underline{8.9578\ \text{amu}} \\
\text{Atomic mass} = 35.4546 &= 35.45\ \ \text{amu} \\
&\text{(Rounded to four significant figures)}
\end{aligned}$$

The final number of significant figures in this case (four) was determined by the rounding rules presented in Chapter 1. Note that the final rounding to four significant figures was not done until *after* the final answer was obtained.

Worked Example 2.3 Average Atomic Mass: Weighted-Average Calculation

Gallium is a metal with a very low melting point—it will melt in the palm of your hand. It has two naturally occurring isotopes: 60.4% is Ga-69 (mass = 68.9257 amu) and 39.6% is Ga-71 (mass = 70.9248 amu). Calculate the atomic mass for gallium.

ANALYSIS We can calculate the average atomic mass for the element by summing up the contributions from each of the naturally occurring isotopes.

BALLPARK ESTIMATE The masses of the two naturally occurring isotopes of gallium differ by 2 amu (68.9 and 70.9 amu). Since slightly more than half of the Ga atoms are the lighter isotope (Ga-69), the average mass will be slightly less than halfway between the two isotopic masses; estimate = 69.8 amu.

SOLUTION

STEP 1: Identify known information.	Ga-69 (60.4% at 68.9257 amu) Ga-71 (39.6% at 70.9248 amu)
STEP 2: Identify the unknown answer and units.	Atomic mass for Ga (in amu) = ?
STEP 3: Identify conversion factors or equations. This equation calculates the average atomic mass as a weighted average of all naturally occurring isotopes.	Atomic mass = $\sum$[(isotopic abundance) × (isotopic mass)]
STEP 4: Solve. Substitute known information and solve.	Atomic mass = (0.604) × (68.9257 amu) = 41.6311 amu + (0.396) × (70.9248 amu) = 28.0862 amu Atomic mass = 69.7 amu (3 significant figures)

BALLPARK CHECK Our estimate (69.8 amu) is close!

Worked Example 2.4 Identifying Isotopes from Atomic Mass and Atomic Number

Identify element X in the symbol $^{194}_{78}X$ and give its atomic number, mass number, number of protons, number of electrons, and number of neutrons.

ANALYSIS The identity of the atom corresponds to the atomic number—78.

SOLUTION

Element X has Z = 78, which shows that it is platinum. (Look inside the front cover for the list of elements.) The isotope $^{194}_{78}Pt$ has a mass number of 194, and we can subtract the atomic number from the mass number to get the number of neutrons. This platinum isotope therefore has 78 protons, 78 electrons, and 194 − 78 = 116 neutrons.

PROBLEM 2.2

Potassium (K) has two naturally occurring isotopes: K-39 (93.12% mass = 38.9637 amu) and K-41 (6.88%; 40.9618 amu). Calculate the atomic mass for potassium. How does your answer compare with the atomic mass given in the list inside the front cover of this book?

PROBLEM 2.3

Bromine, an element present in compounds used as sanitizers and fumigants (for example, ethylene bromide), has two naturally occurring isotopes. Look up the mass numbers of the two naturally occurring isotopes of bromine, along with their percent abundance.

(a) Write the symbols for both isotopes.

(b) Using the masses and natural percent abundances, calculate the average molecular mass for bromine and compare your value to the value found in the periodic table on page 84.

HANDS-ON CHEMISTRY 2.1

Isotopes are used in many applications, including diagnosis and treatment of cancer and other diseases. In this activity, we will explore the structure of some isotopes of a specific element. Take two pieces of construction paper of different colors and cut each into about 25 pieces. Label each piece of one color with an "n" for neutron and each piece of the other color with a "p" for proton.

a. Distribute the pieces of construction paper into three piles as follows. Into pile 1, place six "p" and six "n" pieces. Into pile 2, place six "p" and seven "n" pieces. Into pile 3, place six "p" and eight "n" pieces. How is each pile similar, and how are they different?

b. The three piles represent isotopes of a particular element. Which element? Write the atomic symbols for each isotope.

c. Look up the natural abundance of each isotope and calculate the average atomic mass for this element. How does your answer compare with the atomic mass given in the periodic table?

PROBLEM 2.4

An element used to sanitize water supplies has two naturally occurring isotopes with mass numbers of 35 and 37, and 17 electrons. Write the symbols for both isotopes, including their atomic numbers and mass numbers.

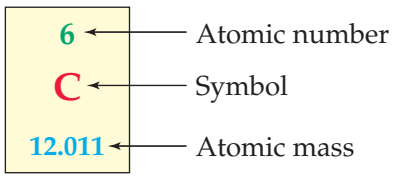
2.4 The Periodic Table

Learning Objective:

- Locate elements on the periodic table and classify them as metals, nonmetals, or metalloids based on their location.

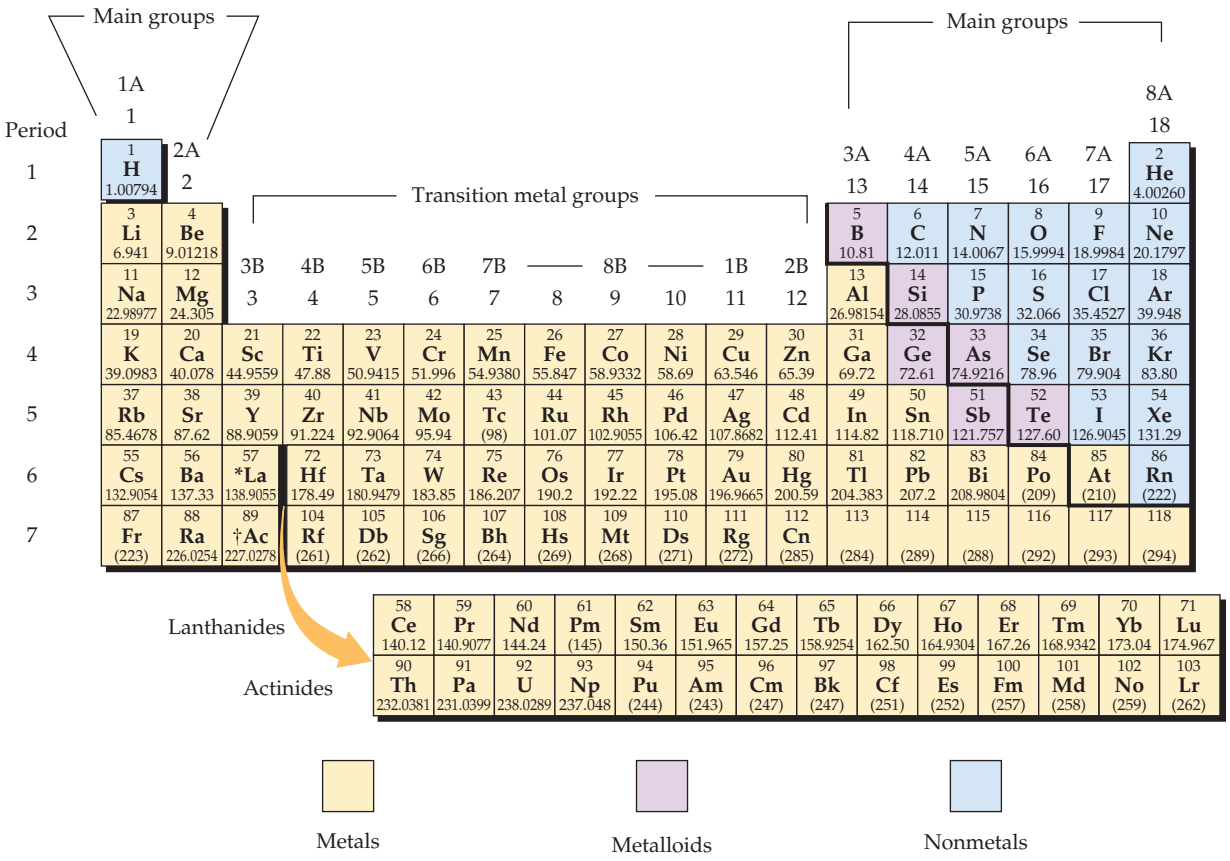
Ten elements have been known since the beginning of recorded history: antimony (Sb), carbon (C), copper (Cu), gold (Au), iron (Fe), lead (Pb), mercury (Hg), silver (Ag), sulfur (S), and tin (Sn). It is worth noting that the symbols for many of these elements are derived from their Latin names, a reminder that they have been known since the time when Latin was the language used for all scholarly work. The first "new" element to be found in several thousand years was arsenic (As), discovered in about 1250. In fact, only 24 elements were known up to the time of the American Revolution in 1776.

As the pace of discovery quickened in the late 1700s and early 1800s, chemists began to look for similarities among elements that might make it possible to draw general conclusions. Numerous attempts were made in the mid-1800s to account for the similarities among groups of elements, but the great breakthrough came in 1869 when the Russian chemist Dmitri Mendeleev organized the elements in order of increasing mass and then organized elements into groups based on similarities in chemical behavior. His table is a forerunner of the modern **periodic table.** The table has boxes for each element that give the symbol, atomic number, and atomic mass of the element:



Periodic table A tabular format listing all known elements where the atomic symbol (top), name of the element (middle), and atomic mass (bottom) are given in each box that represents the element.

The atomic masses for each element in the table are the average masses calculated based on the mass and percent abundance of the naturally occurring stable isotopes. The boxes are arranged in order of increasing atomic number, with the elements arranged in rows and columns as shown in Figure 2.2. An enormous amount of information is embedded in the periodic table, information that gives chemists the ability to explain known chemical behavior of elements and to predict new behavior.



▲ **Figure 2.2**

The periodic table of the elements.

Elements are organized into groups, indicated with numbers and letters. Main group elements are in columns labeled 1A–8A, while the transition metal groups are in columns labeled 1B–8B. Elements to the left and bottom of the periodic table are classified as metals, while elements in the upper right portion are classified as nonmetals.

Metal A malleable element, with a lustrous appearance, that is a good conductor of heat and electricity.

Nonmetal An element that is a poor conductor of heat and electricity.

Metalloid An element whose properties are intermediate between those of a metal and a nonmetal.

One way of classifying the elements is by similarities in physical properties. Of the 118 currently known elements, 94 are classified as metals—aluminum, gold, copper, and zinc, for example. **Metals** are solid at room temperature (except for mercury), usually have a lustrous appearance when freshly cut, are good conductors of heat and electricity, and are malleable rather than brittle. That is, metals can be pounded into different shapes rather than shattering when struck. Note that metals occur on the left side of the periodic table.

Eighteen elements are **nonmetals.** All are poor conductors of heat and electricity. Eleven are gases at room temperature, six are brittle solids, and one is a liquid. Oxygen and nitrogen, for example, are gases present in air; sulfur is a solid found in large underground deposits. Bromine is the only liquid nonmetal. Note that nonmetals occur on the upper right side of the periodic table.

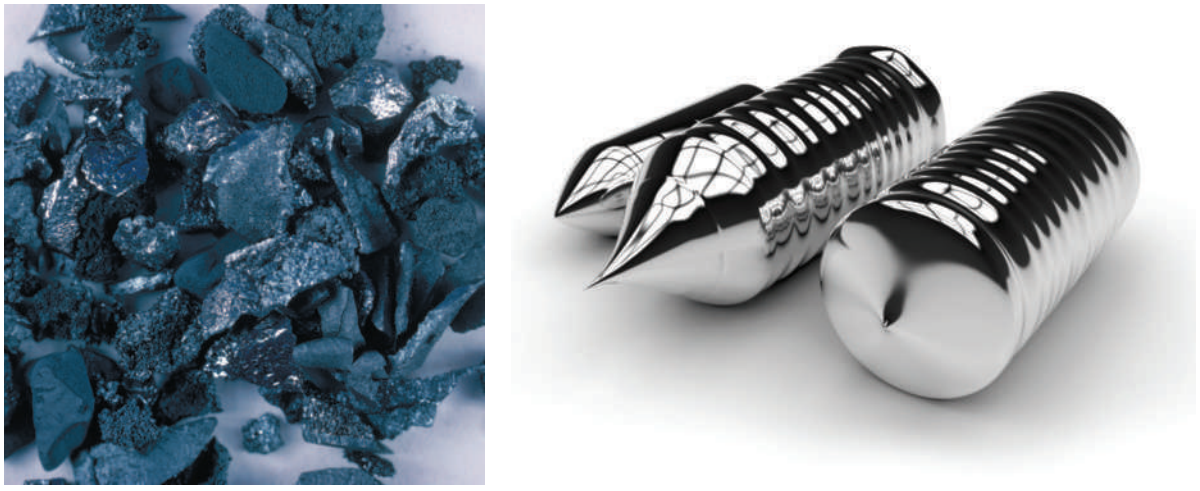
The **metalloids** are located in a zigzag band between the metals on the left and nonmetals on the right side of the periodic table. Although there is some debate as to which elements to include in this list, we include only six in this text: boron, silicon, arsenic, germanium, antimony, and tellurium. The metalloids are so named because their properties are intermediate between those of metals and nonmetals. Pure silicon, for example, has a lustrous or shiny surface, like a metal, but it is brittle, like a nonmetal, and its electrical conductivity lies between that of metals and nonmetals. Some chemistry texts identify polonium as a metalloid, but its chemical behavior and conductivity more closely resemble that of other metals. Others include astatine in the list, but this is purely academic: as a very rare and unstable element, it would be difficult to collect a sample of astatine large enough to obtain reliable data regarding its chemical and physical behavior.

(a) (b) (c)

▲ **Metals: Gold, zinc, and copper.**
(a) Known for its beauty, gold is very unreactive and is used primarily in jewelry and in electronic components. (b) Zinc, an essential trace element in our diets, has industrial uses ranging from the manufacture of brass, to roofing materials, to batteries. (c) Copper is widely used in electrical wiring, in water pipes, and in coins.

(a) (b) (c)

▲ **Nonmetals: Nitrogen, sulfur, and iodine.**
(a) Nitrogen, (b) sulfur, and (c) iodine are essential to all living things. Pure nitrogen, which constitutes almost 80% of air, is a gas at room temperature and does not condense to a liquid until it is cooled to −328 °C. Sulfur, a yellow solid, is found in large underground deposits in Texas and Louisiana. Iodine is a dark violet crystalline solid that was first isolated from seaweed.



(a) (b)

▲ **Metalloids: Boron and silicon.**
(a) Boron is a strong, hard metalloid used in making the composite materials found in military aircraft. (b) Silicon is well known for its use in making computer chips.

Period One of the seven horizontal rows of elements in the periodic table.

Group One of the 18 vertical columns of elements in the periodic table.

Another way of classifying the elements in the periodic table is based on similarities in chemical behavior. Beginning at the upper left corner of the periodic table, elements are arranged by increasing atomic number into seven horizontal rows, called **periods,** and 18 vertical columns, called **groups.** When organized in this way, *the elements in a given group have similar chemical properties.* Lithium, sodium, potassium, and the other elements in group 1A behave similarly. Chlorine, bromine, iodine, and the other elements in group 7A behave similarly and so on throughout the table.

Note that different periods (rows) contain different numbers of elements. The first period contains only two elements, hydrogen and helium; the second and third periods each contain eight elements; the fourth and fifth periods each contain 18; the sixth and seventh periods contain 32. Note also that the 14 elements following lanthanum (the *lanthanides*) and the 14 following actinium (the *actinides*) are pulled out and shown below the others.

Main group element An element in one of the two groups on the left or the six groups on the right of the periodic table.

Transition metal element An element in one of the 10 smaller groups near the middle of the periodic table.

Inner transition metal element An element in one of the 14 groups shown separately at the bottom of the periodic table.

Groups are numbered in two ways, both shown in Figure 2.2. The two large groups on the far left and the six on the far right are called the **main group elements** and are numbered 1A through 8A. The 10 smaller groups in the middle of the table are called the **transition metal elements** and are numbered 1B through 8B. Alternatively, all 18 groups are numbered sequentially from 1 to 18. The 14 groups shown separately at the bottom of the table are called the **inner transition metal elements** and are not numbered.

PROBLEM 2.5

Locate aluminum in the periodic table and give its group number and period number.

PROBLEM 2.6

Identify the group 1B element in period five and the group 2A element in period four.

PROBLEM 2.7

There are five elements in group 5A of the periodic table. Identify them and give the period of each.

PROBLEM 2.8

The six metalloids are boron (B), silicon (Si), germanium (Ge), arsenic (As), antimony (Sb), and tellurium (Te). Locate them in the periodic table and tell where they appear with respect to metals and nonmetals.

PROBLEM 2.9

Locate the following elements in the periodic table, give the corresponding name for each, and classify them according to group (i.e., halogen, noble gas, alkali metal, etc.).

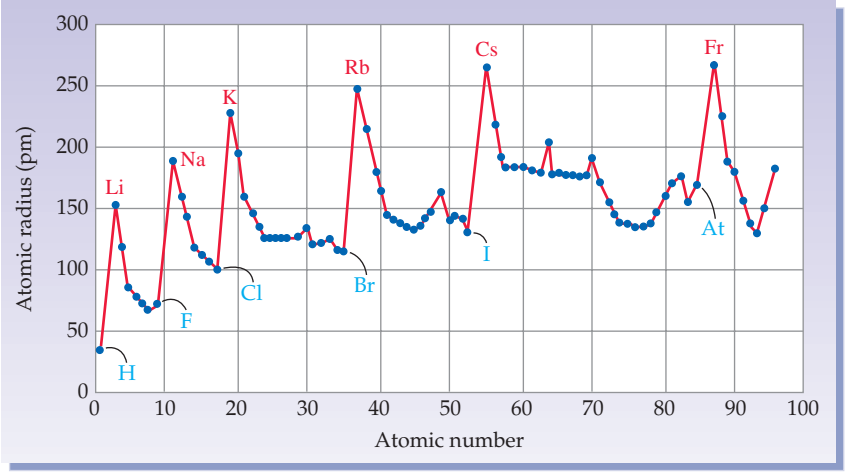
(a) Ti **(b)** Te **(c)** Se **(d)** Sc **(e)** At **(f)** Ar

2.5 Some Characteristics of Different Groups

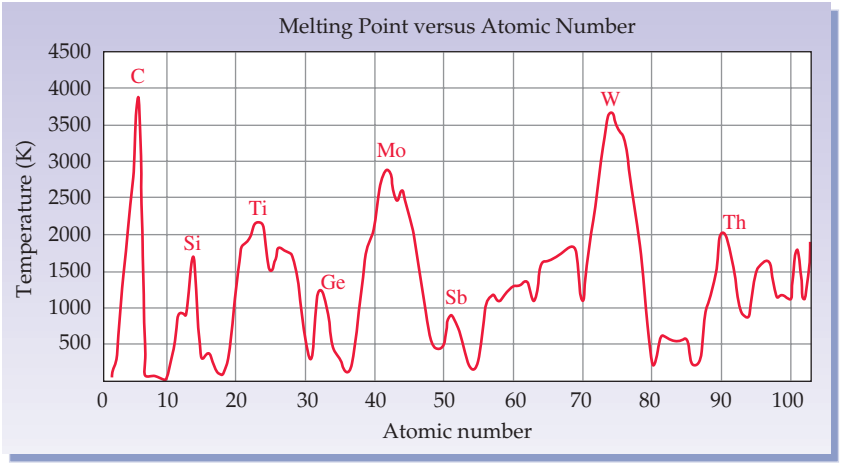
Learning Objective:

- Classify elements and describe chemical behavior based on group membership.

To see why the periodic table has the name it does, look at the graph of atomic radius versus atomic number in Figure 2.3. The graph shows an obvious *periodicity*—a repeating rise-and-fall pattern. Beginning on the left with atomic number 1 (hydrogen), the sizes of the atoms increase to a maximum at atomic number 3 (lithium), then decrease to a minimum, then increase again to a maximum at atomic number 11 (sodium), then decrease, and



◄ Figure 2.3
A graph of atomic radius in picometers (pm) versus atomic number shows a periodic rise and fall pattern.
The maxima occur for atoms of the group 1A elements (Li, Na, K, Rb, Cs, and Fr in red); the minima occur for atoms of the group 7A elements (blue). Accurate data are not available for the group 8A elements.



◄ Figure 2.4
A graph of melting point versus atomic number shows periodic properties similar to the trend in Figure 2.3.
While the maxima and minima are not as sharp as in Figure 2.3, the change in melting points of the elements still shows a similar periodic trend.

so on. It turns out that the local maximum values occur for atoms of group 1A elements—Li, Na, K, Rb, Cs, and Fr—and the local minimum values occur for atoms of the group 7A elements.

There is nothing unique about the periodicity of atomic radii shown in Figure 2.3. The melting points of the first 100 elements, for example, exhibit similar periodic behavior, as shown in Figure 2.4, with a systematic trend of peaks and valleys as you progress through the elements in the periodic table. Many other physical and chemical properties can be plotted in a similar way with similar results. In fact, the various elements in a given group of the periodic table usually show remarkable similarities in many of their chemical and physical properties. Look at the following four groups, for example:

- **Group 1A—Alkali metals:** Lithium (Li), sodium (Na), potassium (K), rubidium (Rb), cesium (Cs), and francium (Fr) are shiny, soft metals with low melting points. All react rapidly (often violently) with water to form products that are highly alkaline, or basic—hence the name **alkali metals.** Because of their high reactivity, the alkali metals are never found in nature in the pure state but only in combination with other elements.
- **Group 2A—Alkaline earth metals:** Beryllium (Be), magnesium (Mg), calcium (Ca), strontium (Sr), barium (Ba), and radium (Ra) are also lustrous, silvery metals but are less reactive than their neighbors in group 1A. Like the alkali metals, the alkaline earths are never found in nature in the pure state.

▲ Sodium, an alkali metal, reacts violently with water to yield hydrogen gas and an alkaline (basic) solution.

Alkali metal An element in group 1A of the periodic table.

Alkaline earth metal An element in group 2A of the periodic table.

Halogen An element in group 7A of the periodic table.

Noble gas An element in group 8A of the periodic table.

- **Group 7A—Halogens:** Fluorine (F), chlorine (Cl), bromine (Br), iodine (I), and astatine (At) are colorful and corrosive nonmetals. All are found in nature only in combination with other elements, such as with sodium in table salt (sodium chloride, NaCl). In fact, the group name **halogen** is taken from the Greek word *hals,* meaning salt.
- **Group 8A—Noble gases:** Helium (He), neon (Ne), argon (Ar), krypton (Kr), xenon (Xe), and radon (Rn) are colorless gases. The elements in this group were labeled the "noble" gases because of their lack of chemical reactivity—helium, neon, and argon do not combine with any other elements, whereas krypton and xenon combine with a very few.

Carbon, the element on which life is based, is a group 4A nonmetal near the top right of the periodic table. Clustered near carbon are other elements often found in living organisms, including oxygen, nitrogen, phosphorus, and sulfur. We will look at the subject of *organic chemistry*—the chemistry of carbon compounds—in Chapters 12–17 and move on to *biochemistry*—the chemistry of living things—in Chapters 18–29.

PROBLEM 2.10

Locate (a) krypton, (b) strontium, (c) nitrogen, and (d) cobalt in the periodic table. Indicate which categories apply to each: (i) metal, (ii) nonmetal, (iii) transition element, (iv) main group element, and (v) noble gas.

PROBLEM 2.11

For each of the following sets of elements, arrange in order of increasing atomic radius:

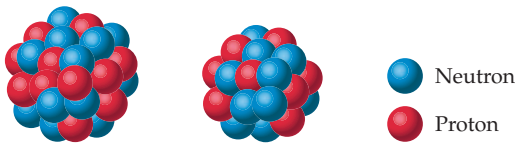
a) Na, Li, Rb, K **b)** Li, O, C, F **c)** Cl, Br, I, F

PROBLEM 2.12

For each set of elements presented in the previous problem, arrange in order of increasing melting point.

KEY CONCEPT PROBLEM 2.13

Identify the elements whose nuclei are shown next. For each, tell its group number, its period number, and whether it is a metal, nonmetal, or metalloid.



(a) (b)

CHEMISTRY IN ACTION

Essential Elements and Group Chemistry

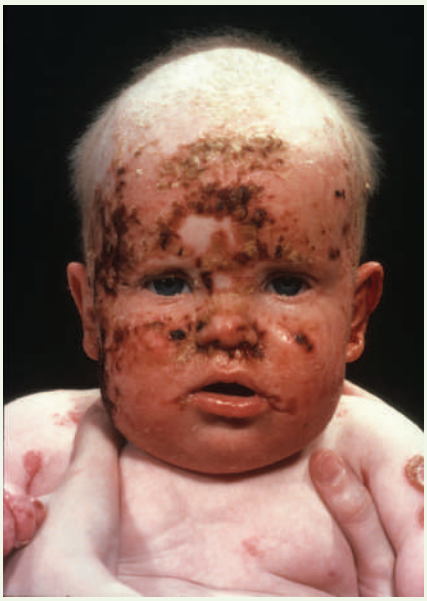
In Chapter 1, we introduced the essential elements—elements that are vital to good health and fitness. In this chapter, we demonstrated how elements in a group exhibit similar chemical properties. As you might expect, the properties of a group influence their role in the metabolism of an organism. As we noted in Chapter 1, these elements are typically not present in the body as free atoms but as ions or combined with other elements in compounds (discussed in Chapter 3). Let's take a look at some of the major players in the different groups:

1A. Alkali metals: Lithium (Li) plays no known physiological role in the body, but the apparent neurological effects of the Li ion in many lithium compounds explains why they are often used as mood stabilizing drugs. Sodium (Na) is considered a macronutrient because of the vital role it plays in regulation of blood volume and blood pressure and transmission of nerve impulses. Potassium (K), like sodium, is also involved in neurological functions and nerve impulse transmission, and a deficiency in K ions can lead to cardiac dysfunctions.

2A. Alkaline earth metals: Magnesium (Mg) ions are important in many enzymatic processes, including energy production and DNA synthesis. Magnesium compounds also are used therapeutically as laxatives and to relieve the symptoms of fibromyalgia, migraines, and premenstrual syndrome. Calcium (Ca) is a major component in teeth and bones and also plays a role in neurotransmission and muscle contraction. An excess of calcium ions is the blood can lead to impaired kidney function and decreased absorption of other important minerals.

7A. Halogens: Fluorine (F) compounds have been added into toothpaste and municipal drinking water supplies to strengthen tooth enamel and increase dental health. Fluorine-containing drugs are used to lower cholesterol, as antidepressants, antibiotics, and anesthetics. Chlorine (Cl) ions play an important role in maintaining salt balance in bodily fluids. Bromine (Br) was initially thought to have no biological function; recent research indicates that it is necessary for tissue development. Iodine (I) is an essential trace element, primarily because of its role as a constituent in thyroxine, a thyroid hormone responsible for regulation of basal metabolism.

1–8B. Transition metals: Probably the most familiar essential transition metal is iron (Fe), a major component in hemoglobin that is responsible for oxygen transport in the blood. But many other transition metals are constituents of enzymes (biological catalysts), including chromium (Cr), cobalt (Co), copper (Cu), molybdenum (Mo), manganese (Mn), and zinc (Zn). Zinc, in particular, is recognized as an essential mineral important to public health. Zinc deficiencies in children are linked to delayed growth and sexual maturation, severe dermatitis, and diarrhea.



▲ This infant is suffering from acrodermatitis enteropathica, a skin condition resulting from an inability to metabolize zinc.

CIA Problem 2.3 Elements from other groups also play important biological roles. Identify each of the following:

a) A group 5A element that is a major component of cell membranes and bones.
b) A group 6A element that is involved in thyroid function and a constituent of enzymes involved in fat metabolism but is toxic in large doses.

CIA Problem 2.4 Locate and identify the group number for each of the transition metals mentioned earlier.

2.6 Electronic Structure of Atoms

Learning Objective:

- Describe the distribution of electrons into shells, subshells, and orbitals around the nucleus of an atom.

Why does the periodic table have the shape it does, with periods of different length? Why are periodic variations observed in atomic radii and in so many other characteristics of the elements? And why do elements in a given group of the periodic table show similar chemical behavior? These questions occupied the thoughts of chemists for more than 50 years after Mendeleev, and it was not until well into the 1920s that the answers were established. Today, we know that *the properties of the elements are determined by the arrangement of electrons in their atoms.*

Our current understanding of the electronic structure of atoms is based on the *quantum mechanical model,* developed by Austrian physicist Erwin Schrödinger in 1926. One of the fundamental assumptions of the model is that electrons have both particle-like and wave-like properties, and that the behavior of electrons can be described using a mathematical equation called a wave function. One consequence of this assumption is that electrons are not perfectly free to move about in an atom.

▲ Stairs are *quantized* because they change height in discrete amounts. A ramp, by contrast, is not quantized because it changes height continuously.

Instead, each electron is restricted to a certain region of space within the atom, depending on the energy level of the electron. Different electrons have different amounts of energy and thus occupy different regions within the atom. Furthermore, the energies of electrons are *quantized* or restricted to having only certain values.

To understand the idea of quantization, think about the difference between stairs and a ramp. A ramp is *not* quantized because it changes height continuously. Stairs, by contrast, *are* quantized because they change height only by a fixed amount. When you walk up a flight of stairs, you can put your foot on each step, but you cannot stand any place between the two steps. Conversely, on a ramp, you can step anywhere on the ramp you like. In the same way, the energy values available to electrons in an atom change only in steps rather than continuously.

The wave functions derived from the quantum mechanical model also provide important information about the location of electrons in an atom. Just as a person can be found by giving his or her address within a state, an electron can be found by giving its "address" within an atom. Furthermore, just as a person's address is composed of several successively narrower categories—city, street, and house number—an electron's address is also composed of successively narrower categories—*shell, subshell,* and *orbital,* which are defined by the quantum mechanical model.

Shell (electron) A grouping of electrons in an atom according to energy.

The electrons in an atom are grouped around the nucleus into **shells,** like the layers in an onion, according to the energy of the electrons. The shell is designated using the letter n; $n = 1$ for the first shell (period 1), $n = 2$ for the second shell (period 2), and so on. The farther a shell is from the nucleus, the larger it is, the more electrons it can hold, the higher the energies of those electrons, and thus the easier they are to remove because they are the farthest away from the positively charged nucleus. The first shell (the one nearest the nucleus) can hold only 2 electrons, the second shell can hold 8, the third shell can hold 18, and the fourth shell can hold 32 electrons.

Shell number:	1	2	3	4
Electron capacity:	2	8	18	32

Subshell (electron) A grouping of electrons in a shell according to the shape of the region of space they occupy.

Within shells, electrons are further grouped into **subshells** of four different types, identified in order of increasing energy by the letters *s, p, d,* and *f.* The first shell has only one subshell, *s.* The second shell has two subshells: an *s* subshell and a *p* subshell. The third shell has an *s, p,* and *d* subshell. The fourth shell has an *s, p, d,* and *f* subshell. Of the four types, we will be concerned mainly with *s* and *p* subshells because most of the elements found in living organisms use only these. A specific subshell is symbolized by writing the number of the shell followed by the letter for the subshell. For example, the designation 3*p* refers to the *p* subshell in the third shell $(n = 3)$. Note that the number of subshells in a given shell is equal to the shell number. For example, shell number 3 has three subshells *(s, p,* and *d).*

Orbital A region of space within an atom where an electron in a given subshell can be found.

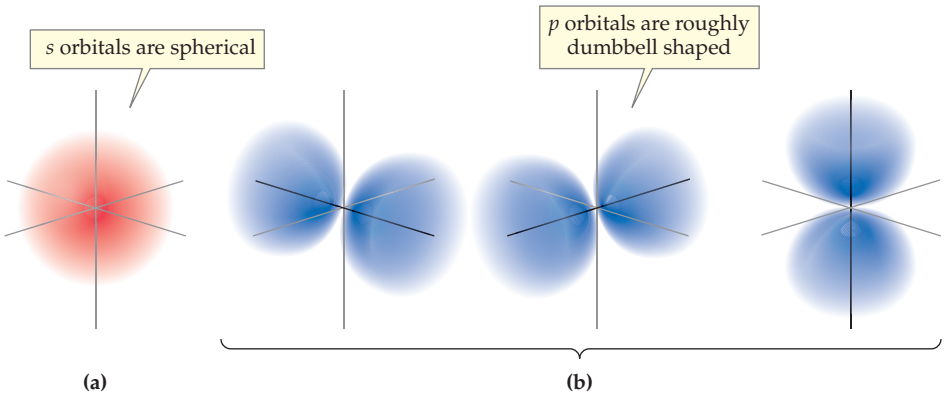
Finally, within each subshell, electrons are grouped into **orbitals,** regions of space within an atom where the specific electrons are most likely to be found. There are different numbers of orbitals within the different kinds of subshells. A given *s* subshell has only one orbital, a *p* subshell has three orbitals, a *d* subshell has five orbitals, and an *f* subshell has seven orbitals. Each orbital can hold only two electrons, which differ in a property known as *spin.* If one electron in an orbital has a clockwise spin, the other electron in the same orbital must have a counterclockwise spin. Since the number of orbitals in a shell increases as n increases, the number of electrons that can be placed in a shell also increases with n, as seen in Table 2.2. The following figure summarizes the configuration of shells, subshells, and orbitals.

Shell number:	1	2	3	4
Subshell designation:	*s*	*s , p*	*s , p , d*	*s , p , d , f*
Number of orbitals:	1	1 , 3	1 , 3 , 5	1 , 3 , 5 , 7

Table 2.2 Electron Distribution in Atoms

Shell Number:	1	2	3	4
Subshell designation:	*s*	*s, p*	*s, p, d*	*s, p, d, f*
Number of orbitals:	1	1, 3	1, 3, 5	1, 3, 5, 7
Number of electrons:	2	2, 6	2, 6, 10	2, 6, 10, 14
Total electron capacity:	2	8	18	32

In the quantum mechanical model, different orbitals have different shapes and orientations. Orbitals in *s* subshells are spherical regions centered about the nucleus, whereas orbitals in *p* subshells are roughly dumbbell-shaped regions where the nucleus is at the midpoint of the dumbbells (Figure 2.5). As shown in Figure 2.5b, the three *p* orbitals in a given subshell are oriented at right angles to one another.



◂ **Figure 2.5**
The shapes of *s* and *p* orbitals. (a) The *s* orbitals and (b) the *p* orbitals. The three *p* orbitals in a given subshell are oriented at right angles to one another. Each orbital can hold only two electrons.

The overall electron distribution within an atom is summarized in Table 2.2 and in the following list:

- The first shell has a maximum capacity of only two electrons. The two electrons have different spins and are in a single 1*s* orbital.
- The second shell has a maximum capacity of eight electrons. Two are in a 2*s* orbital, and 6 are in the three different 2*p* orbitals (two per 2*p* orbital).
- The third shell has a maximum capacity of 18 electrons. Two are in a 3*s* orbital, 6 are in three 3*p* orbitals, and 10 are in five 3*d* orbitals.
- The fourth shell has a maximum capacity of 32 electrons. Two are in a 4*s* orbital, 6 are in three 4*p* orbitals, 10 are in five 4*d* orbitals, and 14 are in seven 4*f* orbitals.

Worked Example 2.5 Atomic Structure: Electron Shells

How many electrons are present in an atom that has its first and second shells filled and has four electrons in its third shell? Name the element.

ANALYSIS The number of electrons in the atom is calculated by adding the total electrons in each shell. We can identify the element from the number of protons in the nucleus, which is equal to the number of electrons in the atom.

SOLUTION
The first shell of an atom holds two electrons in its 1*s* orbital, and the second shell holds eight electrons (two in a 2*s* orbital and six in three 2*p* orbitals). Thus, the atom has a total of $2 + 8 + 4 = 14$ electrons. Since the number of electrons is equal to the number of protons, the element's atomic number $Z = 14$ and must be silicon (Si).

PROBLEM 2.14

How many electrons are present in an atom in which the first and second shells and the 3*s* subshell are filled? Name the element.

HANDS-ON CHEMISTRY 2.2

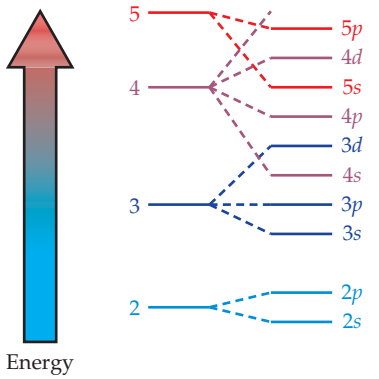
This exercise is designed to help visualize the structure of the atom more closely. The manipulation of an onion will simulate the phenomenal behavior and properties of individual atoms.

a. Cut a medium-sized whole onion in half and remove the outer dry peeling/skin. If we consider the central kernel of the onion as the nucleus, each "layer" would then correspond to a shell containing varying numbers of electrons.

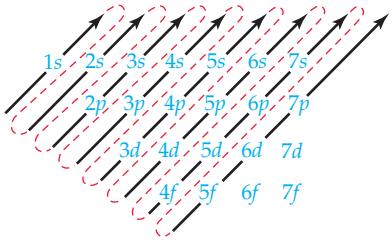
b. How many shells/layers are there in your onion? To which period in the periodic table does this correspond?

c. Note how far each layer is from the "nucleus." What does this imply about the relative attractive forces between each layer and the nucleus?

d. Now peel the successive layers of the onion. How big is the outermost layer compared with the inner layers? What does this imply about the number of electrons that can fit in each layer?



(a)



(b)

▲ **Figure 2.6**
Order of orbital energy levels. (a) An energy-level diagram shows the order in which orbitals will be filled within each shell. Above the 3*p* level, there is some crossover of energies among orbitals in different shells. (b) A simple scheme to remember the order in which the orbitals are filled.

Electron configuration The specific arrangement of electrons in an atom's shells and subshells.

Orbital diagram A representation of the electron distribution into orbitals, in which orbitals are indicated by a line or a box and electrons in each orbital are represented as arrows.

2.7 Electron Configurations

Learning Objective:

- Write the electronic configuration for an atom to describe how electrons are distributed into specific orbitals.

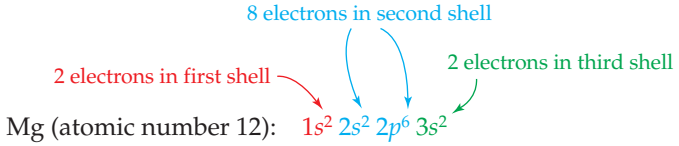
The exact arrangement of electrons in an atom's shells and subshells is called the atom's **electron configuration** and can be predicted by applying three rules:

RULE 1: Electrons occupy the lowest-energy orbitals available, beginning with 1*s*. Within each shell, the orbital energies increase in the order *s, p, d,* and *f*. For the first three periods, the order of energy is as follows: 1*s,* 2*s,* 2*p,* 3*s,* and 3*p*. Across shells, the orbital closer to the nucleus is lower in energy. For example, a 2*s* orbital has lower energy than a 3*s* orbital. As a result, above the 3*p* level the order of how shells are filled is not as straightforward. For example, the 4*s* orbital is lower in energy than the 3*d* orbitals and is therefore filled first. The energy level diagram and simple scheme shown in Figure 2.6 can be used to predict the order in which orbitals are filled. Neither of these diagrams need to be memorized, however, as you can also use the periodic table to determine the order in which orbitals are filled in relation to their placement, shown later in Section 2.8.

RULE 2: Each orbital can hold only two electrons, which must be of opposite spin.

RULE 3: Two or more orbitals with the same energy are each half-filled by one electron before any one orbital is completely filled by the addition of the second electron. For example, one electron is added to each of the three *p* orbitals before a second electron is added to fill an orbital.

Electron configurations of the first 20 elements are shown in Table 2.3. Notice that the number of electrons in each subshell is indicated by a superscript. For example, the notation $1s^2\ 2s^2\ 2p^6\ 3s^2$ for magnesium means that magnesium atoms have two electrons in the first shell, eight electrons in the second shell, and two electrons in the third shell.



In additional to writing the configurations as shown above, we can also use **orbital diagrams.** In the written representation, the superscript in the notation $1s^1$ means that the 1*s* orbital is occupied by only one electron. In an orbital diagram, the 1*s* orbital is indicated by a line or a box and the single electron in this orbital is shown by a single arrow pointing up (↑). A single electron in an orbital is often referred to as being *unpaired.* Two electrons in an orbital are paired, with spins in opposite directions, so they are represented by two arrows pointing in opposite directions (one up, one down).

Table 2.3 Electron Configurations of the First 20 Elements

	Element	Atomic Number	Electron Configuration
H	Hydrogen	1	$1s^1$
He	Helium	2	$1s^2$
Li	Lithium	3	$1s^2\ 2s^1$
Be	Beryllium	4	$1s^2\ 2s^2$
B	Boron	5	$1s^2\ 2s^2\ 2p^1$
C	Carbon	6	$1s^2\ 2s^2\ 2p^2$
N	Nitrogen	7	$1s^2\ 2s^2\ 2p^3$
O	Oxygen	8	$1s^2\ 2s^2\ 2p^4$
F	Fluorine	9	$1s^2\ 2s^2\ 2p^5$
Ne	Neon	10	$1s^2\ 2s^2\ 2p^6$
Na	Sodium	11	$1s^2\ 2s^2\ 2p^6\ 3s^1$
Mg	Magnesium	12	$1s^2\ 2s^2\ 2p^6\ 3s^2$
Al	Aluminum	13	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^1$
Si	Silicon	14	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^2$
P	Phosphorus	15	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^3$
S	Sulfur	16	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^4$
Cl	Chlorine	17	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^5$
Ar	Argon	18	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$
K	Potassium	19	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^1$
Ca	Calcium	20	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2$

As you read through the following electron configurations, check the atomic number and the location of each element in the periodic table (Figure 2.2). See if you can detect the relationship between electron configuration and position in the table.

- **Hydrogen ($Z = 1$):** The single electron in a hydrogen atom is in the lowest-energy, 1*s*, level. The configuration can be represented in either of two ways:

$$\mathbf{H} \quad 1s^1 \quad \text{or} \quad \underset{1s^1}{\boxed{\uparrow}}$$

- **Helium ($Z = 2$):** The two electrons in helium are both in the lowest-energy, 1*s*, orbital, and their spins are *paired,* as represented by up and down arrows ($\uparrow\downarrow$). Helium has a completely filled first shell ($n = 1$) of electrons.

$$\mathbf{He} \quad 1s^2 \quad \text{or} \quad \underset{1s^2}{\boxed{\uparrow\downarrow}}$$

- **Lithium ($Z = 3$):** Lithium has three electrons, so we must now use the orbitals in the second shell, starting with 2*s*. Since electrons are always added to the lowest energy level first, the first two electrons fill the first shell. Next, the second shell begins to fill. The third electron goes into the 2*s* orbital and is unpaired:

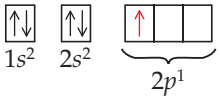
$$\mathbf{Li} \quad 1s^2\ 2s^1 \quad \text{or} \quad \underset{1s^2}{\boxed{\uparrow\downarrow}} \quad \underset{2s^1}{\boxed{\uparrow}}$$

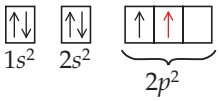
  Because [He] has the configuration of a filled $1s^2$ orbital, it is sometimes substituted for the $1s^2$ orbital in depictions of electron pairing. Using this alternative shorthand notation, the electron configuration for Li is written [He] $2s^1$.

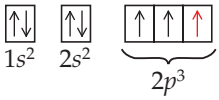
- **Beryllium ($Z = 4$):** For beryllium's four electrons, we continue to use the second shell. The three electrons are configured as they were for lithium, and the fourth electron pairs up to fill the $2s$ orbital:

Be $1s^2\,2s^2$ or  or [He] $2s^2$

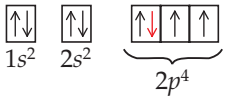
- **Boron ($Z = 5$), Carbon ($Z = 6$), Nitrogen ($Z = 7$):** The next three elements use the three $2p$ orbitals, one at a time. For boron, the fifth electron starts to fill the first $2p$ orbital. Carbon and nitrogen's sixth and seventh electron are placed in the next two orbitals, respectively (instead of filling the first p orbital). Note that representing the configurations with lines and arrows gives more information than the alternative written notations because the filling and pairing of electrons in individual orbitals within the p subshell is shown.

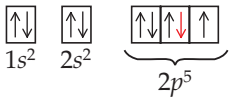
B $1s^2\,2s^2\,2p^1$ or  or [He] $2s^2\,2p^1$

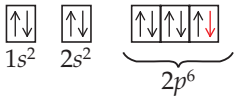
C $1s^2\,2s^2\,2p^2$ or  or [He] $2s^2\,2p^2$

N $1s^2\,2s^2\,2p^3$ or  or [He] $2s^2\,2p^3$

- **Oxygen ($Z = 8$), Fluorine ($Z = 9$), Neon ($Z = 10$):** Electrons now pair up one by one to fill the three $2p$ orbitals and fully occupy the second shell.

O $1s^2\,2s^2\,2p^4$ or  or [He] $2s^2\,2p^4$

F $1s^2\,2s^2\,2p^5$ or  or [He] $2s^2\,2p^5$

Ne $1s^2\,2s^2\,2p^6$ or 

Just as [He] was used as a shorthand notation to indicate the closed-shell configuration $1s^2$, we may also use [Ne] to represent the electron configuration for a completely filled set of orbitals in the second shell, or $1s^2 2s^2 2p^6$. Both helium and neon are noble gases and are located in Group 8A on the periodic table. All of electron configurations of the elements in one period can be written in shorthand using the noble gas that immediately precedes it in the periodic table.

- **Sodium to Calcium ($Z = 11 - 20$):** The pattern seen for lithium through neon is seen again for sodium ($Z = 11$) through argon ($Z = 18$) as the $3s$ and $3p$ subshells fill up. For elements having a third filled shell, we may use [Ar] to represent a completely filled third shell. After argon, however, the first crossover in subshell energies occurs. As indicated in Figure 2.6, the $4s$ subshell is lower in energy than the $3d$ subshell and is filled first. Potassium ($Z = 19$) and calcium ($Z = 20$), therefore, have the following electron configurations:

K $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^1$ or [Ar]$4s^1$ **Ca** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^2$ or [Ar]$4s^2$

After calcium we enter the transition metals, and the subsequent electrons for these elements would be placed into the next lowest energy orbitals, or the $3d$.

Worked Example 2.6 Atomic Structure: Electron Configurations

Show how the electron configuration of magnesium can be assigned.

ANALYSIS Magnesium, $Z = 12$, has 12 electrons to be placed in specific orbitals. Assignments are made by putting two electrons in each orbital, according to the order shown in Figure 2.6.

- The first two electrons are placed in the 1*s* orbital $(1s^2)$.
- The next two electrons are placed in the 2*s* orbital $(2s^2)$.
- The next six electrons are placed in the three available 2*p* orbitals $(2p^6)$.
- The remaining two electrons are both put in the 3*s* orbital $(3s^2)$.

SOLUTION

Magnesium has the configuration $1s^2 2s^2 2p^6 3s^2$ or $[\text{Ne}]3s^2$.

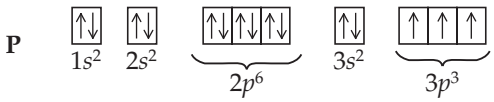
Worked Example 2.7 Electron Configurations: Orbital-Filling Diagrams

Write the electron diagram of phosphorus, $Z = 15$, using up and down arrows to show how the electrons in each orbital are paired.

ANALYSIS Phosphorus has 15 electrons, which occupy orbitals according to the order shown in Figure 2.6.

- The first two are paired and fill the first shell $(1s^2)$.
- The next eight fill the second shell $(2s^2 2p^6)$. All electrons are paired.
- The remaining five electrons enter the third shell, where two fill the 3*s* orbital $(3s^2)$ and three occupy the 3*p* subshell, one in each of the three *p* orbitals.

SOLUTION



PROBLEM 2.15

An element has completely filled $n = 1$ and $n = 2$ shells and has six electrons in the $n = 3$ shell. Identify the element and its major group (i.e., main group, transition, etc.). Is it a metal or a nonmetal? Identify the orbital in which the last electron is found.

PROBLEM 2.16

Write electron configurations for the following elements. (You can check your answers in Table 2.3.)

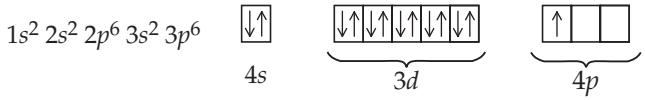
(a) C **(b)** P **(c)** Cl **(d)** K

PROBLEM 2.17

For an atom containing 33 electrons, identify the incompletely filled subshell and show the paired and/or unpaired electrons in this subshell using up and down arrows.

KEY CONCEPT PROBLEM 2.18

Identify the atom with the following orbital-filling diagram.



2.8 Electron Configurations and the Periodic Table

Learning Objective:

- Identify the valence shell electrons for an atom, and which subshell of electrons *(s, p, d, f)* correlate with which groups in the periodic table.

s-Block element A main group element that results from the filling of an *s* orbital.

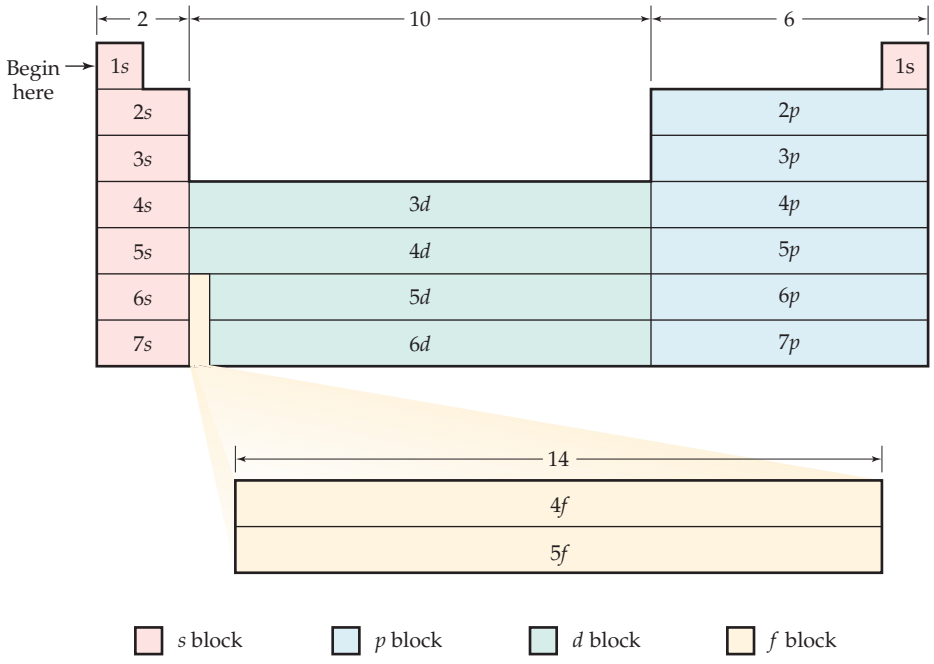
p-Block element A main group element that results from the filling of *p* orbitals.

d-Block element A transition metal element that results from the filling of *d* orbitals.

f-Block element An inner transition metal element that results from the filling of *f* orbitals.

How is an atom's electron configuration related to its chemical behavior, and why do elements with similar behavior occur in the same group of the periodic table? As shown in Figure 2.7, the periodic table can be divided into four regions, or *blocks,* of elements according to the electron shells and subshells occupied by *the subshell filled last.*

- The main group 1A and 2A elements on the left side of the table (plus He) are called the ***s*-block elements** because an *s* subshell is filled last in these elements.
- The main group 3A–8A elements on the right side of the table (except He) are the ***p*-block elements** because a *p* subshell is filled last in these elements.
- The transition metals in the middle of the table are the ***d*-block elements** because a *d* subshell is filled last in these elements.
- The inner transition metals detached at the bottom of the table are the ***f*-block elements** because an *f* subshell is filled last in these elements.



▶ **Figure 2.7**
The blocks of elements in the periodic table correspond to filling the different types of subshells. Beginning at the top left and going across successive rows of the periodic table provides a method for remembering the order of orbital filling: $1s \rightarrow 2s \rightarrow 2p \rightarrow 3s \rightarrow 3p \rightarrow 4s \rightarrow 3d \rightarrow 4p$, and so on.

Thinking of the periodic table as outlined in Figure 2.7 provides a simple way to remember the order of orbital filling shown previously in Figure 2.6. Beginning at the top left corner of the periodic table, the first row contains only two elements (H and He) because only two electrons are required to fill the *s* orbital in the first shell, $1s^2$. The second row begins with two *s*-block elements (Li and Be) and continues with six *p*-block elements (B through Ne), so electrons fill the next available *s* orbital (2*s*) and then the first available *p* orbitals (2*p*). The third row is similar to the second row, so the 3*s* and 3*p* orbitals are filled next. The fourth row again starts with 2 *s*-block elements (K and Ca) but is then followed by 10 *d*-block elements (Sc through Zn) and 6 *p*-block elements (Ga through Kr). Thus, the order of orbital filling is 4*s* followed by the first

available *d* orbitals (3*d*) followed by 4*p*. Continuing through successive rows of the periodic table gives the entire filling order, identical to that shown in Figure 2.6.

$$1s \longrightarrow 2s \longrightarrow 2p \longrightarrow 3s \longrightarrow 3p \longrightarrow 4s \longrightarrow 3d \longrightarrow 4p \longrightarrow 5s \longrightarrow$$
$$4d \longrightarrow 5p \longrightarrow 6s \longrightarrow 4f \longrightarrow 5d \longrightarrow 6p \longrightarrow 7s \longrightarrow 5f \longrightarrow 6d \longrightarrow 7p$$

But why do the elements in a given group of the periodic table have similar properties? The answer emerges when you look at Table 2.4, which gives electron configurations for elements in the main groups 1A, 2A, 7A, and 8A. Focusing only on the electrons in the outermost shell, or **valence shell,** *elements in the same group of the periodic table have similar electron configurations in their valence shells.* The group 1A elements, for example, all have one **valence electron,** ns^1 (where n represents the number of the valence shell: $n = 2$ for Li, $n = 3$ for Na, $n = 4$ for K, and so on). The group 2A elements have two valence electrons (ns^2). The group 7A elements have seven valence electrons $(ns^2\, np^5)$. For example, fluorine (F) has the electron configuration of $1s^2\mathbf{2s^2 2p^5}$ (valence electrons in bold). The group 8A elements (except He) have eight valence electrons $(ns^2\, np^6)$. You might also notice that the group numbers from 1A through 8A give the numbers of valence electrons for the elements in each main group. It is worth noting that the valence electrons are those in the outermost shell *(n)*—not necessarily in the orbitals that were filled last!

Valence shell The outermost electron shell of an atom.

Valence electron An electron in the valence shell of an atom.

Table 2.4 Valence-Shell Electron Configurations for Groups 1A, 2A, 7A, and 8A Elements

Group	Element	Atomic Number	Valence-Shell Electron Configuration
1A	Li (lithium)	3	$2s^1$
	Na (sodium)	11	$3s^1$
	K (potassium)	19	$4s^1$
	Rb (rubidium)	37	$5s^1$
	Cs (cesium)	55	$6s^1$
2A	Be (beryllium)	4	$2s^2$
	Mg (magnesium)	12	$3s^2$
	Ca (calcium)	20	$4s^2$
	Sr (strontium)	38	$5s^2$
	Ba (barium)	56	$6s^2$
7A	F (fluorine)	9	$2s^2\, 2p^5$
	Cl (chlorine)	17	$3s^2\, 3p^5$
	Br (bromine)	35	$4s^2\, 4p^5$
	I (iodine)	53	$5s^2\, 5p^5$
8A	He (helium)	2	$1s^2$
	Ne (neon)	10	$2s^2\, 2p^6$
	Ar (argon)	18	$3s^2\, 3p^6$
	Kr (krypton)	36	$4s^2\, 4p^6$
	Xe (xenon)	54	$5s^2\, 5p^6$

What is true for the main group elements is also true for the other groups in the periodic table: atoms within a given group have the same number of valence electrons and have similar electron configurations. *Because the valence electrons are the most loosely held, they are the most important in determining an element's properties.* Similar electron configurations thus explain why the elements in a given group of the periodic table have similar chemical behavior.

We have seen that elements in a given group have similar chemical behavior because they have similar valence electron configurations, and that many chemical properties exhibit periodic trends across the periodic table. The *chemical* behavior of nearly all the elements can be predicted based on their position in the periodic table, and this will be examined in more detail in Chapters 3 and 4. Similarly, the *nuclear* behavior of the different isotopes of a given element is related to the configuration of the nucleus (i.e., the number of neutrons and protons) and will be examined in Chapter 11.

Worked Example 2.8 Electron Configurations: Valence Electrons

Write the electron configuration for the following elements, using both the complete and the shorthand notations. Indicate which electrons are the valence electrons.

(a) Na **(b)** Cl **(c)** Zr

ANALYSIS Locate the row and the block in which each of the elements is found in Figure 2.7. The location can be used to determine the complete electron configuration and to identify the valence electrons.

SOLUTION

(a) Na (sodium) is located in the third row and in the first column of the *s*-block. Therefore, all orbitals up to the 3*s* are completely filled, and there is one electron in the 3*s* orbital.

Na: $1s^2\ 2s^2\ 2p^6\ \underline{3s^1}$ or $[\text{Ne}]\ \underline{3s^1}$ (valence electrons are underlined)

(b) Cl (chlorine) is located in the third row and in the fifth column of the *p*-block. Therefore, there are five electrons in the 3*p* orbital.

Cl: $1s^2\ 2s^2\ 2p^6\ \underline{3s^2\ 3p^5}$ or $[\text{Ne}]\ \underline{3s^2\ 3p^5}$

(c) Zr (zirconium) is located in the fifth row and in the second column of the *d*-block. All orbitals up to the 4*d* are completely filled, and there are two electrons in the 4*d* orbitals. Note that the 4*d* orbitals are filled after the 5*s* orbitals in both Figures 2.6 and 2.7.

Zr: $1s^2\ 2s^2\ 2p^6\ 3s^1\ 3p^6\ 4s^2\ 3d^{10}\ 4p^6\ \underline{5s^2}\ 4d^2$ or $[\text{Kr}]\ \underline{5s^2}\ 4d^2$

Worked Example 2.9 Electron Configurations: Valence-Shell Configurations

Using *n* to represent the number of the valence shell, write a general valence-shell configuration for the elements in group 6A.

ANALYSIS The elements in group 6A have six valence electrons. In each element, the first two of these electrons are in the valence *s* subshell, giving ns^2, and the next four electrons are in the valence *p* subshell, giving np^4.

SOLUTION

For group 6A, the general valence-shell configuration is $ns^2\ np^4$.

Worked Example 2.10 Electron Configurations: Inner Shells versus Valence Shell

How many electrons are in a tin atom? Give the number of electrons in each shell. How many valence electrons are there in a tin atom? Write the valence-shell configuration for tin.

ANALYSIS The total number of electrons will be the same as the atomic number for tin $(Z = 50)$. The number of valence electrons will equal the number of electrons in the valence shell.

SOLUTION

Checking the periodic table shows that tin (Sn) has atomic number 50 and is in group 4A. The number of electrons in each shell is

Shell number:	1	2	3	4	5
Number of electrons:	2	8	18	18	4

As expected from the group number, tin has four valence electrons. They are in the 5*s* and 5*p* subshells and have the configuration $5s^2\ 5p^2$. Although there are *f* orbitals available in the $n = 4$ shell, the 5*s* orbital is of lower energy than the 4*f* orbitals, and so will fill first. Hence, there are only 18 electrons in the $n = 4$ shell.

PROBLEM 2.19

Write the electron configuration for the following elements, using both the complete and the shorthand notations. Indicate which electrons are the valence electrons.

(a) F **(b)** Al **(c)** As

PROBLEM 2.20

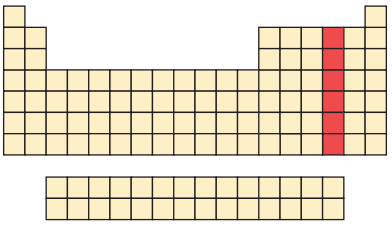
Identify the group in which all the elements have the valence-shell configuration ns^2.

PROBLEM 2.21

For chlorine, identify the group number, give the number of electrons in each occupied shell, and write its valence-shell configuration.

KEY CONCEPT PROBLEM 2.22

Identify the group number and write the general valence-shell configuration (e.g., ns^1 for group 1A elements) for the elements indicated in red in the following periodic table.



2.9 Electron-Dot Symbols

Learning Objective:

- Write Lewis dot symbols to represent the valence electrons for a given atom.

Valence electrons play such an important role in the behavior of atoms that it is useful to have a method for including them with atomic symbols. In an **electron-dot symbol** (also called Lewis symbols), dots are placed around the atomic symbol to indicate the number of valence electrons present. A group 1A atom, such as sodium, has a single dot; a group 2A atom, such as magnesium, has two dots; a group 3A atom, such as boron, has three dots; and so on.

Electron-dot (Lewis) symbol An atomic symbol with dots placed around it to indicate the number of valence electrons.

Table 2.5 gives electron-dot symbols for atoms of the first few elements in each main group. As shown, the dots are distributed around the four sides of the element symbol, singly at first until each of the four sides has one dot. As more electron dots are added they will form pairs, with no more than two dots on a side. Note that helium differs from other noble gases in having only two valence electrons rather than eight. Nevertheless, helium is considered a member of group 8A because its properties resemble those of the other noble gases and because its highest occupied subshell is filled $(1s^2)$.

Table 2.5 Electron-Dot Symbols for Some Main Group Elements

1A	2A	3A	4A	5A	6A	7A	Noble Gases
H·							He:
Li·	·Be·	·B·	·C·	·N:	·O:	·F:	:Ne:
Na·	·Mg·	·Al·	·Si·	·P:	·S:	·Cl:	:Ar:
K·	·Ca·	·Ga·	·Ge·	·As:	·Se:	·Br:	:Kr:

Worked Example 2.11 Electron Configurations: Electron-Dot Symbols

Write the electron-dot symbol for any element X in group 5A.

ANALYSIS The group number, 5A, indicates five valence electrons. The first four are distributed singly around the four sides of the element symbol, and any additional are placed to form electron pairs.

SOLUTION


(5 electrons)

PROBLEM 2.23

Write the electron-dot symbol for any element X in group 3A.

PROBLEM 2.24

Write electron-dot symbols for radon, lead, xenon, and radium.

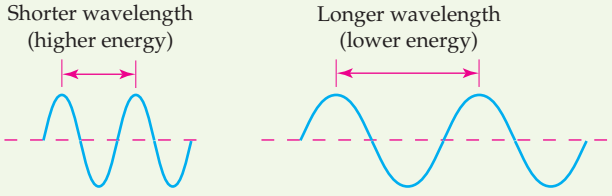
PROBLEM 2.25

When an electron in a strontium atom drops from the excited state to the ground state, it emits red light, as explained in the following Chemistry in Action feature. When an electron in a copper atom drops from the excited state to the ground state, it emits blue light. What are the approximate wavelengths of the red light and the blue light? Which color is associated with higher energy?

CHEMISTRY IN ACTION

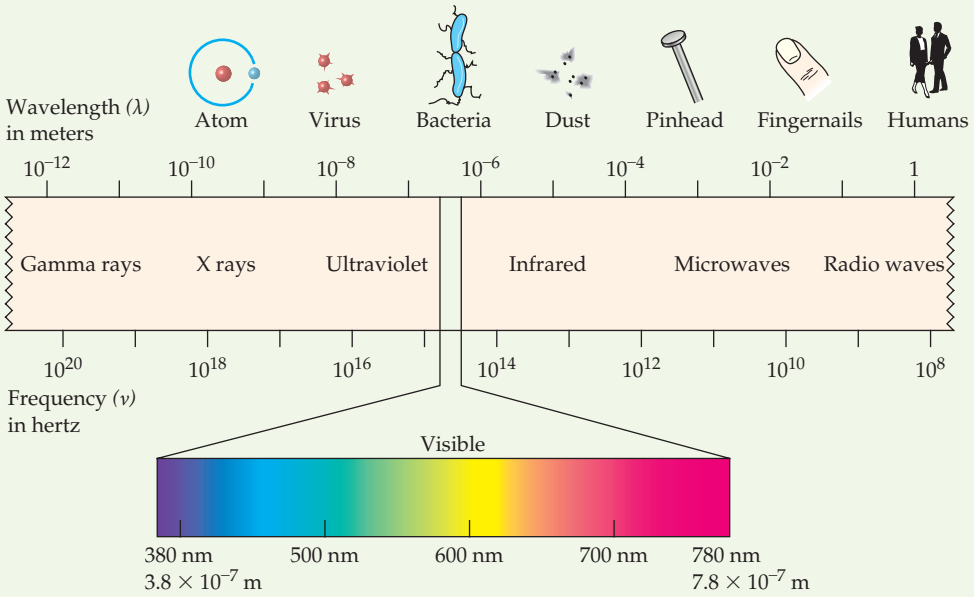
Atoms and Light

What we see as *light* is really a wave of energy moving through space. The shorter the length of the wave (the *wavelength*), the higher the energy; the longer the wavelength, the lower the energy.



What happens when a beam of electromagnetic energy collides with an atom? Remember that electrons are located in orbitals based on their energy levels. An atom with its electrons in their usual, lowest-energy locations is said to be in its *ground state.* If the amount of electromagnetic energy is just right, an electron can be kicked up from its usual energy level to a higher one. Energy from an electrical discharge or in the form of heat can also boost electrons to higher energy levels. With one of its electrons promoted to a higher energy, an atom is said to be *excited.* The excited state does not last long, though, because the electron quickly drops back to its more stable, ground-state energy level, releasing its extra energy in the process. If the released energy falls in the range of visible light (400–800 nm), we can see the result. Many practical applications, from neon lights to fireworks, are the result of this phenomenon.

▲ This chest X ray equipment uses high energy, short wavelength electromagnetic radiation to generate diagnostic images.



▲ The electromagnetic spectrum consists of a continuous range of wavelengths, with the familiar visible region accounting for only a small portion near the middle of the range.

The interaction of light with matter has many significant impacts. The UV radiation (200–350 nm) from the sun has enough energy to cause sunburn and, with chronic long-term exposure, can lead to skin cancers. Higher energy radiation (X rays) is used in many diagnostic applications, while even higher energies (gamma rays) can be used to kill cancer cells. In clinical applications, the concentration of certain biologically important metals in body fluids, such as blood or urine, is measured by sensitive instruments (such as the spectrophotometer mentioned at the beginning of this chapter), relying on the principle of electron excitation, where metal atoms will emit light of a specific wavelength corresponding to electronic transitions in the atom. These instruments measure the intensity of color produced in a flame by lithium (red), sodium (yellow), and potassium (violet), to determine the concentrations of these metals, which should be in a certain range to ensure good health. If the levels of these and other essential metals are outside the optimal range, it may be an indication of poor nutrition or certain diseases.

CIA Problem 2.5 Which type of electromagnetic energy in the following pairs is of higher energy?

(a) Infrared, ultraviolet
(b) Gamma waves, microwaves
(c) Visible light, X rays

CIA Problem 2.6 Why do you suppose ultraviolet rays from the sun are more damaging to the skin than visible light?

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Explain the major assumptions of atomic theory, and name and identify the properties of the subatomic particles that make up an atom.** All matter is composed of *atoms.* An atom is the smallest and simplest unit into which a sample of an element can be divided while maintaining the properties of the element. Atoms are made up of subatomic particles called *protons, neutrons,* and *electrons.* Protons have a positive electrical charge, neutrons are electrically neutral, and electrons have a negative electrical charge. The protons and neutrons in an atom are present in a dense, positively charged central region called the *nucleus.* Electrons are situated a relatively large distance away from the nucleus, leaving most of the atom as empty space *(see Problems 31–40, 83, 85, 89, and 95).*

- **Identify atoms of an element based on the number of protons in the nucleus.** Elements differ according to the number of protons their atoms contain, a value called the element's *atomic number* (Z). All atoms of a given element have the same number of protons and an equal number of electrons. The number of neutrons in an atom is not predictable but is generally equal to or greater than the number of protons. The total number of protons plus neutrons in an atom is called the atom's *mass number* (A) *(see Problems 43, 46, and 82).*

- **Write the symbols for different isotopes of an element and use relative abundances and atomic masses of isotopes to calculate the average atomic mass of an element.** The symbol for an atom is written using the symbol for the element (e.g., C for carbon), including

the atomic number *(Z)* as a subscript on the left, and the atomic mass *(A)* as a superscript. An atom of carbon-12 (6 protons + 6 neutrons) would be represented as $^{12}_{6}C$. Atoms with identical numbers of protons and electrons but different numbers of neutrons are called *isotopes.* The atomic mass of an element is the weighted average mass of atoms of the element's naturally occurring isotopes *(see Problems 27, 40–49, 52, and 96).*

- **Locate elements on the periodic table and classify them as metals, nonmetals, or metalloids based on their location.** The majority of elements are identified as metals and are located to the left/bottom of the periodic table. Only 18 elements are identified as nonmetals, and they are located to the upper right of the periodic table. Metalloids are located on a diagonal between the metals and nonmetals *(see Problems 26, 52–57, 86, and 88).*
- **Classify elements and describe chemical behavior based on group membership.** Elements are organized into the *periodic table,* consisting of 7 rows, or *periods,* and 18 columns, or *groups.* The two columns on the left side of the table and the six columns on the right are called the *main group elements.* The 10 columns in the middle are the *transition metal groups,* and the 14 columns pulled out and displayed below the main part of the table are called the *inner transition metal groups (see Problems 27, 56–61, 80–82, 97, and 98).*
- **Describe the distribution of electrons into shells, subshells, and orbitals around the nucleus of an atom.** The electrons surrounding an atom are grouped into layers, or *shells.* Within each shell, electrons are grouped into *subshells,* and within each subshell into *orbitals*—regions of space in which electrons are most likely to be found. The *s* orbitals are spherical, and the *p* orbitals are dumbbell-shaped. Each shell can hold a specific number of electrons. The first shell can hold 2 electrons, the second shell can hold 8 electrons, the third shell can hold 18 electrons, and so on *(see Problems 50, 51, and 62–69).*
- **Write the electronic configuration for an atom to describe how electrons are distributed into specific orbitals.** The electron configuration of an element is predicted by assigning the element's electrons into shells and orbitals, beginning with the lowest-energy orbital. For example, the first shell can hold 2 electrons in an *s* orbital ($1s^2$); the second shell can hold 8 electrons in one *s* and three *p* orbitals ($2s^2 2p^6$); the third shell can hold 18 electrons in one *s,* three *p,* and five *d* orbitals ($3s^2\ 3p^6\ 3d^{10}$); and so on *(see Problems 29, 30, 68–74, 83, 84, 86, 87, and 90–94).*
- **Identify the valence shell electrons for an atom, and which subshell of electrons *(s, p, d, f)* correlate with which groups in the periodic table.** The valence electrons for an atom are found in the outermost shell and correspond to the location of the element in the periodic table. The number of valence electrons for the main group elements corresponds to the group number. The valence electrons for the 1A and 2A elements are located in *s* orbitals, while the valence electrons for groups 3A–8A are in *p* orbitals. Electrons in the *d* orbitals are associated with the transition metals, while *f* orbitals are associated with the inner transition metals (lanthanide and actinide series). Within a given group in the table, elements have the same number of valence electrons in their valence shell and similar electron configurations *(see Problems 28, 53, 74–79, 84, 86–88, and 94).*
- **Write Lewis dot symbols to represent the valence electrons for a given atom.** The number of valence electrons is determined by the location of the element in the periodic table. The Lewis dot symbol for an atom is written as the chemical symbol for the element (C for carbon) with the valence electrons represented as dots around the symbol. If there are only four (or fewer) valence electrons, they are written as single dots above, below, and to the left and right sides of the symbol. If there are more than four valence electrons, then the extra electrons are added to form electron pairs *(see Problems 78, 81, and 86).*

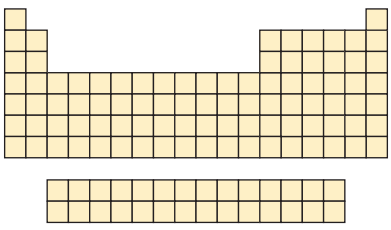
KEY WORDS

Alkali metal, *p. 87*
Alkaline earth metal, *p. 87*
Atom, *p. 77*
Atomic mass unit (amu), *p. 77*
Atomic number *(Z),* *p. 79*
Atomic theory, *p. 77*
Atomic mass, *p. 81*
***d*-Block element,** *p. 96*
Electron, *p. 77*
Electron configuration, *p. 92*
Electron-dot (Lewis) symbol, *p. 99*
***f*-Block element,** *p. 96*
Group, *p. 86*
Halogen, *p. 88*
Inner transition metal element, *p. 86*
Isotopes, *p. 80*
Main group element, *p. 86*
Mass number *(A),* *p. 80*
Metal, *p. 84*
Metalloid, *p. 84*
Neutron, *p. 77*
Noble gas, *p. 88*
Nonmetal, *p. 84*
Nucleus, *p. 78*
Orbital, *p. 90*
Orbital diagram, *p. 92*
Periodic table, *p. 83*
***p*-Block element,** *p. 96*
Period, *p. 86*
Proton, *p. 77*
***s*-Block element,** *p. 96*
Shell (electron), *p. 90*
Subatomic particles, *p. 77*
Subshell (electron), *p. 90*
Transition metal element, *p. 86*
Valence electron, *p. 97*
Valence shell, *p. 97*

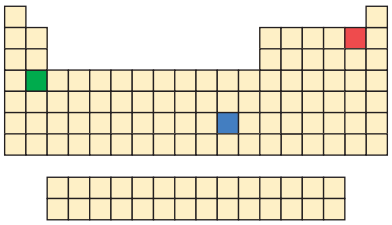
UNDERSTANDING KEY CONCEPTS

2.26 Where on the following outline of a periodic table do the indicated elements or groups of elements appear?

(a) Alkali metals
(b) Halogens
(c) Alkaline earth metals
(d) Transition metals
(e) Hydrogen
(f) Helium
(g) Metalloids



2.27 Is the element marked in red on the following periodic table likely to be a gas, a liquid, or a solid? What is the atomic number of the element in blue? Name at least one other element that is likely to be similar to the element in green.

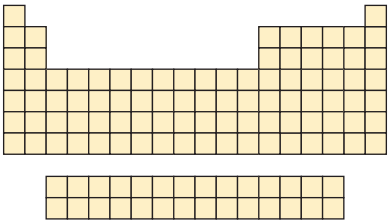


2.28 Use the following blank periodic table to show where the elements matching the following descriptions appear.

(a) Elements with the valence-shell electron configuration $ns^2\ np^5$

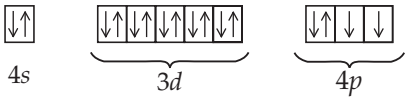
(b) An element whose third shell contains two *p* electrons

(c) Elements with a completely filled valence shell



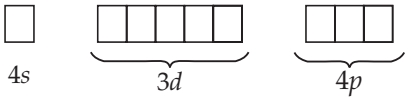
2.29 What atom has the following orbital-filling diagram?

$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$



2.30 Use the following orbital-filling diagram to show the electron configuration for As:

$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$



ADDITIONAL PROBLEMS

ATOMIC THEORY AND THE COMPOSITION OF ATOMS (SECTION 2.1–2.3)

2.31 What four fundamental assumptions about atoms and matter make up modern atomic theory?

2.32 How do atoms of different elements differ?

2.33 Find the mass in grams of one atom of the following elements:

(a) Bi, atomic mass 208.9804 amu

(b) Xe, atomic mass 131.29 amu

(c) He, atomic mass 4.0026 amu

2.34 Find the mass in atomic mass units of the following:

(a) 1 O atom, with a mass of 2.66×10^{-23} g

(b) 1 Br atom, with a mass of 1.31×10^{-22} g

2.35 What is the mass in grams of 6.022×10^{23} N atoms of mass 14.01 amu?

2.36 What is the mass in grams of 6.022×10^{23} O atoms of mass 16.00 amu?

2.37 How many O atoms of mass 15.99 amu are in 15.99 g of oxygen?

2.38 How many C atoms of mass 12.00 amu are in 12.00 g of carbon?

2.39 What are the names of the three subatomic particles? What are their approximate masses in atomic mass units, and what electrical charge does each have?

2.40 Where within an atom are the three types of subatomic particles located?

2.41 Give the number of neutrons in each naturally occurring isotope of argon: argon-36, argon-38, argon-40.

2.42 Give the number of protons, neutrons, and electrons in the following isotopes:

(a) Al-27 **(b)** $^{28}_{14}$Si

(c) B-11 **(d)** $^{115}_{47}$Ag

2.43 Which of the following symbols represent isotopes of the same element? Explain.

(a) $^{19}_{9}X$ **(b)** $^{19}_{10}X$

(c) $^{21}_{9}X$ **(d)** $^{21}_{12}X$

2.44 Give the name and the number of neutrons in each isotope listed in Problem 2.43.

2.45 Write the symbols for the following isotopes:

(a) Its atoms contain 6 protons and 8 neutrons.

(b) Its atoms have mass number 39 and contain 19 protons.

(c) Its atoms have mass number 20 and contain 10 electrons.

2.46 Write the symbols for the following isotopes:

(a) Its atoms contain 50 electrons and 70 neutrons.

(b) Its atoms have $A = 56$ and $Z = 26$.

(c) Its atoms have $A = 226$ and contain 88 electrons.

2.47 One of the most widely used isotopes in medical diagnostics is technetium-99*m* (the *m* indicates that it is a *metastable* isotope). Write the symbol for this isotope, indicating both mass number and atomic number.

2.48 Naturally occurring copper is a mixture of 69.17% Cu-63 with a mass of 62.93 amu and 30.83% Cu-65 with a mass of 64.93 amu. What is the atomic mass of copper?

2.49 Naturally occurring lithium is a mixture of 92.58% Li-7 with a mass of 7.016 amu and 7.42% Li-6 with a mass of 6.015 amu. What is the atomic mass of lithium?

THE PERIODIC TABLE (SECTIONS 2.4–2.6)

2.50 Why does the third period in the periodic table contain eight elements?

2.51 Why does the fourth period in the periodic table contain 18 elements?

2.52 Americium, atomic number 95, is used in household smoke detectors. What is the symbol for americium? Is americium a metal, a nonmetal, or a metalloid?

2.53 What subshell is being filled for the metalloid elements?

2.54 Answer the following questions for the elements from scandium through zinc:

(a) Are they metals or nonmetals?

(b) To what general class of elements do they belong?

(c) What subshell is being filled by electrons in these elements?

2.55 Answer the following questions for the elements from cerium through lutetium:

(a) Are they metals or nonmetals?

(b) To what general class of elements do they belong?

(c) What subshell is being filled by electrons in these elements?

2.56 For (a) rubidium (b) tungsten, (c) germanium, and (d) krypton, which of the following terms apply? (i) metal, (ii) nonmetal, (iii) metalloid (iv) transition element, (v) main group element, (vi) noble gas, (vii) alkali metal, (viii) alkaline earth metal.

2.57 For (a) calcium, (b) palladium, (c) carbon, and (d) radon, which of the following terms apply? (i) metal, (ii) nonmetal, (iii) metalloid, (iv) transition element, (v) main group element, (vi) noble gas, (vii) alkali metal, (viii) alkaline earth metal.

2.58 Name an element in the periodic table that you would expect to be chemically similar to sulfur.

2.59 Name an element in the periodic table that you would expect to be chemically similar to potassium.

2.60 What elements in addition to lithium make up the alkali metal family?

2.61 What elements in addition to fluorine make up the halogen family?

ELECTRON CONFIGURATIONS (SECTIONS 2.6–2.9)

2.62 What is the maximum number of electrons that can go into an orbital?

2.63 What are the shapes and locations within an atom of *s* and *p* orbitals?

2.64 What is the maximum number of electrons that can go into the first shell? The second shell? The third shell?

2.65 What is the total number of orbitals in the third shell? The fourth shell?

2.66 How many subshells are there in the third shell? The fourth shell? The fifth shell?

2.67 How many orbitals would you expect to find in the last subshell of the fifth shell? How many electrons would you need to fill this subshell?

2.68 How many electrons are present in an atom with its 1*s*, 2*s*, and 2*p* subshells filled? What is this element?

2.69 How many electrons are present in an atom with its 1*s*, 2*s*, 2*p*, 3*s*, 3*p*, and 4*s* subshells filled and with two electrons in the 3*d* subshell? What is this element?

2.70 Use arrows to show electron pairing in the valence *p* subshell of

(a) Sulfur **(b)** Bromine **(c)** Silicon

2.71 Use arrows to show electron pairing in the 5*s* and 4*d* orbitals of

(a) Rubidium **(b)** Niobium **(c)** Rhodium

2.72 Determine the number of unpaired electrons for each of the atoms in Problems 2.70 and 2.71.

2.73 Without looking back in the text, write the electron configurations for the following:

(a) Titanium $Z = 22$ **(b)** Phosphorus, $Z = 15$

(c) Argon, $Z = 18$ **(d)** Lanthanum, $Z = 57$

2.74 How many electrons does the element with $Z = 12$ have in its valence shell? Write the electron-dot symbol for this element.

2.75 How many valence electrons do group 4A elements have? Explain. Write a generic electron-dot symbol for elements in this group.

2.76 Identify the valence subshell occupied by electrons in beryllium and arsenic atoms.

2.77 What group in the periodic table has the valence-shell configuration $ns^2\ np^3$?

2.78 Give the number of valence electrons and draw electron-dot symbols for atoms of the following elements:

(a) Kr **(b)** C **(c)** Ca

(d) K **(e)** B **(f)** Cl

2.79 Using *n* for the number of the valence shell and write a general valence-shell configuration for the elements in group 6A and in group 2A.

CONCEPTUAL PROBLEMS

2.80 What elements in addition to helium make up the noble gas family?

2.81 Hydrogen is placed in group 1A on many periodic charts, even though it is not an alkali metal. On other periodic charts, however, hydrogen is included with group 7A even though it is not a halogen. Explain. (Hint: Draw electron-dot symbols for H and for the 1A and 7A elements.)

2.82 What is the atomic number of the yet-undiscovered element directly below francium (Fr) in the periodic table?

2.83 Give the number of electrons in each shell for lead.

2.84 Identify the highest-energy occupied subshell in atoms of the following elements:

(a) Iodine **(b)** Scandium

(c) Arsenic **(d)** Aluminum

2.85 **(a)** What is the mass (in amu and in grams) of a single atom of Carbon-12?

(b) What is the mass (in grams) of 6.02×10^{23} atoms of Carbon-12?

(c) Based on your answer to part (b), what would be the mass of 6.02×10^{23} atoms of Sodium-23?

2.86 An unidentified element is found to have an electron configuration by shell of 2 8 18 8 2. To what group and period does this element belong? Is the element a metal or a

nonmetal? How many protons does an atom of the element have? What is the name of the element? Write its electron-dot symbol.

2.87 Germanium, atomic number 32, is used in building semiconductors for microelectronic devices, and has an electron configuration by shell of 2 8 18 4.

(a) Write the electronic configuration for germanium.

(b) In what shell and orbitals are the valence electrons?

2.88 Tin, atomic number 50, is directly beneath germanium (Problem 2.87) in the periodic table. What electron configuration by shell would you expect tin to have? Is tin a metal or a nonmetal?

2.89 A blood sample is found to contain 8.6 mg/dL of Ca. How many atoms of Ca are present in 8.6 mg? The atomic mass of Ca is 40.08 amu.

2.90 What is wrong with the following electron configurations?

(a) Ni $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^{10}$

(b) N $1s^2\ 2p^5$

(c) Si $1s^2\ 2s^2\ 2p$ 

(d) Mg $1s^2\ 2s^2\ 2p^6\ 3s$ 

2.91 Not all elements follow exactly the electron-filling order described in Figure 2.6. Atoms of which elements are represented by the following electron configurations?

(a) $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^5\ 4s^1$

(b) $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^{10}\ 4s^1$

(c) $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^{10}\ 4s^2\ 4p^6\ 4d^5\ 5s^1$

(d) $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^{10}\ 4s^2\ 4p^6\ 4d^{10}\ 5s^1$

2.92 What similarities do you see in the electron configurations for the atoms in Problem 2.91? How might these similarities explain their anomalous electron configurations?

2.93 Based on the identity of the elements whose electron configurations are given in Problem 2.91, write the electron configurations for the element with atomic number $Z = 79$.

2.94 What orbital is filled last in the most recently discovered element 117?

GROUP PROBLEMS

2.95 Look up one of the experiments by the scientists discussed in the Chemistry in Action on page 78, and explain how it contributed to our understanding of atomic structure.

2.96 Do a web search to identify each of the following elements/isotopes and indicate the number of neutrons, protons, and electrons in an atom of the element/isotope:

(a) A radioactive isotope used in cancer treatments. (There may be more than one answer!)

(b) The element having the greatest density.

(c) An element with Z < 90 that is *not* found in nature.

2.97 Tellurium $(Z = 52)$ has a *lower* atomic number than iodine $(Z = 53)$, yet it has a *higher* atomic mass (127.60 amu for Te vs. 126.90 amu for I). How is this possible? Can you find any other instances in the periodic table where two adjacent elements exhibit a similar behavior, that is, the element with the lower atomic number has a higher atomic mass?

2.98 Look again at the trends illustrated in Figures 2.3 and 2.4.

(a) How do the peaks/valleys correlate with locations in the periodic table?

(b) Are there other chemical properties that also exhibit periodic trends? What are they?

3

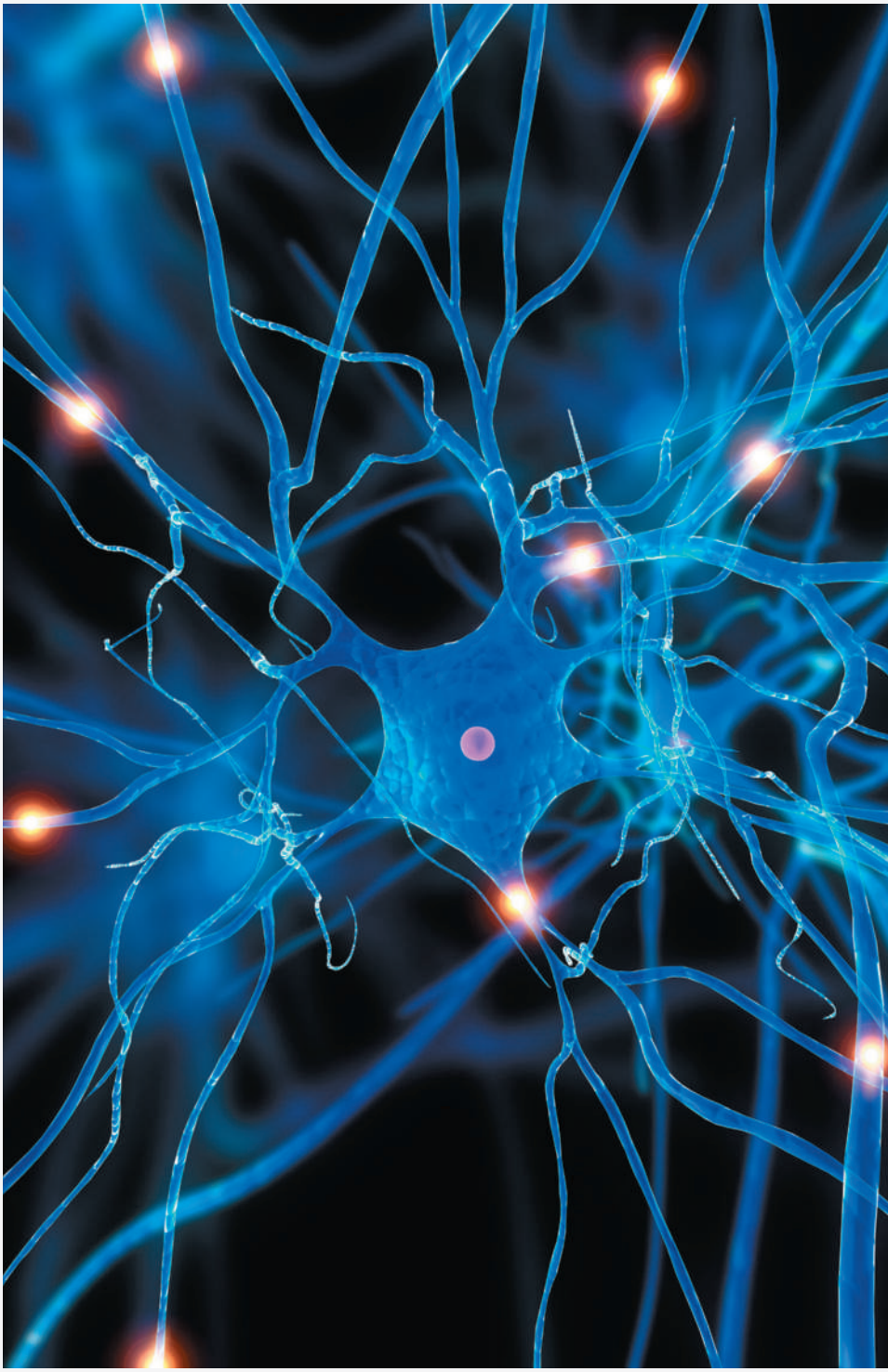
Ionic Compounds

CONTENTS

CONCEPTS TO REVIEW

A. The Periodic Table (Sections 2.4 and 2.5)

B. Electron Configurations (Sections 2.7 and 2.8)



▲ Ions play critical roles in many cellular processes, including signal transmission between nerve cells as simulated above.

In previous chapters, we mentioned the importance of various elements for good health, identifying individual elements as *macro*nutrients (needed in large amounts) or *micro*nutrients (needed in lesser amounts). Of equal significance is the chemical form of the element; what is the chemical nature of the compounds in which an element is found? Many of these macro- and micronutrients, for example, exist as *ions,* or charged particles, and play critical roles in different cells within the body. Calcium ions, for example, are necessary for strong teeth and bones; sodium and potassium ions are necessary for signal transmission in nerve cells, such as those depicted in the artistic

rendition in the chapter opening picture; and chloride ions are an important component of gastric juices found in the stomach. Disruptions in the transport or metabolism of these ions is linked to various diseases, including cystic fibrosis, neuropathy (chronic nerve pain), and osteoporosis, which we will discuss in greater detail in the Chemistry in Action feature on page 127.

There are more than 19 million known chemical compounds, ranging in size from small *diatomic* (two-atom) substances like carbon monoxide (CO) to deoxyribonucleic acid (DNA), which can contain several *billion* atoms linked together in a precise way. In the next two chapters, we will examine how atoms are held together in chemical compounds. We can describe the forces that hold atoms together as *chemical bonds*. All chemical bonds result from the electrical attraction between opposite charges—between positively charged nuclei and negatively charged electrons. As a result, the way that different elements form bonds is related to their different electron configurations and the changes that take place as each atom tries to achieve a more stable electron configuration. There are two types of chemical bonds: *ionic bonds* and *covalent bonds*. In this chapter, we look at how ions are formed, the ionic bonds that occur between ions of opposite charge, and at the behavior of ionic compounds. In the next chapter, we will look at covalent bonds.

3.1 Ions

Learning Objective:

- Describe ion formation processes and distinguish between anions and cations.

A general rule noted by early chemists is that metals, on the left side of the periodic table, tend to form compounds with nonmetals, on the right side of the table. The alkali metals of group 1A, for instance, react with the halogens of group 7A to form a variety of compounds. Sodium chloride (table salt), formed by the reaction of sodium with chlorine, is a familiar example. The names and chemical formulas of some other compounds containing elements from groups 1A and 7A include:

Potassium iodide, KI	Added to table salt to provide the iodide ion that is needed by the thyroid gland
Sodium fluoride, NaF	Added to many municipal water supplies to provide fluoride ion for the prevention of tooth decay
Sodium iodide, NaI	Used in laboratory scintillation counters to detect radiation (see Section 11.8)

The compositions and the properties of these alkali metal–halogen compounds are similar. For instance, the two elements always combine in a 1:1 ratio: one alkali metal atom for every halogen atom. Each compound has a high melting point (all are over 773.15 K or 500 °C); each is a stable, white, crystalline solid; and each is soluble in water. Furthermore, a water solution containing each compound conducts electricity, a property that gives a clue as to the kind of chemical bond holding the atoms together.

▲ A solution of sodium chloride in water conducts electricity, allowing the bulb to light.

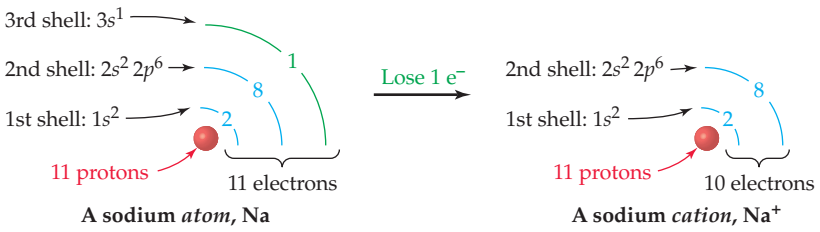
Electricity can only flow through a medium containing charged particles that are free to move. The electrical conductivity of metals, for example, results from the movement of negatively charged electrons through the metal. But what charged particles might be present in the water solutions of alkali metal–halogen compounds? To answer this question, think about the composition of atoms. Atoms are electrically neutral because they contain equal numbers of protons and electrons. By gaining or losing one or more electrons, however, an atom can be converted into a charged particle called an **ion.**

Ion An electrically charged atom or group of connected atoms.

Recall from Chapter 2 that the number of negative electrons in a neutral atom is equal to the number of positive protons in the nucleus of that atom. Therefore, the *loss* of one or more electrons from a neutral atom gives a *positively* charged ion called a **cation** (*cat*-ion). As we saw in Section 2.8, sodium and other alkali metal atoms have a single electron in their valence shell and an electron configuration symbolized as ns^1,

Cation A positively charged ion.

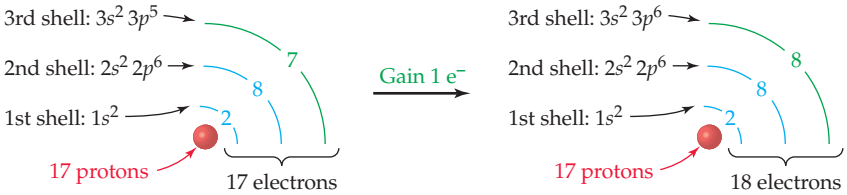
where n represents the shell number. By losing this electron, an alkali metal is converted to a positively charged cation with a stable noble gas configuration.



A sodium *atom*, Na **A sodium *cation*, Na^+**

Anion A negatively charged ion.

Conversely, the *gain* of one or more electrons by a neutral atom gives a *negatively* charged ion called an **anion** (*an*-ion). Chlorine and other halogen atoms have ns^2np^5 valence electrons and will readily gain an additional electron to fill their valence subshell with eight electrons, thereby forming negatively charged anions.



A chlorine *atom*, Cl **A chlorine *anion*, Cl^-**

LOOKING AHEAD The tendency to gain or lose electrons is not limited to atoms in ionic compounds and forms the basis of an important class of chemical reactions (redox reactions), which will be discussed in Chapter 5.

The symbol for a cation is written by adding the positive charge as a superscript to the symbol for the element; an anion symbol is written by adding the negative charge as a superscript. If one electron is lost or gained, the charge is $+1$ or -1 but the number 1 is omitted in the notation, as in Na^+ and Cl^-. If two or more electrons are lost or gained, however, the charge is ± 2 or greater and the number *is* used, as in Ca^{2+} and N^{3-}.

In the sections that follow, we will discuss the reasons why metals tend to form cations and nonmetals tend to form anions, how we can predict the charges associated with the respective ions, and how these ions combine to form compounds.

PROBLEM 3.1

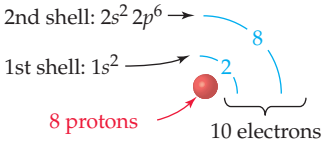
Magnesium atoms lose two electrons when they react. Write the symbol of the ion that is formed. Is it a cation or an anion?

PROBLEM 3.2

Sulfur atoms gain two electrons when they react. Write the symbol of the ion that is formed. Is it a cation or an anion?

KEY CONCEPT PROBLEM 3.3

Write the atomic symbol for the ion depicted here. Is it a cation or an anion?



3.2 Ions and the Octet Rule

Learning Objective:

- Use the octet rule and electron configurations to explain the charge associated with ions.

We have seen that alkali metal atoms have a single valence-shell electron, ns^1. The electron-dot symbol X· is consistent with this valence electron configuration. Halogens, having seven valence electrons, ns^2np^5, can be represented using :$\ddot{\text{X}}$· as the electron-dot

symbol. Noble gases can be represented as $:\ddot{\underset{\cdot\cdot}{X}}:$, since they have eight valence electrons, ns^2np^6. Both the alkali metals and the halogens are extremely reactive, undergoing many chemical reactions and forming many compounds. The noble gases, however, are quite different. They are the least reactive of all elements.

Now look at sodium chloride and similar ionic compounds. When sodium or any other alkali metal reacts with chlorine or any other halogen, the metal transfers an electron from its valence shell to the valence shell of the halogen. Sodium thereby changes its valence-shell electron configuration from $2s^22p^63s^1$ in the atom to $2s^22p^6(3s^0)$ in the Na^+ ion, and chlorine changes from $3s^23p^5$ in the atom to $3s^23p^6$ in the Cl^- ion. *As a result, both sodium and chlorine gain noble gas electron configurations, with eight valence electrons.* The Na^+ ion has eight electrons in the $n = 2$ shell, matching the electron configuration of neon. The Cl^- ion has eight electrons in the $n = 3$ shell, matching the electron configuration of argon.

$$\underset{1s^2\,2s^2\,2p^6\,3s^1}{Na} + \underset{1s^2\,2s^2\,2p^6\,3s^2\,3p^5}{Cl} \longrightarrow \underbrace{Na^+}_{\substack{1s^2\,2s^2\,2p^6 3s^0 \\ \text{Neon configuration}}} + \underbrace{Cl^-}_{\substack{1s^2\,2s^2\,2p^6\,3s^2\,3p^6 \\ \text{Argon configuration}}}$$

$$Na^{\cdot} + \cdot\ddot{\underset{\cdot\cdot}{Cl}}: \longrightarrow Na^+ + :\ddot{\underset{\cdot\cdot}{Cl}}:^-$$

Having eight valence electrons (filled *s* and *p* subshells) leads to stability and lack of chemical reactivity. In fact, observations of many chemical compounds have shown that main group elements frequently combine in such a way that each winds up with eight valence electrons, called an *electron octet*. This conclusion is summarized in a statement called the **octet rule.**

Octet rule The tendency of atoms to gain or lose electrons to achieve a stable, noble gas configuration, that is, a completely filled subshell containing eight electrons.

Main group *metals* lose electrons to form cations and attain an electron configuration like that of the noble gas just *before* them in the periodic table. Main group *nonmetals* gain electrons to form anions and an electron configuration like that of the noble gas just *after* them in the periodic table. In both cases, the product ions have filled *s* and *p* subshells with eight electrons in their valence electron shell. We can use this tendency to explain why metals form cations and nonmetals form anions, as well as to predict the most likely charge of the ions that are formed.

Worked Example 3.1 Electron Configurations: Octet Rule for Cations

Write the electron configuration of magnesium $(Z = 12)$. Show how many electrons a magnesium atom must lose to form an ion with a filled shell (eight electrons) and write the configuration of the ion. Explain the reason for the ion's charge, and write the ion's symbol.

ANALYSIS Write the electron configuration of magnesium as described in Section 2.7 and count the number of electrons in the valence shell.

SOLUTION

Magnesium has the electron configuration $1s^22s^22p^63s^2$. Since the second shell contains an octet of electrons $(2s^22p^6)$ and the third shell is only partially filled $(3s^2)$, magnesium can achieve a valence-shell octet by losing the two electrons in the 3*s* subshell. The result is formation of a doubly charged cation, Mg^{2+}, with the neon configuration:

$$Mg^{2+} \qquad 1s^22s^22p^6 \text{ (Neon configuration or [Ne])}$$

A neutral magnesium atom has 12 protons and 12 electrons. With the loss of two electrons, there is an excess of two protons, accounting for the +2 charge of the ion, Mg^{2+}.

Worked Example 3.2 Electron Configurations: Octet Rule for Anions

How many electrons must a nitrogen atom, $Z = 7$, gain to attain a noble gas configuration? Write the electron-dot and ion symbols for the ion formed.

ANALYSIS Write the electron configuration of nitrogen, and identify how many more electrons are needed to reach a noble gas configuration.

SOLUTION

Nitrogen, a group 5A element, has the electron configuration $1s^2 2s^2 2p^3$. The second shell contains five electrons $(2s^2 2p^3)$ and needs three more to reach an octet. The result is formation of a triply charged anion, N^{3-}, with eight valence electrons, matching the neon configuration:

$$N^{3-} \qquad 1s^2 2s^2 2p^6 \quad \text{(Neon configuration)} \qquad :\ddot{N}:^{3-}$$

PROBLEM 3.4

Write the electron configuration of potassium, $Z = 19$, and show how a potassium atom can attain a noble gas configuration.

PROBLEM 3.5

How many electrons must an aluminum atom, $Z = 13$, lose to attain a noble gas configuration? Write the symbol for the ion formed.

KEY CONCEPT PROBLEM 3.6

Which atom in the reaction depicted here gains electrons and which loses electrons? Draw the electron-dot symbols for the resulting ions.

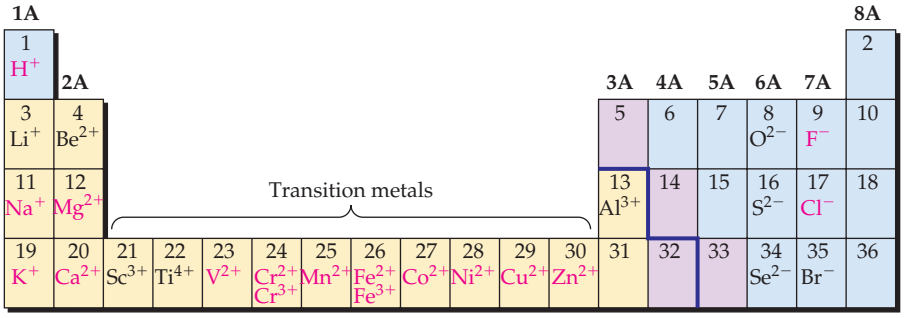
$$X: + \cdot\ddot{Y}\cdot \longrightarrow ?$$

3.3 Ions of Some Common Elements

Learning Objective:

- Use the periodic table to predict the charge associated with ions of main group elements.

The periodic table is the key to understanding and remembering which elements form ions and which do not. As shown in Figure 3.1, atoms of elements in the same group tend to form ions of the same charge. The metals of groups 1A–3A, for example, form cations with charges identical to their group number (i.e., 1A elements form cations with +1 charge, etc.). The ions of these elements all have noble gas configurations as a



▶ Figure 3.1
Common ions formed by elements in the first four periods.
Ions important in biological chemistry are shown in magenta.

result of electron loss from their valence *s* subshells. (Note in the following equations that the electrons being lost are shown as products.)

Group 1A: $M\cdot \rightarrow M^+ + e^-$
$(M = Li, Na, K, Rb, or\ Cs)$

Group 2A: $M: \rightarrow M^{2+} + 2e^-$
$(M = Be, Mg, Ca, Sr, Ba, or\ Ra)$

Four of these ions, Na^+, K^+, Mg^{2+}, and Ca^{2+}, are present in body fluids, where they play extremely important roles in biochemical processes.

The only group 3A element commonly encountered in ionic compounds is aluminum, which forms Al^{3+} by loss of three electrons from its valence *s* and *p* subshells. Aluminum is not thought to be an essential element in the human diet, although it is known to be present in some organisms.

As we move to the right, elements in Group 4A would have to gain or lose too many electrons to achieve an octet. Therefore, the first three elements in groups 4A (C, Si, Ge) and 5A (N, P, As) do not ordinarily form cations or anions. The bonding of these elements is largely covalent and will be described in Chapter 4. Carbon, in particular, is the key element on which life is based. Together with hydrogen, nitrogen, phosphorus, and oxygen, carbon is present in all the essential biological compounds that we will be describing throughout the latter half of this book.

The group 6A elements, oxygen and sulfur, form ions having noble gas configurations, achieved by gaining two electrons:

Group 6A: $\cdot\ddot{O}\cdot + 2\,e^- \longrightarrow :\ddot{O}:^{2-}$

$\cdot\ddot{S}\cdot + 2\,e^- \longrightarrow :\ddot{S}:^{2-}$

The halogens can form ions by gaining one electron:

Group 7A: $\cdot\ddot{X}: + e^- \longrightarrow :\ddot{X}:^-$
(X = F, Cl, Br, I)

Transition metals lose electrons to form cations, some of which are present in the human body. The charges of transition metal cations are not as predictable as those of main group elements, however, because many transition metal atoms can lose one or more *d* electrons in addition to losing valence *s* electrons. For example, iron $(\ldots 3s^2 3p^6 3d^6 4s^2)$ forms Fe^{2+} by losing two electrons from the 4*s* subshell and also forms Fe^{3+} by losing an additional electron from the 3*d* subshell. Looking at the electron configuration for iron shows why the octet rule is limited to main group elements: transition metal cations generally do not have noble gas configurations because they would have to lose *all* their *d* electrons.

Important Points about Ion Formation and the Periodic Table:

- **Metals form cations by losing one or more electrons.**
  - Group 1A and 2A metals form +1 and +2 ions, respectively (e.g., Li^+ and Mg^{2+}), to achieve a noble gas configuration.
  - Transition metals can form cations of more than one charge (e.g., Fe^{2+} and Fe^{3+}) by losing a combination of valence-shell *s* electrons and inner-shell *d* electrons.
- **Reactive nonmetals form anions by gaining one or more electrons to achieve a noble gas configuration.**
  - Group 6A nonmetals oxygen and sulfur form the anions O^{2-} and S^{2-}.
  - Group 7A elements (the halogens) form −1 ions, for example, F^- and Cl^-.
- **Group 8A elements (the noble gases) are unreactive.**
- **Ionic charges of main group elements can be predicted using the group number and the octet rule.**
  - For 1A and 2A metals: cation charge = group number
  - For nonmetals in groups 5A, 6A, and 7A: anion charge = 8 − (group number)

Worked Example 3.3 Formation of Ions: Gain/Loss of Valence Electrons

Which of the following ions is likely to form?
(a) S^{3-} **(b)** Si^{2+} **(c)** Sr^{2+}

ANALYSIS Count the number of valence electrons in each ion. For main group elements, only ions with a valence octet of electrons are likely to form.

SOLUTION

(a) Sulfur (S) is in group 6A, has six valence electrons, and needs only two more to reach an octet. Gaining two electrons gives an S^{2-} ion with a noble gas configuration but gaining three electrons does not. The S^{3-} ion is, therefore, unlikely to form.

(b) Silicon (Si) is a nonmetal in group 4A. Like carbon, it does not form ions because it would have to gain or lose too many electrons (four) to reach a noble gas electron configuration. The Si^{2+} ion does not have an octet and will not form.

(c) Strontium (Sr), a metal in group 2A, has only two outer-shell electrons and can lose both to reach a noble gas configuration. The Sr^{2+} ion has an octet and, therefore, forms easily.

PROBLEM 3.7

Iron is an important component of hemoglobin, a large biomolecule responsible for oxygen transport (Chapters 18 and 19). Find the common ions formed by iron in Figure 3.1. Which ion of iron is found in hemoglobin, and what is its electron configuration?

PROBLEM 3.8

Write symbols, both with and without electron dots, for the ions formed by the following processes:

(a) Gain of two electrons by selenium
(b) Loss of two electrons by barium
(c) Gain of one electron by bromine

PROBLEM 3.9

Blood serum in healthy adults normally contains approximately 3.2 mg/mL of sodium ions (Na^+) and approximately 3.5 mg/mL of chloride ions (Cl^-). How many milliliters of blood serum would be needed to obtain 1.0 g of Na^+? To obtain 1.0 g of Cl^-?

3.4 Periodic Properties and Ion Formation

Learning Objective:

- Explain the formation of anions and cations based on periodic trends.

As we have seen, metals on the left side of the periodic table tend to lose electrons, whereas nonmetals on the right side of the periodic table tend to gain electrons. But how does this trend change as you move across a row in the periodic table and why? The answers are related to the ease with which an atom gains or loses an electron.

The ease with which an atom *loses* an electron to form a positively charged cation is measured by a property called the atom's **ionization energy,** defined as the energy required to remove one electron from a single atom in the gaseous state. Conversely, the ease with which an atom *gains* an electron to form a negatively charged anion is

Ionization energy The energy required to remove one valence electron from a single atom in the gaseous state.

measured by a property called **electron affinity,** defined as the energy released on adding an electron to a single atom in the gaseous state.

Electron affinity The energy released on adding an electron to a single atom in the gaseous state.

$$\textbf{Ionization energy}\ (\text{energy is added}) \quad \text{Atom} + \text{Energy} \xrightarrow{\text{Lose } e^-} \text{Cation} + \text{Electron}$$

$$\textbf{Electron affinity}\ (\text{energy is released}) \quad \text{Atom} + \text{Electron} \xrightarrow{\text{Gain } e^-} \text{Anion} + \text{Energy}$$

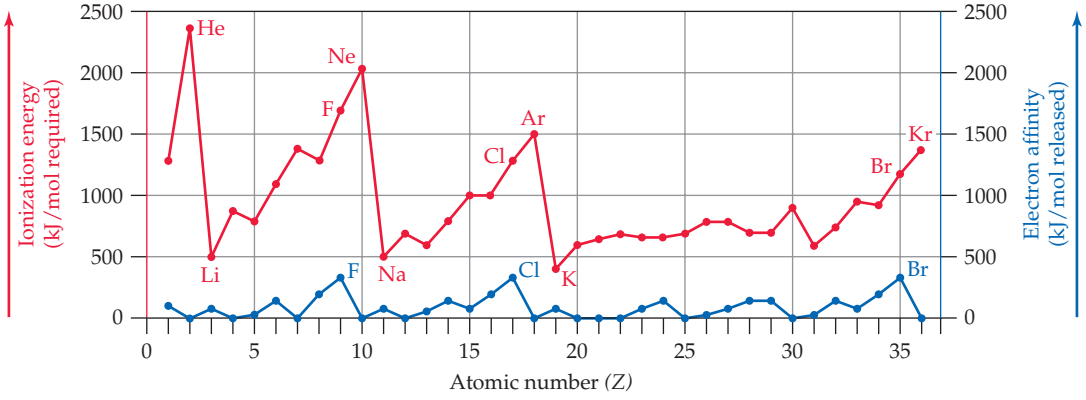
The relative magnitudes of ionization energies and electron affinities for elements in the first four rows of the periodic table are shown in Figure 3.2. Note the repeating pattern in Figure 3.2, beginning with small ionization energies for the 1A elements and a gradual increase as we move across a row, ending with very large ionization energies for the noble gases. Because ionization energy measures the amount of energy that must be *added* to pull an electron away from a neutral atom, the small values shown in Figure 3.2 for alkali metals (Li, Na, K) and other elements on the left side of the periodic table mean that these elements lose an electron easily. Conversely, the large values shown for halogens (F, Cl, Br) and noble gases (He, Ne, Ar, Kr) on the right side of the periodic table mean that these elements do not lose an electron easily. Another interesting feature in Figure 3.2 is the energy plateau after potassium (K). Remember from Chapter 2 that the electronic configuration for the fourth row transition metals is $4s^2\ 3d^x$; the ionization energy is related to the loss of a $4s$ electron, whose energy level remains fairly constant as you move across the row.

Electron affinities, in contrast, measure the amount of energy *released* when an atom gains an electron. Although electron affinities are small compared to ionization energies, the halogens nevertheless have the largest values and, therefore, gain an electron most easily, whereas metals have the smallest values and do not gain an electron easily.

Alkali metal
- Small ionization energy—electron easily lost
- Small electron affinity—electron not easily gained
- *Net result:* Cation formation is favored

Halogen
- Large ionization energy—electron not easily lost
- Large electron affinity—electron easily gained
- *Net result:* Anion formation is favored

As noted in Section 3.3 and illustrated in Figure 3.2, the main group elements near the *middle* of the periodic table—boron ($Z = 5$, group 3A), carbon ($Z = 6$, group 4A),



▲ **Figure 3.2**

Relative ionization energies (red) and electron affinities (blue) for elements in the first four rows of the periodic table. Those elements having a value of zero for electron affinity do not accept an electron. Note that the alkali metals (Li, Na, K) have the lowest ionization energies and lose an electron most easily, whereas the halogens (F, Cl, Br) have the highest electron affinities and gain an electron most easily. The noble gases (He, Ne, Ar, Kr) neither gain nor lose an electron easily.

and nitrogen ($Z = 7$, group 5A)—neither lose nor gain electrons easily and thus do not readily form ions. In the next chapter, we will see that these elements tend to form covalent bonds instead.

Worked Example 3.4 Periodic Trends: Ionization Energy

Look at the periodic trends in Figure 3.2, and predict where the ionization energy of rubidium is likely to fall on the chart.

ANALYSIS Identify the group number of rubidium (group 1A), and find where other members of the group appear in Figure 3.2.

SOLUTION
Rubidium (Rb) is the alkali metal below potassium (K) in the periodic table. Since the alkali metals Li, Na, and K all have ionization energies near the bottom of the chart, the ionization energy of rubidium is probably similar.

Worked Example 3.5 Periodic Trends: Formation of Anions and Cations

Which element is likely to lose an electron more easily, Mg or S?

ANALYSIS Identify the group numbers of the elements, and find where members of those groups appear in Figure 3.2.

SOLUTION
Magnesium, a group 2A element on the left side of the periodic table, has a relatively low ionization energy and loses an electron easily. Sulfur, a group 6A element on the right side of the table, has a higher ionization energy and loses an electron less easily.

PROBLEM 3.10

Look at the periodic trend for ionization energies in Figure 3.2. How would you expect the ionization energies for Rb and Cs to compare with the other members of the 1A group? Look up these values to confirm your expectation.

PROBLEM 3.11

Which element in the following pairs is likely to lose an electron more easily?

(a) Be or B **(b)** Ca or Co **(c)** Sc or Se

PROBLEM 3.12

Which element in the following pairs is likely to gain an electron more easily?

(a) H or He **(b)** S or Si **(c)** Cr or Mn

3.5 Naming Monoatomic Ions

Learning Objective:

- Name common monoatomic anions and cations.

Main group metal cations in groups 1A, 2A, and 3A are named by identifying the metal, followed by the word *ion,* as in the following examples:

K^+	Mg^{2+}	Al^{3+}
Potassium ion	Magnesium ion	Aluminum ion

It is sometimes a little confusing to use the same name for both a metal and its ion, and you may occasionally have to stop and think about what is meant. For example, it is common practice in nutrition and health-related fields to talk about sodium or potassium

in the bloodstream. Because both sodium and potassium *metals* react violently with water, however, they cannot possibly be present in blood as neutral atoms. The references are to dissolved sodium and potassium *ions*.

Transition metals, such as iron or chromium, and many metals found in the *p*-block, such as tin and lead, can form more than one type of cation. To avoid confusion, a method is needed to differentiate between ions of these metals. Two systems are used. The first is an old system that gives the ion with the smaller charge the word ending *-ous* and the ion with the larger charge the word ending *-ic*.

CHEMISTRY IN ACTION

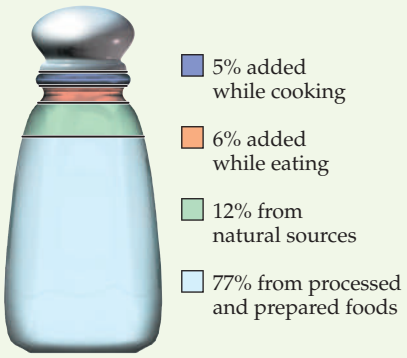
Salt

If you are like most people, you feel a little guilty about reaching for the salt shaker at mealtime. The notion that high salt intake and high blood pressure go hand in hand is surely among the most highly publicized pieces of nutritional lore ever to appear.

Although sodium is a macronutrient that we need—it plays a critical role in charge balance and ion transport in cell membranes—too much sodium has been linked to both hypertension and kidney ailments. Hypertension can be caused by a number of factors, including congenital conditions, reactions to some medications, and certain diseases, including thyroid problems. Regardless of the cause, hypertension can be aggravated by high salt consumption and, in extreme cases, must be controlled by medication and dietary restrictions. The recommended daily intake (RDI) for sodium is 2300 mg, which translates to roughly 4 g of salt. However, the average adult in most industrialized countries consumes over twice this amount, with most of it coming from processed foods.

What should an individual do? The best answer, as in so many things, is to use moderation and common sense. People with hypertension should make a strong effort to lower their sodium intake; others might be well advised to choose unsalted snacks, monitor their consumption of processed food, and read nutrition labels for sodium content.

CIA Problem 3.1 What is the RDI for sodium for adults, and what amount of table salt (in grams) contains this quantity of sodium?



CIA Problem 3.2 In the beginning of this chapter, we identified potassium iodide (KI) as an additive in table salt to provide the iodide ion needed by the thyroid. Look up the approximate amount of iodide in iodized salt and the daily adult intake of iodide recommended by the U.S. Food and Drug Administration (FDA).

The second is a newer system in which the charge on the ion is given as a Roman numeral in parentheses right after the metal name. For example:

	Cr^{2+}	Cr^{3+}
Old name:	Chrom*ous* ion	Chrom*ic* ion
New name:	Chromium(II) ion	Chromium(III) ion

We will generally emphasize the new system in this book, but it is important to understand both systems because the old system is often found on labels of commercially supplied chemicals. The small differences between the names in either system illustrate the importance of reading a name very carefully before using a chemical.

There are significant differences between compounds consisting of the same two elements but having different charges on the cation. In treating iron-deficiency anemia, for example, iron(II) compounds are preferable because the body absorbs them considerably better than iron(III) compounds.

The names of some common transition metal cations are listed in Table 3.1. Notice that the old names of the copper, iron, and tin ions are derived from their Latin names *(cuprum, ferrum,* and *stannum).*

Table 3.1 Names of Some Transition Metal Cations

Element	Symbol	Old Name	New Name
Chromium	Cr^{2+} Cr^{3+}	Chromous Chromic	Chromium(II) Chromium(III)
Copper	Cu^{+} Cu^{2+}	Cuprous Cupric	Copper(I) Copper(II)
Iron	Fe^{2+} Fe^{3+}	Ferrous Ferric	Iron(II) Iron(III)
Mercury	*Hg_2^{2+} Hg^{2+}	Mercurous Mercuric	Mercury(I) Mercury(II)
Tin	Sn^{2+} Sn^{4+}	Stannous Stannic	Tin(II) Tin(IV)

*This cation is composed of two mercury atoms, each of which has an average charge of +1.

Table 3.2 Names of Some Common Anions

Element	Symbol	Name
Bromine	Br^{-}	Bromide ion
Chlorine	Cl^{-}	Chloride ion
Fluorine	F^{-}	Fluoride ion
Iodine	I^{-}	Iodide ion
Oxygen	O^{2-}	Oxide ion
Sulfur	S^{2-}	Sulfide ion

Anions are named by replacing the ending of the element name with *-ide,* followed by the word *ion* (Table 3.2). For example, the anion formed by fluor*ine* is the fluor*ide* ion, and the anion formed by sulf*ur* is the sulf*ide* ion.

PROBLEM 3.13

Name the following ions:

(a) Cu^{2+} **(b)** F^{-} **(c)** Mg^{2+} **(d)** S^{2-}

PROBLEM 3.14

Write the symbols for the following ions:

(a) Silver(I) ion **(b)** Iron(II) ion
(c) Cuprous ion **(d)** Telluride ion

PROBLEM 3.15

Ringer's solution is used intravenously to adjust ion concentrations in body fluids. Look up the composition of Ringer's solution and identify the major ions it contains. Give the names and symbols of these ions (including the ionic charge).

3.6 Polyatomic Ions

Learning Objective:

- Identify the name, formula, and charge of common polyatomic ions.

Polyatomic ion An ion that is composed of more than one atom.

Ions that are composed of more than one atom are called **polyatomic ions.** Most polyatomic ions contain oxygen and another element, and their chemical formulas include subscripts to show how many of each type of atom are present. Sulfate ion, for example, is composed of one sulfur atom and four oxygen atoms and has a −2 charge: SO_4^{2-}. The atoms in a polyatomic ion are held together by covalent bonds, which will be discussed in Chapter 4, and the entire group of atoms acts as a single unit. A polyatomic ion is charged because it contains a total number of electrons different from the total number of protons in the combined atoms. For example, the individual atoms in the sulfate ion

contribute 48 electrons—the S atom has 16 electrons, and the four O atoms contain 8 electrons each. The sulfate ion, however, has two extra electrons for a total of 50, hence the −2 charge.

The most common polyatomic ions are listed in Table 3.3. Note that the ammonium ion, NH_4^+, and the hydronium ion, H_3O^+, are the only cations; all the others are anions. These ions are encountered so frequently in chemistry, biology, and medicine that there is no alternative but to memorize their names and formulas. Fortunately, there are only a few of them.

Table 3.3 Some Common Polyatomic Ions

Name	Formula	Name	Formula
Hydronium ion	H_3O^+	Nitrate ion	NO_3^-
Ammonium ion	NH_4^+	Nitrite ion	NO_2^-
Acetate ion	$CH_3CO_2^-$	Oxalate ion	$C_2O_4^{2-}$
Carbonate ion	CO_3^{2-}	Permanganate ion	MnO_4^-
Hydrogen carbonate ion	HCO_3^-	Phosphate ion	PO_4^{3-}
Chromate ion	CrO_4^{2-}	Hydrogen phosphate ion (biphosphate ion)	HPO_4^{2-}
Dichromate ion	$Cr_2O_7^{2-}$	Dihydrogen phosphate ion	$H_2PO_4^-$
Cyanide ion	CN^-	Sulfate ion	SO_4^{2-}
Hydroxide ion	OH^-	Hydrogen sulfate ion (bisulfate ion)	HSO_4^-
Hypochlorite ion	OCl^-	Sulfite ion	SO_3^{2-}

Note in Table 3.3 that several pairs of ions—CO_3^{2-} and HCO_3^-, for example—are related by the presence or absence of a hydrogen ion, H^+. In such instances, the ion with the hydrogen is sometimes named using the prefix *bi-*. Thus, CO_3^{2-} is the carbonate ion, and HCO_3^- is the hydrogen carbonate ion; similarly, SO_4^{2-} is the sulfate ion, and HSO_4^- is the bisulfate ion.

PROBLEM 3.16

Name the following ions:

(a) NO_3^- **(b)** CN^- **(c)** OH^- **(d)** HPO_4^{2-}

PROBLEM 3.17

Which of the biologically important ions (see the following Chemistry in Action feature) belong to Group 1A? To Group 2A? To the transition metals? To the halogens? Which are polyatomic?

CHEMISTRY IN ACTION

Biologically Important Ions

The human body requires many different ions for proper functioning. Several of these ions, such as Ca^{2+}, Mg^{2+}, and HPO_4^{2-}, are used as structural materials in bones and teeth in addition to having other essential functions. Although 99% of Ca^{2+} is contained in bones and teeth, small amounts in body fluids play a vital role in transmission of nerve impulses. Other ions, including essential transition metal ions such as Fe^{2+}, are required for specific chemical reactions in the body. And still others, such as K^+, Na^+, and Cl^-, are present in fluids throughout the body.

To maintain charge neutrality in solution, the total negative charge (from anions) must balance the total positive

(Continued)

charge (from cations). Several monatomic anions, and several polyatomic anions, especially HCO_3^- and HPO_4^{2-}, are present in body fluids where they help balance the cation charges. Some of the most important ions and their functions are shown in the accompanying table.

Some Biologically Important Ions

Ion	Location	Function	Dietary Source
Ca^{2+}	Outside cell; 99% of Ca^{2+} is in bones and teeth as $Ca_3(PO_4)_2$ and $CaCO_3$	Bone and tooth structure; necessary for blood clotting, muscle contraction, and transmission of nerve impulses	Milk, whole grains, leafy vegetables
Fe^{2+}	Blood hemoglobin	Transports oxygen from lungs to cells	Liver, red meat, leafy green vegetables
K^+	Fluids inside cells	Maintain ion concentrations in cells; regulate insulin release and heartbeat	Milk, oranges, bananas, meat
Na^+	Fluids outside cells	Protect against fluid loss; necessary for muscle contraction and transmission of nerve impulses	Table salt, seafood
Mg^{2+}	Fluids inside cells; bone	Present in many enzymes; needed for energy generation and muscle contraction	Leafy green plants, seafood, nuts
Cl^-	Fluids outside cells; gastric juice	Maintain fluid balance in cells; help transfer CO_2 from blood to lungs	Table salt, seafood
HCO_3^-	Fluids outside cells	Control acid–base balance in blood	By-product of food metabolism
HPO_4^{2-}	Fluids inside cells; bones and teeth	Control acid–base balance in cells	Fish, poultry, milk

CIA Problem 3.3 Where are most of the calcium ions found in the body?

CIA Problem 3.4 Excess sodium ion is considered hazardous, but a certain amount is necessary for normal body functions. What is the purpose of sodium in the body?

3.7 Ionic Bonds

Learning Objective:

- Explain the nature of the ionic bonds holding ions together in ionic compounds.

Ionic bond The electrical attractions between ions of opposite charge in an ionic compound.

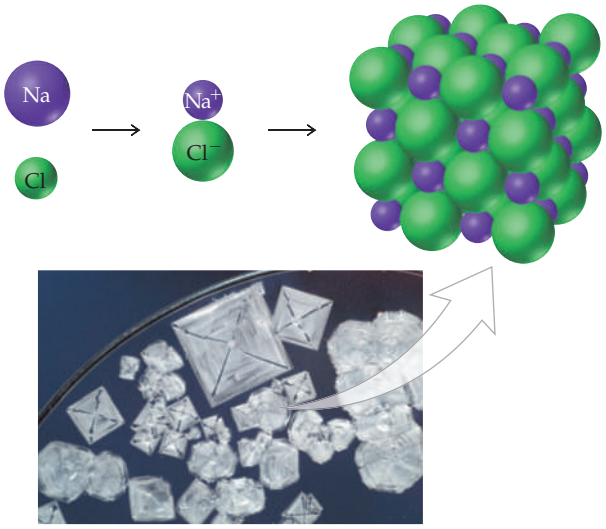
Look again at the reaction between sodium and chlorine introduced in Section 3.2. When sodium reacts with chlorine, the product is sodium chloride, a compound completely unlike either of the elements from which it is formed. Sodium is a soft, silvery metal that reacts violently with water, and chlorine is a corrosive, poisonous, green gas (Figure 3.3a). When chemically combined, however, an electron is transferred from the sodium atom to the chlorine atom to produce our familiar table salt containing Na^+ ions and Cl^- ions. Because opposite electrical charges attract each other, the positive Na^+ ion and negative Cl^- ion are held together by an **ionic bond.**

The product that results—sodium chloride (NaCl)—is electrically neutral because the positive charge of each Na^+ ion is balanced by the negative charge of each Cl^- ion. When a vast number of sodium atoms transfer electrons to an equally vast number of chlorine atoms, a visible crystal of sodium chloride results. In this crystal, equal numbers of Na^+ and Cl^- ions are packed together in a regular arrangement. Each positively charged Na^+ ion is surrounded by six negatively charged Cl^- ions, and each Cl^- ion is

(a) (b)

◂ **Figure 3.3**
(a) Chlorine is a toxic green gas, sodium is a reactive metal, and sodium chloride is a harmless white solid. (b) Sodium metal burns with an intense yellow flame when immersed in chlorine gas, yielding white sodium chloride "smoke."

surrounded by six Na^+ ions (Figure 3.4). This packing arrangement allows each ion to be stabilized by the attraction of unlike charges on its six nearest-neighbor ions, while being as far as possible from ions of like charge.



▲ **Figure 3.4**
The arrangement of Na^+ and Cl^- ions in a sodium chloride crystal.
Each positively charged Na^+ ion is surrounded by six negatively charged Cl^- ions, and each Cl^- ion is surrounded by six Na^+ ions. The crystal is held together by ionic bonds—the attraction between oppositely charged ions that are formed by the transfer of electrons between atoms.

Because of the three-dimensional arrangement of ions in a sodium chloride crystal, we cannot speak of specific ionic bonds between specific pairs of ions. Rather, there are many ions attracted by ionic bonds to their nearest neighbors. We therefore speak of the whole NaCl crystal as being an **ionic solid** and of such compounds as being **ionic compounds.** The same is true of all compounds composed of ions.

Ionic solid A crystalline solid held together by ionic bonds.

Ionic compound A compound that contains ionic bonds.

3.8 Formulas of Ionic Compounds

Learning Objective:

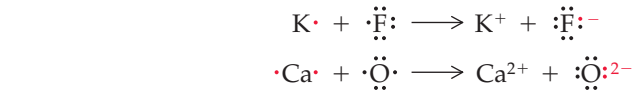
- Determine the formula of ionic compounds based on the formulas and charges of the cations and anions.

Since all chemical compounds are neutral, it is relatively easy to figure out the formulas of ionic compounds. Once the ions are identified, all we need to do is decide how many ions of each type give a total charge of zero. Thus, the chemical formula of an ionic compound tells the ratio of anions and cations.

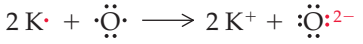
If the ions have the same charge, only one of each ion is needed:

$$K^+ \text{ and } F^+ \text{ form } KF$$
$$Ca^{2-} \text{ and } O^{2-} \text{ form } CaO$$

This makes sense when we look at how many electrons must be gained or lost by each atom in order to satisfy the octet rule. For the formation of KF and CaO, electrons must be transferred from the metals to the nonmetals to form their respective cations and anions. This process can be represented as:

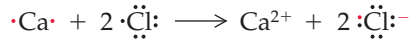


For each case, the electrons being transferred are represented in red, and each of the product ions has an electron configuration equivalent to a noble gas (i.e., a complete octet). The charges on the anions and cations are equal, but opposite in sign, so the charges cancel. If the ions have different charges, however, unequal numbers of anions and cations must combine in order to have a net charge of zero. When potassium and oxygen combine, for example, it takes two K^+ ions to balance the -2 charge of the O^{2-} ion. Put another way, it takes two K atoms to provide the two electrons needed in order to complete the octet for the O atom:



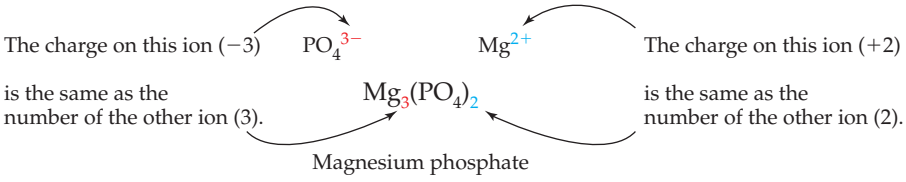
$$2\,K^+ \text{ and } O^{2-} \text{ form } K_2O$$

The situation is reversed when a Ca^{2+} ion reacts with a Cl^- ion. One Ca atom can provide two electrons; each Cl atom requires only one electron to achieve a complete octet. Thus, there is one Ca^{2+} cation for every two Cl^- anions:



$$Ca^{2+} \text{ and } 2\,Cl^- \text{ form } CaCl_2$$

It sometimes helps when writing the formulas for an ionic compound to remember that, when the two ions have different charges, the number of one ion is equal to the charge on the other ion. In magnesium phosphate, for example, the charge on the magnesium ion is +2 and the charge on the polyatomic phosphate ion is −3. Thus, there must be three magnesium ions with a total charge of $3 \times (+2) = +6$ and two phosphate ions with a total charge of $2 \times (-3) = -6$ for overall neutrality.

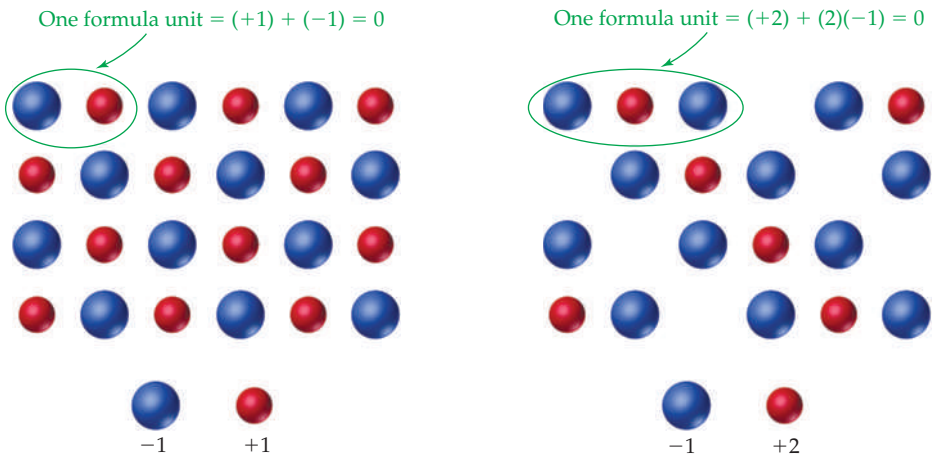


The formula of an ionic compound shows the lowest possible ratio of atoms in the compound and is thus known as a *simplest formula*. Because there is no such thing as a single neutral *particle* of an ionic compound, however, we use the term **formula unit** to identify the smallest possible neutral *unit* (Figure 3.5). For NaCl, the formula unit is one Na^+ ion and one Cl^- ion; for K_2SO_4, the formula unit is two K^+ ions and one SO_4^{2-} ion; for CaF_2, the formula unit is one Ca^{2+} ion and two F^- ions; and so on.

Formula unit The formula that identifies the smallest neutral unit of an ionic compound.

Once the number and kinds of ions in a compound are known, the formula is written using the following rules:

- List the cation first and the anion second; for example, NaCl rather than ClNa.
- Do not write the charges of the ions; for example, KF rather than K^+F^-.
- Use parentheses around a polyatomic ion formula if it has a subscript; for example, $Al_2(SO_4)_3$ rather than Al_2SO_{43}.



◀ **Figure 3.5**
Formula units of ionic compounds. The sum of charges on the ions in a formula unit equals zero.

Worked Example 3.6 Ionic Compounds: Writing Formulas

Write the formula for the compound formed by calcium ions and nitrate ions.

ANALYSIS Knowing the formula and charges on the cation and anion (Figure 3.1 and Table 3.3), we determine how many of each are needed to yield a neutral formula (zero charge) for the ionic compound.

SOLUTION
The two ions are Ca^{2+} and NO_3^-. Two nitrate ions, each with a −1 charge, will balance the +2 charge of the calcium ion.

$$Ca^{2+} \quad \text{Charge} = 1 \times (+2) = +2$$
$$2NO_3^- \quad \text{Charge} = 2 \times (-1) = -2$$

Since there are two ions, the nitrate formula must be enclosed in parentheses:

$$Ca(NO_3)_2 \quad \text{Calcium nitrate}$$

PROBLEM 3.18

Write the formulas for the ionic compounds that are formed for each of the following ion combinations:

(a) Iodide ion and magnesium ion
(b) Oxide ion and aluminum ion
(c) Phosphate ion and Iron(II)
(d) Sulfate ion and Chromium(III)

PROBLEM 3.19

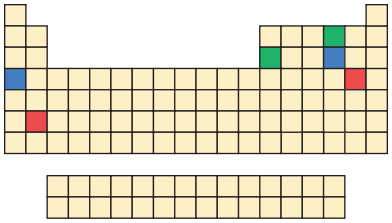
The ionic compound containing ammonium ion and carbonate ion gives off the odor of ammonia, a property put to use in smelling salts for reviving someone who has fainted. Write the formula for this compound.

PROBLEM 3.20

An *astringent* is a compound that causes proteins in blood, sweat, and other body fluids to coagulate, a property put to use in antiperspirants. Two safe and effective astringents are the ionic compounds of aluminum with sulfate ion and with acetate ion. Write the formulas of both.

KEY CONCEPT PROBLEM 3.21

Three ionic compounds are represented on this periodic table—red cation with red anion, blue cation with blue anion, and green cation with green anion. Give a likely formula for each compound.



HANDS-ON CHEMISTRY 3.1

Obtain a set of Lego building blocks and separate them into groups that are one, two, and three units long (if you do not have access to a physical set of blocks, visit www.buildwithchrome.com/builder). The blocks will represent anions and cations that have charges of 1, 2, and 3, respectively. If possible, try to have multiple colors within each group. Label the blocks in each group as follows:

–*One unit long:* Label as Na^+, K^+, Cl^-, and NO_3^-.
–*Two units long:* Label as Mg^{2+}, Ca^{2+}, Fe^{2+}, O^{2-}, and SO_4^{2-}.
–*Three units long:* Label as Al^{3+}, Fe^{3+}, N^{3-}, and PO_4^{3-}.

Try to have at least three blocks for each ion in a given group and, if possible, keep the colors consistent for a given ion; for example, let all Na^+ ions be black, all Cl^- ions be yellow, all O^{2-} ions be blue, and so on.

Using the blocks, assemble the following compounds by matching anion and cation blocks. Starting with the cation block, connect an anion on top of it. If the anion layer is not long enough for the two layers to match up exactly, add another anion of the same type beside it on top of the cation layer. If the anion layer extends over the end of the cation layer, add another cation to the bottom layer. When the cation and anion layers match exactly in length, count how many of the cation and anion blocks were necessary to determine the formula of the ionic compound.

Try building the compounds suggested next, or make up your own combinations. Just be sure that each compound has a cation and an anion!

a) Cation = Na^+ Anion = SO_4^{2-}
b) Cation = Fe^{2+} Anion = NO_3^-
c) Cation = Mg^{2+} Anion = PO_4^{3-}
d) Cation = Fe^{3+} Anion = O^{2-}

3.9 Naming Ionic Compounds

Learning Objective:

- Based on the cations and anions in the chemical formula, write the name of ionic compounds.

Ionic compounds are named by citing first the cation and then the anion, with a space between words. There are two kinds of ionic compounds, and the rules for naming them are slightly different.

Type I: Ionic compounds containing cations of main group elements (1A, 2A, aluminum). Since the charges on these cations do not vary, we do not need to specify the charge on the cation as discussed in Section 3.5. For example, NaCl is sodium chloride and $MgCO_3$ is magnesium carbonate.

Type II: Ionic compounds containing metals that can exhibit more than one charge. Since some metals, including the transition metals, often form more than one ion, we need to specify the charge on the cation in these compounds. Either the old *(-ous, -ic)* or the new (Roman numerals) system described in Section 3.5 can be used. Thus, $FeCl_2$ is called iron(II) chloride (or ferrous chloride) and $FeCl_3$ is called iron(III) chloride (or ferric chloride). Note that we do *not* name these compounds iron *di*chloride or iron *tri*-chloride—once the charge on the metal is known, the number of anions needed to yield a neutral compound is also known and does not need to be included as part of the compound name. Table 3.4 lists some common ionic compounds and their uses.

Table 3.4 Some Common Ionic Compounds and Their Applications

Chemical Name (Common Name)	Formula	Applications
Ammonium carbonate	$(NH_4)_2CO_3$	Smelling salts
Calcium hydroxide (hydrated lime)	$Ca(OH)_2$	Mortar, plaster, whitewash
Calcium oxide (lime)	CaO	Lawn treatment, industrial chemical
Lithium carbonate (lithium)	Li_2CO_3	Treatment of bipolar disorder
Magnesium hydroxide (milk of magnesia)	$Mg(OH)_2$	Antacid
Magnesium sulfate (Epsom salts)	$MgSO_4$	Laxative, anticonvulsant
Potassium permanganate	$KMnO_4$	Antiseptic, disinfectant*
Potassium nitrate (saltpeter)	KNO_3	Fireworks, matches, and desensitizer for teeth
Silver nitrate	$AgNO_3$	Antiseptic, germicide
Sodium hydrogen carbonate (baking soda)	$NaHCO_3$	Baking powder, antacid, mouthwash, deodorizer
Sodium hypochlorite	NaOCl	Disinfectant, active ingredient in household bleach
Zinc oxide	ZnO	Skin protection, in calamine lotion

*Antiseptics and disinfectants can also be harmful or toxic to nonharmful microorganisms but are used specifically to prevent infection from harmful microorganisms.

Because the formula unit for an ionic compound must be neutral, we can unambiguously write the formula from the name of the compound and vice versa. As we shall see in Chapter 4, covalent bonding between atoms can produce a much greater variety of compounds. The rules for naming covalent compounds must be able to accommodate multiple combinations of elements (e.g., CO and CO_2).

Worked Example 3.7 Ionic Compounds: Formulas and Ionic Charges

Sodium and calcium both form a wide variety of ionic compounds. Write formulas for the following compounds:

(a) Sodium bromide and calcium bromide

(b) Sodium sulfide and calcium sulfide

(c) Sodium sulfate and calcium sulfate

(d) Sodium phosphate and calcium phosphate

ANALYSIS Using the formulas and charges for the cations and the anions (from Tables 3.2 and 3.3), we determine how many of each cation and anion are needed to yield a formula that is neutral.

SOLUTION

(a) The cations are sodium (Na) and calcium (Ca). Sodium, as a 1A metal would have a +1 charge (Na^+); calcium, as a 2A metal, would have a +2 charge (Ca^{2+}). The anion (bromide) is in group 7A and would have a −1 charge (Br^-). In order for the charges to be neutral, the respective compound formulas are NaBr and $CaBr_2$.

(b) Again, the cations are Na^+ and Ca^{2+}. The anion (sulfide) is in group 6A and would have a −2 charge. The neutral formulas are Na_2S and CaS.

(c) The cations are Na^+ and Ca^{2+}. The anion (sulfate) is a polyatomic ion with a −2 charge (SO_4^{2-}). Neutral formulas = Na_2SO_4 and $CaSO_4$.

(d) Cations = Na^+ and Ca^{2+}. The anion (phosphate) is a polyatomic ion with −3 charge (PO_4^{3-}). Neutral formulas = Na_3PO_4 and $Ca_3(PO_4)_2$.

Worked Example 3.8 Naming Ionic Compounds

Name the following compounds using Roman numerals to indicate the charges on the cations where necessary:

(a) KF **(b)** $MgCl_2$ **(c)** $AuCl_3$ **(d)** Fe_2O_3

ANALYSIS For main group metals, the charge is determined from the group number, and no Roman numerals are necessary. For transition metals, the charge on the metal can be determined from the total charge(s) on the anion(s).

—continued on next page

—continued from previous page

SOLUTION

(a) Potassium fluoride. No Roman numeral is necessary because a group 1A metal forms only one cation.

(b) Magnesium chloride. No Roman numeral is necessary because magnesium (group 2A) forms only Mg^{2+}.

(c) Gold(III) chloride. The three Cl^- ions require a +3 charge on the gold for a neutral formula. Since gold is a transition metal that can form other ions, the Roman numeral is necessary to specify the +3 charge.

(d) Iron(III) oxide. Because the three oxide anions (O^{2-}) have a total negative charge of −6, the two iron cations must have a total charge of +6. Thus, each is Fe^{3+}, and the charge on each is indicated by the Roman numeral (III).

PROBLEM 3.22

The compound Ag_2S is responsible for much of the tarnish found on silverware. Name this compound, and give the charge on the silver ion.

PROBLEM 3.23

Name the following compounds:

(a) SnO_2 **(b)** $Ca(CN)_2$ **(c)** Na_2CO_3
(d) Cu_2SO_4 **(e)** $Ba(OH)_2$ **(f)** $Fe(NO_3)_2$

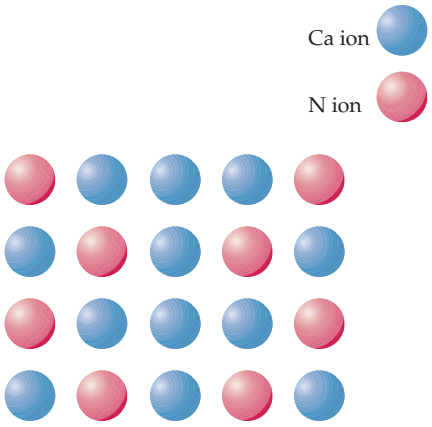
PROBLEM 3.24

Write formulas for the following compounds:

(a) Lithium phosphate
(b) Copper(II) carbonate
(c) Aluminum sulfite
(d) Cuprous fluoride
(e) Ferric sulfate
(f) Ammonium chloride

KEY CONCEPT PROBLEM 3.25

The ionic compound calcium nitride is represented here. What is the formula for calcium nitride, and what are the charges on the calcium and nitride ions?



HANDS-ON CHEMISTRY 3.2

Using the same building block set from the previous Hands-On Chemistry activity, build the following compounds and identify the chemical formula. Refer to the names of common ions in Tables 3.1–3.3 as needed.

a) Chromic phosphate
b) Ferrous chloride
c) Ferric nitrate
d) Ammonium sulfite

3.10 Some Properties of Ionic Compounds

Learning Objective:

- Identify the properties of ionic compounds, and explain how the nature of the ionic bond is reflected in the physical properties of ionic compounds.

Like sodium chloride, ionic compounds are usually crystalline solids. Different ions vary in size and charge; therefore, they are packed together in crystals in different ways. The ions in each compound settle into a pattern that efficiently fills space and allows for maximum interaction with adjacent ions of opposite charge.

Because the ions in an ionic solid are held rigidly in place by attraction to their neighbors, they cannot move about. Once an ionic solid is dissolved in water, however, the ions can move freely, thereby making ionic compounds good conductors of electricity in a solution. Ionic compounds dissolve in water if the attraction between water and the ions overcomes the attraction of the ions for one another. Compounds like sodium chloride are very soluble in water and can be dissolved to make solutions of high concentration. Do not be misled, however, by the ease with which sodium chloride and other familiar ionic compounds dissolve in water. Many other ionic compounds, such as magnesium hydroxide or barium sulfate, are not water soluble, because the attractive forces between these ions and water is not sufficient to overcome the ionic attractions in the crystals.

Ionic compounds also have high melting and boiling points. The attractive force between oppositely charged cations and anions is extremely strong, so the ions need to gain a large amount of energy to overcome the attractions between one another. At higher boiling or melting points, more energy is needed. Sodium chloride, for example, melts at 1074 K and boils at 1686 K; potassium iodide melts at 954 K and boils at 1603 K.

Despite the strength of ionic bonds, ionic solids shatter if struck sharply. A blow disrupts the orderly arrangement of cations and anions, forcing particles of like electrical charge closer together. The proximity of like charges creates repulsive energies that split the crystal apart.

▲ The melting point of sodium chloride is 1074 K.

PROBLEM 3.26

The melting points of NaCl, KCl, and RbCl are 1074 K, 1043 K, and 991 K, respectively. Based on this, which compound exhibits the strongest ionic bonds, and which exhibits the weakest? How is this trend related to the relative size of the cations?

CHEMISTRY IN ACTION

Ionic Liquids

Imagine a substance that could help solve the problems of nuclear waste, make solar energy more efficient, and revolutionize the development of biomass-based renewable energies. When discussing ionic substances, most of us think of hard, crystalline materials like common table salt (see the Chemistry in Action feature on p. 115), with high melting points. But ionic liquids have very different properties, including low melting points, high viscosity, low-to-moderate electrical conductivity, and low volatility, which make them suitable for the varied uses described previously.

Although the details of the discovery of ionic liquids are in dispute, one of the first *room temperature ionic liquids* (or RTILs), ethylammonium nitrate, was synthesized in 1914 by Paul Walden. Most RTILs developed since then consist of a bulky, asymmetric organic cation (see Organic Chemistry in Chapters 12–19) combined with a variety of anions.

▲ Protic ionic liquids (PIL) are used to extract lignin from biomass (right) leaving behind the solid, energy-rich cellulose (left) to be converted into biofuels.

Bulky cations provide unique solvent properties, enabling them to dissolve substances that are not very soluble in more conventional solvents. Their low volatility also makes

(Continued)

them attractive as "green," or environmentally friendly, solvents. Consider the practice of using biomass as a fuel source. One common approach is to convert sugar or starch (from corn, beets, or cane sugar) into ethanol by the process of fermentation. But the major component of these and most other plants is cellulose. Cellulose is a polymer (see the Chemistry in Action feature on p. 155) composed of many sugars joined together in a long chain. Cellulose is chemically similar to starch but is neither highly soluble in most solvents nor subject to fermentation. RTILs can be used to dissolve cellulose at moderate temperatures and facilitate its breakdown into simple fermentable sugars. Most of the cellulose in biomass, however, is also combined with lignin—an integral component of the cell walls of plants. Lignin can be separated and removed from biomass by dissolving it in RTIL solutions, providing a simple and relatively inexpensive method for recovering cellulose for biofuel applications. At a volume of nearly 700 billion tons of the earth's biomass, cellulose represents an important renewable energy source. The ability to isolate and convert cellulose into fuel will certainly help meet our expanding energy needs.

CIA Problem 3.5 Most ionic substances are solids at room temperature. Explain why the RTILs discussed in this application are liquids rather than solids

CIA Problem 3.6 Ionic liquids are being evaluated for use in a moon-based spinning-liquid telescope. Which properties of ionic liquids make them particularly well suited for this application?

3.11 H^+ and OH^- Ions: An Introduction to Acids and Bases

In Chapter 10, we will look at the chemical behavior of acids and bases and their importance in many areas of chemistry. Acid–base chemistry is so significant that it requires a full chapter for adequate coverage. The importance of acids and bases will be evident as they reappear in later chapters related to organic and biochemistry.

Learning Objective:

- Identify the ions associated with acids and bases.

Two of the most important ions we will be discussing in the remainder of this book are the hydrogen cation (H^+) and the hydroxide anion (OH^-). Since a hydrogen *atom* contains one proton and one electron, a hydrogen *cation* is simply a proton because it has lost its single electron. A hydroxide anion (OH^-), by contrast, is a polyatomic ion in which an oxygen atom is covalently bonded to a hydrogen atom (covalent bonds are discussed in Chapter 4). Although much of Chapter 10 is devoted to the chemistry of H^+ and OH^- ions, it is worth taking a preliminary look now.

Acid A substance that provides H^+ ions in water.

Base A substance that provides OH^- ions in water.

The importance of the H^+ cation and the OH^- anion is that they are fundamental to the concepts of *acids* and *bases*. In fact, one definition of an **acid** is a substance that provides H^+ ions when dissolved in water; for example, HCl, HNO_3, H_2SO_4, and H_3PO_4. One definition of a **base** is a substance that provides OH^- ions when dissolved in water; for example, NaOH, KOH, and $Ba(OH)_2$.

Hydrochloric acid (HCl), nitric acid (HNO_3), sulfuric acid (H_2SO_4), and phosphoric acid (H_3PO_4) are among the most common acids. When any of these substances is dissolved in water, H^+ ions are formed along with the corresponding anion (Table 3.5).

The behavior of polyprotic acids, or acids that provide more than one H^+ ion per acid molecule, will be discussed in more detail in Chapter 10.

Different acids can provide different numbers of H^+ ions per acid molecule. Hydrochloric acid, for instance, provides one H^+ ion per acid molecule; sulfuric acid can provide two H^+ ions per acid molecule; and phosphoric acid can provide three H^+ ions per acid molecule.

Sodium hydroxide (NaOH; also known as *lye* or *caustic soda*), potassium hydroxide (KOH; also known as *caustic potash*), and barium hydroxide [$Ba(OH)_2$] are examples of bases. When any of these compounds dissolves in water, OH^- anions go into solution along with the corresponding metal cation. Sodium hydroxide and potassium hydroxide provide one OH^- ion per formula unit; barium hydroxide provides two OH^- ions per formula unit, as indicated by its formula, $Ba(OH)_2$.

PROBLEM 3.27

Which of the following compounds are acids, and which are bases? Explain.

(a) HF **(b)** $Ca(OH)_2$ **(c)** LiOH **(d)** HCN

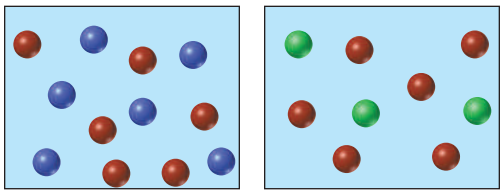
Table 3.5 Some Common Acids and the Anions Derived from Them

Acids		Anions	
Acetic acid	CH_3COOH	Acetate ion	*CH_3COO^-
Carbonic acid	H_2CO_3	Hydrogen carbonate ion	HCO_3^-
		Carbonate ion	CO_3^{2-}
Hydrochloric acid	HCl	Chloride ion	Cl^-
Nitric acid	HNO_3	Nitrate ion	NO_3^-
Nitrous acid	HNO_2	Nitrite ion	NO_2^-
Phosphoric acid	H_3PO_4	Dihydrogen phosphate ion	$H_2PO_4^-$
		Hydrogen phosphate ion	HPO_4^{2-}
		Phosphate ion	PO_4^{3-}
Sulfuric acid	H_2SO_4	Hydrogen sulfate ion	HSO_4^-
		Sulfate ion	SO_4^{2-}

*Sometimes written $C_2H_3O_2^-$ or as $CH_3CO_2^-$.

KEY CONCEPT PROBLEM 3.28

One of these pictures represents a solution of HCl and one represents a solution of H_2SO_4. Which is which?



(a) (b)

CHEMISTRY IN ACTION

Osteoporosis

At the beginning of the chapter we discussed the importance of dietary calcium ions for the formation of strong teeth and bones. Bone consists primarily of two components, one mineral and one organic. About 70% of bone is the ionic compound *hydroxyapatite,* $Ca_{10}(PO_4)_6(OH)_2$, called the *trabecular,* or spongy, bone. This mineral component is intermingled in a complex matrix with about 30% by mass of fibers of the protein *collagen,* called the *cortical,* or compact, bone. Hydroxyapatite gives bone its hardness and strength, whereas collagen fibers add flexibility and resistance to breaking.

Total bone mass in the body increases from birth until reaching a maximum in the mid 30s. By the early 40s, however, an age-related decline in bone mass begins to occur in both sexes. Bone density decreases, and the microarchitecture of bones is disrupted, resulting in weakening of bone structure, particularly in the wrists, hips, and spine. Should this thinning of bones become too great and the bones become too porous and brittle, a clinical condition called osteoporosis can result. Osteoporosis is, in fact, the most common of all bone diseases, affecting approximately 25 million people in the United States. Approximately 1.5 million bone fractures each year are caused by osteoporosis, at an estimated health-care cost of $14 billion.

Although both sexes are affected by osteoporosis, the condition is particularly common in postmenopausal women, who undergo bone loss at a rate of 2–3% per year over and above that of the normal age-related loss. The cumulative lifetime bone loss, in fact, may approach 40–50% in women versus 20–30% in men. It has been estimated that half of all women over the age of 50 years will have an osteoporosis-related bone fracture at some point in their life. Other risk factors, in addition to sex, include being thin, being sedentary, having a family history of osteoporosis, smoking, and having a diet low in calcium.

No cure exists for osteoporosis, but treatment for its prevention and management includes estrogen-replacement

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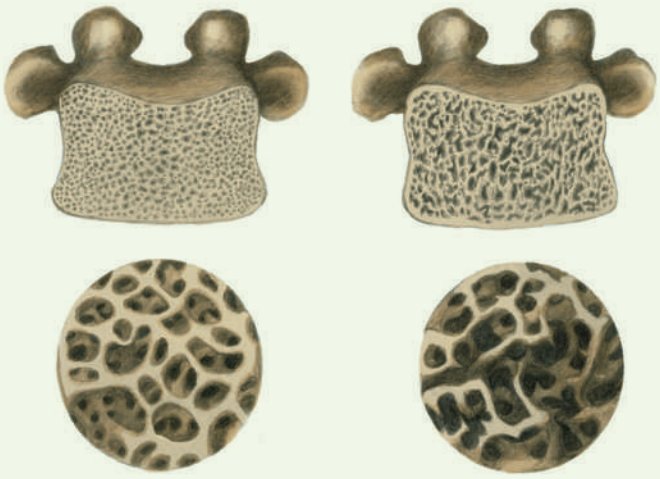


▲ These images represent a healthy vertebra (left) and one showing the effects of osteoporosis (right).

therapy for postmenopausal women as well as several approved medications called *bisphosphonates* that bind to the calcium in bone, slowing down bone loss by inhibiting the action of *osteoclasts,* or cells that break down bone tissue. Calcium supplements are also recommended, as is appropriate weight-bearing exercise. In addition, treatment with sodium fluoride is under active investigation and shows considerable promise. Fluoride ion reacts with hydroxyapatite to give *fluorapatite,* in which OH^- ions are replaced by F^-, increasing both bone strength and density.

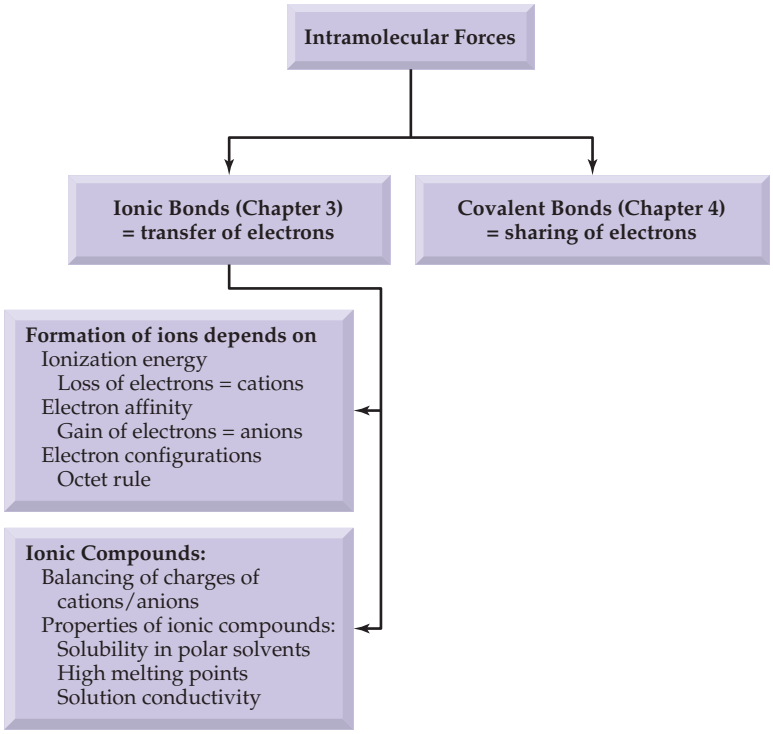
$$\underset{\text{Hydroxyapatite}}{Ca_{10}(PO_4)_6(OH)_2} + 2\,F^- \longrightarrow \underset{\text{Fluorapatite}}{Ca_{10}(PO_4)_6F_2}$$

CIA Problem 3.7 Name each ion in hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$; give its charge; and show that the formula represents a neutral compound.

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Describe ion formation processes and distinguish between anions and cations.** Atoms are converted into *cations* by the loss of one or more electrons [resulting in a positive (+) charge] and into *anions* by the gain of one or more electrons [resulting in a negative (−) charge] *(see Problems 32, 33, 40–43, 46, 48, 49, 54, and 55).*
- **Use the octet rule and electron configurations to explain the charge associated with ions.** A valence-shell electron configuration of eight electrons in filled *s* and *p* subshells leads to stability and lack of reactivity, as typified by the noble gases in group 8A. According to the *octet rule,* atoms of main group elements tend to form ions in which they have gained or lost the appropriate number of electrons to reach a stable electronic configuration of a noble gas *(see Problems 3, 37–39, 44, 45, 47, 78, 79, 84, and 86).*
- **Use the periodic table to predict the charge associated with ions of main group elements.** The ionic charge can be predicted from the group number and the octet rule. For main group metals, the charge on the cation is equal to the group number. For nonmetals, the charge on the anion is equal to 8 − [group number] *(see Problems 29, 30, and 52–55).*
- **Explain the formation of anions and cations based on periodic trends.** Periodic variations in *ionization energy,* the amount of energy that must be supplied to remove an electron from an atom, show that metals lose electrons more easily than nonmetals. As a result, metals usually form cations. Similar periodic variations in *electron affinity,* the amount of energy released on adding an electron to an atom, show that reactive nonmetals gain electrons more easily than metals. As a result, reactive nonmetals usually form anions *(see Problems 50–53, 56, 57, and 85).*
- **Name common monoatomic anions and cations.** Cations have the same name as the metal from which they are derived. Monatomic anions have the name ending *-ide.* For metals that form more than one ion, a Roman numeral equal to the charge on the ion is added to the name of the cation. Alternatively, the ending *-ous* is added to the name of the cation with the lesser charge and the ending *-ic* is added to the name of the cation with the greater charge *(see Problems 58–61).*
- **Identify the name, formula, and charge of common polyatomic ions.** Polyatomic ions consist of groups of atoms that are joined by covalent bonds (Chapter 4) but having an overall charge. The names, formulas, and charges of common polyatomic ions are summarized in Table 3.3 *(see Problems 62, 63, 88, and 89).*
- **Explain the nature of the ionic bonds holding ions together in ionic compounds.** Ionic compounds are composed of cations and anions that are formed by the transfer of electrons; these ions are held together by *ionic bonds,* which result from the attraction between opposite electrical charges *(see Problems 48, 49, and 57).*
- **Determine the formula of ionic compounds based on the formulas and charges of the cations and anions.** Ionic compounds must contain appropriate numbers of anions and cations to maintain overall neutrality, thereby providing a means of determining their chemical formulas *(see Problems 34–36, 64–67, and 70).*
- **Based on the cations and anions in the chemical formula, write the name of ionic compounds.** To name an ionic compound, the cation name is given first, with the charge of the metal ion indicated if necessary. The name of the anion is given second using the *-ide* suffix as appropriate (for a monatomic anion) or the name of the polyatomic anion *(see Problems 68–73, 80, 82, 83, and 87–90).*
- **Identify the properties of ionic compounds and explain how the nature of the ionic bond is reflected in the physical properties of ionic compounds.** Ionic compounds conduct electricity when dissolved in water because the charged particles (ions) act as mobile charge carriers. Ionic compounds are generally crystalline solids with high melting points and high boiling points because of the strong electrostatic attraction between ions in the solid state *(see Problems 49 and 50).*
- **Identify the ions associated with acids and bases.** The hydrogen ion (H^+) and the hydroxide ion (OH^-) are among the most important ions in chemistry because they are fundamental to the idea of acids and bases. According to one common definition, an *acid* is a substance that yields H^+ ions when dissolved in water and a base is a substance that yields OH^- ions when dissolved in water *(see Problems 74–77 and 81).*

CONCEPT MAP: ELECTROSTATIC FORCES



▲ **Figure 3.3 Concept Map.** As illustrated in this concept map, ionic bonds represent one type of intramolecular force holding elements together in compounds. Elements form ions by gaining or losing electrons to obtain a stable electronic configuration. The tendency to gain/lose electrons is reflected in the magnitude of the ionization energies or electron affinities of the elements. Properties of ionic compounds (high melting points, solubility in polar solvents, solution conductivity) are a consequence of the charges on the ions and the strong electrostatic attractions between ions.

KEY WORDS

Acid, *p. 126*
Anion, *p. 108*
Base, *p. 126*
Cation, *p. 107*
Electron affinity, *p. 113*
Formula unit, *p. 120*
Ion, *p. 107*
Ionic bond, *p. 118*
Ionic compound, *p. 119*
Ionic solid, *p. 119*
Ionization energy, *p. 112*
Octet rule, *p. 109*
Polyatomic ion, *p. 116*

UNDERSTANDING KEY CONCEPTS

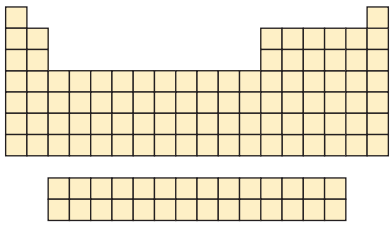
3.29 Where on the blank outline of the periodic table are the following elements found?

(a) Elements that commonly form only one type of cation

(b) Elements that commonly form anions

(c) Elements that can form more than one type of cation

(d) Elements that do not readily form either anions or cations

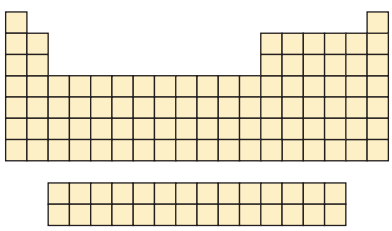


3.30 Where on the blank outline of the periodic table are the following elements found?

(a) Elements that commonly form +2 ions

(b) Elements that commonly form −2 ions

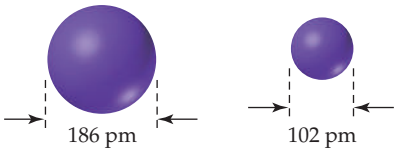
(c) An element that forms a +3 ion



3.31 Write the symbols for the ions represented in the following drawings.

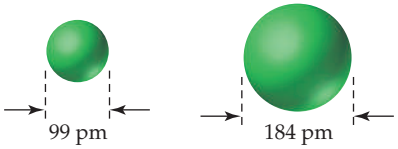
(a) **(b)** **(c)** **(d)**

3.32 One of these drawings represents an Na atom, and one represents an Na^+ ion. Tell which is which, and explain why there is a difference in size.



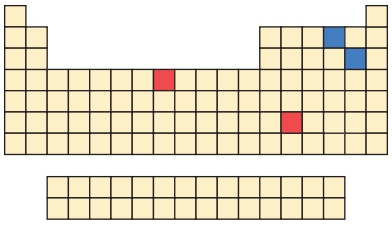
(a) **(b)**

3.33 One of these drawings represents a Cl atom and one represents a Cl^- ion. Tell which is which, and explain why there is a difference in size.

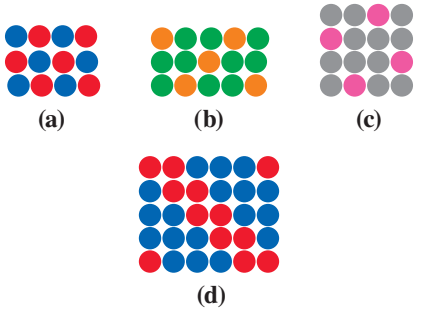


(a) **(b)**

3.34 The elements in red in the periodic table can form cations having more than one charge. Write the formulas and names of the compounds that are formed between the red cations and the blue anions depicted in the periodic table.

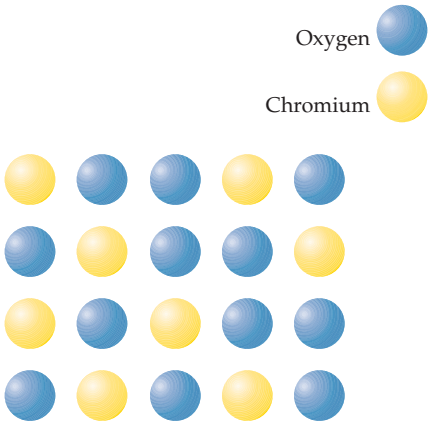


3.35 Each of these drawings (a)–(d) represents one of the following ionic compounds: $PbBr_2$, ZnS, CrF_3, and Al_2O_3. Which is which?



(a) **(b)** **(c)** **(d)**

3.36 The ionic compound formed between chromium and oxygen is shown here. Name the compound and write its formula. (Hint: When naming the compound, remember that chromium is a transition metal cation and can have more than one possible charge.)



ADDITIONAL PROBLEMS

IONS AND THE OCTET RULE (SECTIONS 3.1 AND 3.2)

3.37 What is the *octet rule*?

3.38 What roles do the octet rule and the position of an element in the periodic table play in determining the charge on an ion?

3.39 Why do H and He not obey the octet rule?

3.40 Write the symbol for an ion that contains 34 protons and 36 electrons.

3.41 What is the charge of an ion that contains 21 protons and 19 electrons?

3.42 Identify the element X in the following ions and tell which noble gas has the same electron configuration.

(a) X^{2+}, a cation with 36 electrons

(b) X^-, an anion with 36 electrons

3.43 Element Z forms an ion Z^{3+}, which contains 31 protons. What is the identity of Z, and how many electrons does Z^{3+} have?

3.44 Write the electron configuration for the following ions:

(a) Rb^+ **(b)** Br^- **(c)** S^{2-}

(d) Ba^{2+} **(e)** Al^{3+}

3.45 Based on the following atomic numbers and electronic configurations write the symbols for the following ions:

(a) $Z = 20$; $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$

(b) $Z = 8$; $1s^2\ 2s^2\ 2p^6$

(c) $Z = 22$; $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^2$

(d) $Z = 19$; $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$

(e) $Z = 13$; $1s^2\ 2s^2\ 2p^6$

IONS AND IONIC BONDING (SECTION 3.3)

3.46 Write equations for loss or gain of electrons by atoms that result in formation of the following ions:

(a) Ca^{2+} **(b)** Au^{+} **(c)** F^{-} **(d)** Cr^{3+}

3.47 Write electronic configurations and symbols for the ions formed by the following:

(a) Gain of three electrons by phosphorus

(b) Loss of one electron by lithium

(c) Loss of two electrons by cobalt

(d) Loss of three electrons by thallium

3.48 Tell whether each statement about ions is true or false. If a statement is false, explain why.

(a) A cation is formed by addition of one or more electrons to an atom.

(b) Group 4A elements tend to lose four electrons to yield ions with a +4 charge.

(c) Group 4A elements tend to gain four electrons to yield ions with a −4 charge.

(d) The individual atoms in a polyatomic ion are held together by covalent bonds.

3.49 Tell whether each statement about ionic solids is true or false. If a statement is false, explain why.

(a) Ions are randomly arranged in ionic solids.

(b) All ions are the same size in ionic solids.

(c) Ionic solids can often be shattered by a sharp blow.

(d) Ionic solids have low boiling points.

PERIODIC PROPERTIES AND ION FORMATION (SECTION 3.4)

3.50 Looking only at the periodic table, tell which member of each pair of atoms has the larger ionization energy and thus loses an electron less easily:

(a) Li and O **(b)** Li and Cs

(c) K and Zn **(d)** Mg and N

3.51 Looking only at the periodic table, tell which member of each pair of atoms has the larger electron affinity and thus gains an electron more easily:

(a) Li and S **(b)** Ba and I

(c) Ca and Br

3.52 Which of the following ions are likely to form? Explain.

(a) Li^{2+} **(b)** K^{-} **(c)** Mn^{3+}

(d) Zn^{4+} **(e)** Ne^{+}

3.53 What is the charge on the cation formed from the following elements? For those elements that form more than one cation, indicate the ionic charges most commonly observed.

(a) Magnesium **(b)** Tin

(c) Mercury **(d)** Aluminum

3.54 Write the electron configurations of Cr^{2+} and Cr^{3+}.

3.55 Write the electron configurations of Co, Co^{2+}, and Co^{3+}.

3.56 Would you expect the ionization energy of Li^{+} to be less than, greater than, or the same as the ionization energy of Li? Explain.

3.57 **(a)** Write equations for the loss of an electron by a K atom and the gain of an electron by a K^{+} ion.

(b) What is the relationship between the equations?

(c) What is the relationship between the ionization energy of a K atom and the electron affinity of a K^{+} ion?

SYMBOLS, FORMULAS, AND NAMES FOR IONS (SECTIONS 3.5 AND 3.6)

3.58 Name the following ions:

(a) S^{2-} **(b)** Sn^{2+} **(c)** Sr^{2+}

(d) Mg^{2+} **(e)** Au^{+}

3.59 Name the following ions in both the old and the new systems:

(a) Cr^{2+} **(b)** Fe^{3+} **(c)** Hg^{2+}

3.60 Write symbols for the following ions:

(a) Selenide ion **(b)** Oxide ion

(c) Silver(I) ion

3.61 Write symbols for the following ions:

(a) Ferrous ion **(b)** Tin(IV) ion

(c) Lead(II) ion **(d)** Chromic ion

3.62 Write formulas for the following ions:

(a) Hydroxide ion **(b)** Bisulfate ion

(c) Acetate ion **(d)** Permanganate ion

(e) Hypochlorite ion **(f)** Nitrate ion

(g) Carbonate ion **(h)** Dichromate ion

3.63 Name the following ions:

(a) NO_2^{-} **(b)** CrO_4^{2-}

(c) NH_4^{+} **(d)** HPO_4^{2-}

NAMES AND FORMULAS FOR IONIC COMPOUNDS (SECTIONS 3.8 AND 3.9)

3.64 Write the formula for the following substances:

(a) Sodium hydrogen carbonate (baking soda)

(b) Potassium nitrate (a backache remedy)

(c) Calcium carbonate (an antacid)

(d) Ammonium nitrate (first aid cold packs)

3.65 Write the formula for the following compounds:

(a) Calcium hypochlorite, used as a swimming pool disinfectant

(b) Copper(II) sulfate, used to kill algae in swimming pools

(c) Sodium phosphate, used in detergents to enhance cleaning action

3.66 Complete the table by writing in the formula of the compound formed by each pair of ions:

	S^{2-}	Cl^-	PO_4^{3-}	CO_3^{2-}
Copper(II)	CuS			
Ca^{2+}				
NH_4^+				
Ferric ion				

3.67 Complete the table by writing in the formula of the compound formed by each pair of ions:

	O^{2-}	HSO_4^-	HPO_4^{2-}	$C_2O_4^{2-}$
K^+	K_2O			
Ni^{2+}				
NH_4^+				
Chromous				

3.68 Write the name of each compound in the table for Problem 3.66.

3.69 Write the name of each compound in the table for Problem 3.67.

3.70 Name the following substances:

(a) $MgCO_3$ **(b)** $Ca(CH_3CO_2)_2$

(c) AgCN **(d)** $Na_2Cr_2O_7$

3.71 Name the following substances:

(a) $Fe(OH)_2$ **(b)** $KMnO_4$

(c) Na_2CrO_4 **(d)** $Ba_3(PO_4)_2$

3.72 Which of the following formulas is most likely to be correct for calcium phosphate?

(a) Ca_2PO_4 **(b)** $CaPO_4$

(c) $Ca_2(PO_4)_3$ **(d)** $Ca_2(PO_4)_2$

3.73 Fill in the missing information to give the correct formula for each compound:

(a) $Al_?(SO_4)_?$ **(b)** $(NH_4)_?(PO_4)_?$

(c) $Rb_?(SO_4)_?$

ACIDS AND BASES (SECTION 3.11)

3.74 What is the difference between an acid and a base?

3.75 Identify the following substances as either an acid or a base:

(a) H_2CO_3 **(b)** HCN

(c) $Mg(OH)_2$ **(d)** KOH

3.76 Write equations to show how the substances listed in Problem 3.75 give ions when dissolved in water.

3.77 Give the formula and the name of the anions for the acids in Problem 3.75. (Hint: The H^+ ion is the cation in the acids.)

CONCEPTUAL PROBLEMS

3.78 Explain why the hydride ion, H^-, has a noble gas configuration.

3.79 The H^- ion (Problem 3.78) is stable but the Li^- ion is not. Explain.

3.80 Many compounds containing a metal and a nonmetal are not ionic, yet they are named using the Roman numeral system for ionic compounds described in Section 3.5. Write the chemical formulas for the following such compounds.

(a) Chromium(VI) oxide

(b) Vanadium(V) chloride

(c) Manganese(IV) oxide

(d) Molybdenum(IV) sulfide

3.81 The arsenate ion has the formula AsO_4^{3-}. Write the formula of the corresponding acid that contains this anion. (Hint: The cation for the corresponding acid is H^+.)

3.82 The names given for the following compounds are incorrect. Write the correct name for each compound.

(a) Cu_3PO_4, copper(III) phosphate

(b) Na_2SO_4, sodium sulfide

(c) MnO_2, manganese(II) oxide

(d) $AuCl_3$, gold chloride

(e) $Pb(CO_3)_2$, lead(II) acetate

(f) Ni_2S_3, nickel(II) sulfide

3.83 The formulas given for the following compounds are incorrect. Write the correct formula for each compound.

(a) Cobalt(II) cyanide, $CoCN_2$

(b) Uranium(VI) oxide, UO_6

(c) Tin(II) sulfate, $Ti(SO_4)_2$

(d) Manganese(IV) oxide, MnO_4

(e) Potassium phosphate, K_2PO_4

(f) Calcium phosphide, CaP

(g) Lithium bisulfate, $Li(SO_4)_2$

(h) Aluminum hydroxide, $Al_2(OH)_3$

3.84 How many protons, electrons, and neutrons are in each of these ions?

(a) $^{16}O^{2-}$ **(b)** $^{89}Y^{3+}$

(c) $^{133}Cs^+$ **(d)** $^{81}Br^-$

3.85 Element X reacts with element Y to give a product containing X^{3+} ions and Y^{2-} ions.

(a) Is element X likely to be a metal or a nonmetal?

(b) Is element Y likely to be a metal or a nonmetal?

(c) What is the formula of the product?

(d) What groups of the periodic table are elements X and Y likely to be in?

3.86 Identify each of the ions having the following charges and electron configurations:

(a) X^{4+}; $[Ar]\,4s^0 3d^3$ **(b)** X^+; $[Ar]\,4s^0 3d^{10}$

(c) X^{4+}; $[Ar]\,4s^0 3d^0$

GROUP QUESTIONS

3.87 The term "alum" refers to a group of ionic compounds that contain a monovalent cation (M^+), a trivalent cation (M^{3+}), and sulfate anions. Perform a web search to find:

(a) The chemical formulas of at least two different alum compounds.

(b) At least three common uses or applications of alum compounds.

3.88 One commercially available calcium supplement contains calcium gluconate. Look up the formula for calcium gluconate. Identify the charges on the calcium and gluconate ions. Are the calcium and gluconate ions monoatomic or polyatomic? Explain.

3.89 Borax is a common household and commercial chemical. Look up the chemical formula for borax. What is the anion in borax and the correct chemical name for the anion? (Hint: It is a polyatomic ion.)

3.90 Sodium fluoride reacts with hydroxyapatite to give fluorapatite, which increases both bone strength and density. Another fluoride compound is included in many toothpaste products to strengthen teeth enamel and prevent cavities. Do some research to identify this fluoride compound and give the name and formula of the compound.

4

Molecular Compounds

CONTENTS

CONCEPTS TO REVIEW

A. The Periodic Table (Sections 2.4 and 2.5)
B. Electron Configurations (Sections 2.7 and 2.8)
C. The Octet Rule (Section 3.2)
D. Electron-Dot Symbols (Section 2.9)

▲ The opiate drugs derived from these poppy plants can produce very different physiological effects based on slight differences in chemical structures.

We saw in the preceding chapter that ionic compounds are crystalline solids composed of positively and negatively charged ions. Not all substances, however, are ionic. In fact, with the exception of table salt (NaCl), baking soda ($NaHCO_3$), lime for the garden (CaO), and a few others, most of the compounds we come into contact with on a daily basis are *not* crystalline, brittle, high-melting ionic solids. We are much more likely to encounter gases (like those in air), liquids (such as water), low-melting solids (such as butter), and flexible solids (like plastics). All these materials are composed of *molecules*

rather than ions, all contain *covalent* bonds rather than ionic bonds, and all consist primarily of nonmetal atoms rather than metals.

As an example, consider the active ingredients in many over-the-counter drugs—they consist largely of the elements carbon, hydrogen, nitrogen, and oxygen. However, the myriad ways in which these elements can be combined lead to literally thousands of unique compounds with different chemical formulas, having different chemical and physical properties. In some cases, two compounds can have identical chemical formulas and structures but slightly different three-dimensional orientations of atoms in the compound that result in dramatically different behaviors. For example, dextromethorphan and levomethorphan have identical molecular formulas and are very similar to morphine and codeine—opiate drugs derived from the poppy plant. But very slight differences in the three-dimensional arrangement of atoms can affect the chemical and physiological behavior of these substances. Dextromethorphan, for example, is a safe and effective cough suppressant, whereas levomethorphan is a highly addictive opiate. In this chapter, we will explore the nature of covalent bonds, how they contribute to molecular shapes and properties, and some of the conventions used to name molecular compounds so that we can distinguish one from another.

4.1 Covalent Bonds

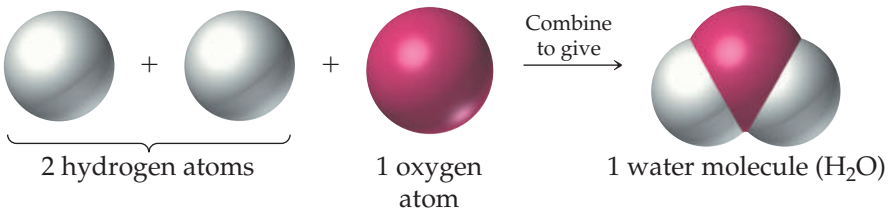
Learning Objectives:

- Describe the nature of covalent bonds and how they are formed.
- Differentiate between ionic and covalent bonds.

How do we describe the bonding in carbon dioxide, water, polyethene, and the many millions of nonionic compounds that make up our bodies and much of the world around us? Simply put, the bonds in such compounds are formed by the sharing of electrons between atoms (unlike ionic bonds, which involve the complete transfer of electrons from one atom to another). The bond formed when atoms share electrons is called a **covalent bond,** and the group of atoms held together by covalent bonds is called a **molecule.** A single molecule of water, for example, contains two hydrogen atoms and one oxygen atom covalently bonded to one another. We might visualize a water molecule using a space-filling model as shown here:

Covalent bond A bond formed by sharing electrons between atoms.

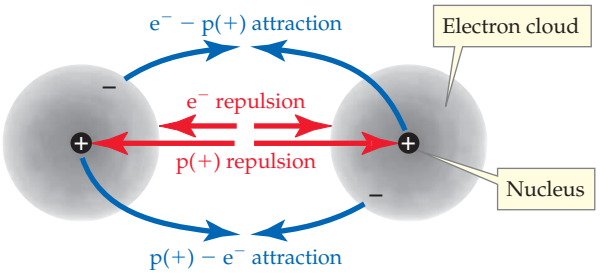
Molecule A group of atoms held together by covalent bonds.



Recall that according to the *octet rule* (Section 3.5), main group elements tend to undergo reactions that leave them with completed outer subshells with eight valence electrons (or two for hydrogen), so that they have a noble gas electron configuration. Although metals and reactive nonmetals can achieve an electron octet by gaining or losing an appropriate number of electrons to form ions, nonmetals can also achieve an electron octet by *sharing* an appropriate number of electrons in covalent bonds.

A simple example of how covalent bond formation occurs is the bond between two hydrogen atoms in a hydrogen molecule, H_2. Recall that a hydrogen *atom* consists of a positively charged nucleus and a single, negatively charged 1*s* valence electron, which we represent as H· using the electron-dot symbol. When two hydrogen atoms come together, electrostatic interactions occur. Some of these interactions are repulsive—the two positively charged nuclei repel each other, and the two negatively charged electrons repel each other. Other interactions, however, are attractive—each nucleus attracts both electrons, and each electron attracts both nuclei (Figure 4.1). Other factors, such as

orbital energy levels and stable electronic configurations, contribute to making the attractive forces stronger than the repulsive forces, so that a covalent bond is formed and the hydrogen atoms stay together.

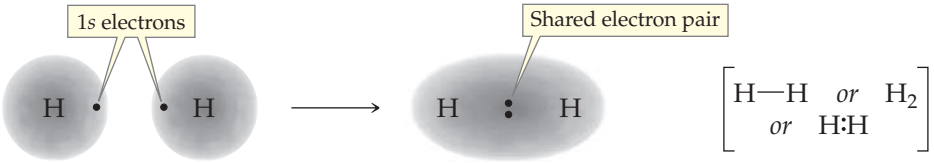


▲ **Figure 4.1**
A covalent H—H bond is the net result of attractive and repulsive forces.
The nucleus–electron attractions (blue arrows) are greater than the nucleus–nucleus and electron–electron repulsions (red arrows), resulting in a net attractive force that holds the atoms together to form an H_2 molecule.

In essence, the electrons act as a kind of "glue" to bind the two nuclei together into an H_2 molecule. Both nuclei are simultaneously attracted to the same electrons and are held together, much as two tug-of-war teams pulling on the same rope are held together.

▲ The two teams are joined together because both are holding onto the same rope. In a similar way, two atoms are bonded together when both hold onto the same electrons.

Covalent bond formation in the H—H molecule can be visualized by imagining that the spherical 1*s* orbitals from the two individual atoms *overlap* and blend together to give an egg-shaped region in the H_2 molecule. Each hydrogen atom now "owns" one valence shell electron and "shares" one provided by the other H atom. The two electrons occupy the central region between the two H nuclei, giving both atoms a share in two valence electrons, and the $1s^2$ electron configuration of the noble gas helium. For simplicity, the shared pair of electrons in a covalent bond is often represented as a line between atoms. Thus, the symbols H—H, H:H, and H_2 all represent a hydrogen molecule.

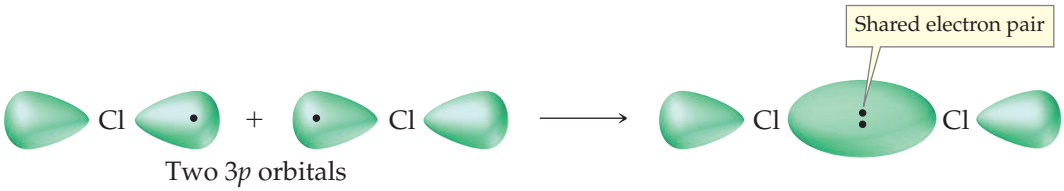


Bond length The optimum distance between nuclei in a covalent bond.

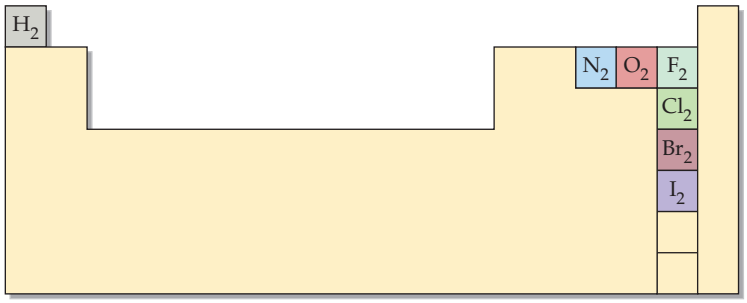
As you might imagine, the magnitudes of the various attractive and repulsive forces between nuclei and electrons in a covalent bond depend on how close the atoms are to each other. If the atoms are too far apart, the attractive forces are small and no bond exists. If the atoms are too close, the repulsive interaction between nuclei is so strong that it pushes the atoms apart. Thus, there is an optimum point where net attractive forces are maximized and where the H_2 molecule is most stable. This optimum distance between nuclei is called the **bond length** and is 74 pm $(7.4 \times 10^{-11}\,\text{m})$ in the H_2 molecule. Typically, the bond length is slightly less than the sum of the atomic radii of the two atoms involved in the covalent bond.

As another example of covalent bond formation, look at the chlorine molecule, Cl_2. An individual chlorine atom has seven valence electrons and the valence-shell electron configuration $3s^2 3p^5$. Using the electron-dot symbols for the valence electrons, each Cl atom can be represented as :Cl·. The 3*s* orbital and two of the three 3*p* orbitals are filled by two electrons each, but the third 3*p* orbital holds only one electron. When two chlorine atoms approach each other, the unpaired 3*p* electrons are shared by both atoms in a covalent bond. Each chlorine atom in the resultant Cl_2 molecule now "owns" six outer-shell electrons and "shares" two more, giving each a valence-shell octet like that of the noble gas argon. We can represent the formation of a covalent bond between chlorine atoms as (where the red dots represent shared electrons once the bond is formed).

Such bond formation can also be pictured as the overlap of the 3*p* orbitals containing the single electrons, with resultant formation of a region of high electron density between the nuclei.



Similar to H_2 and Cl_2, other elements can achieve stable electron configurations by forming *diatomic* molecules (Figure 4.2): nitrogen (N_2) and oxygen (O_2) are colorless, odorless, nontoxic gases present in air; fluorine (F_2) is a pale yellow, highly reactive gas; bromine (Br_2) is a dark red, toxic liquid; and iodine (I_2) is a violet crystalline solid.



▲ **Figure 4.2**
Diatomic elements in the periodic table.

PROBLEM 4.1

Draw the iodine molecule using electron-dot symbols and indicate the shared electron pair. What noble gas configuration do the iodine atoms have in an iodine (I_2) molecule?

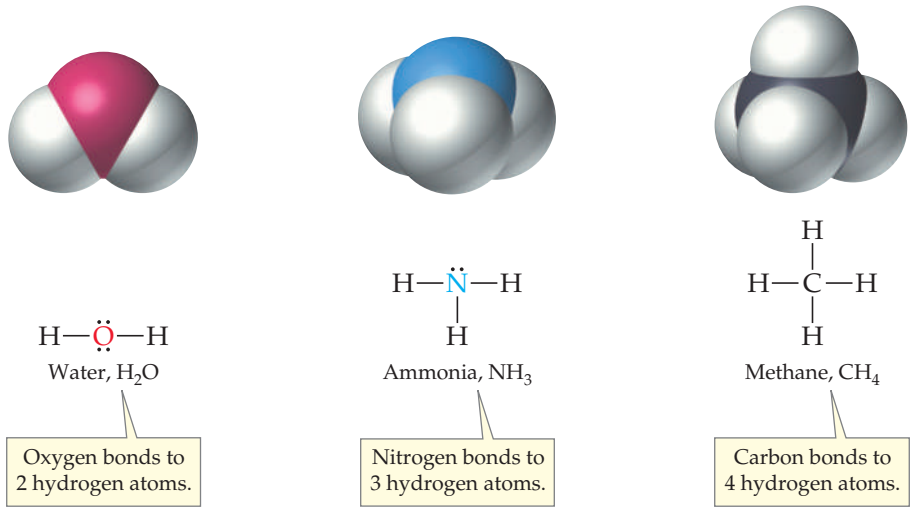
4.2 Covalent Bonds and the Periodic Table

Learning Objective:

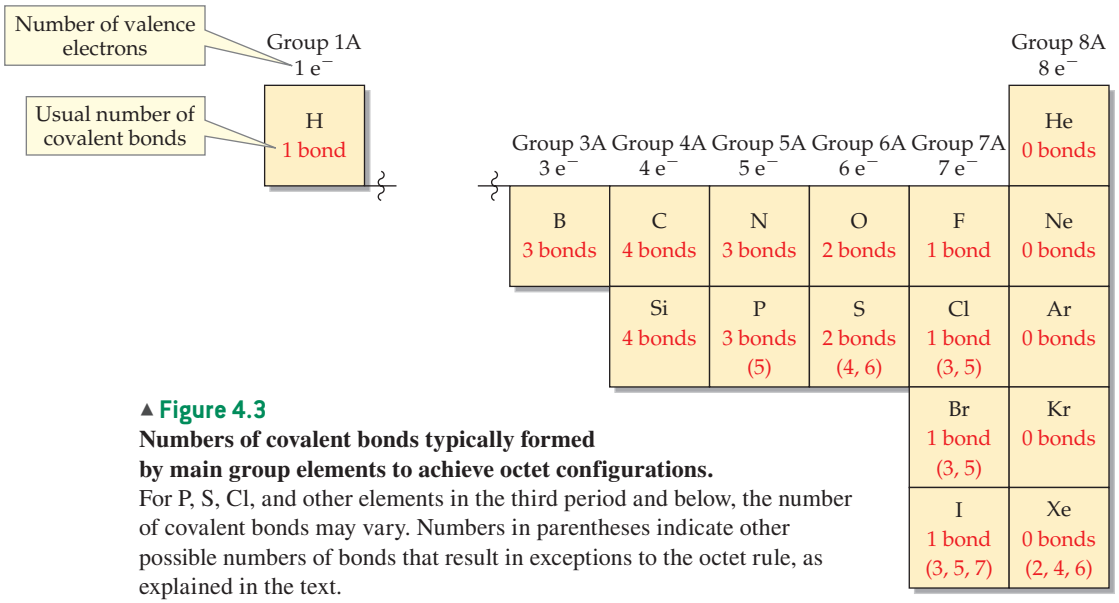
- Predict the number of covalent bonds an atom will form based on its position in the periodic table.

Covalent bonds can form between unlike atoms as well as between like atoms, making possible a vast number of **molecular compounds.** Water molecules, for example, consist of two hydrogen atoms joined by covalent bonds to a single oxygen atom, H_2O; ammonia molecules consist of three hydrogen atoms covalently bonded to a nitrogen atom, NH_3; and methane molecules consist of four hydrogen atoms covalently bonded to a carbon atom, CH_4.

Molecular compound A compound that consists of atoms joined by covalent bonds to form molecules rather than ions.



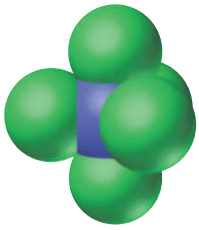
Note that in all of these examples, each atom shares enough electrons to achieve a noble gas configuration: two electrons for hydrogen and octets for oxygen, nitrogen, and carbon. Hydrogen, with one valence electron ($H\cdot$), needs one more electron to achieve a noble gas configuration (that of helium) and thus forms one covalent bond. Oxygen, with six valence electrons ($\cdot\ddot{O}\cdot$), needs two more electrons to have an octet; this happens when oxygen forms two covalent bonds. Nitrogen, with five valence electrons ($\cdot\ddot{N}\cdot$), needs three more electrons to achieve an octet and thus forms three covalent bonds. Carbon, with four valence electrons ($\cdot\dot{C}\cdot$), needs four more electrons and thus forms four covalent bonds. Figure 4.3 summarizes the number of covalent bonds typically formed by common main group elements.



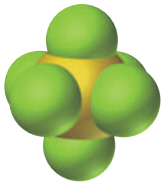
▲ Figure 4.3
Numbers of covalent bonds typically formed by main group elements to achieve octet configurations.
For P, S, Cl, and other elements in the third period and below, the number of covalent bonds may vary. Numbers in parentheses indicate other possible numbers of bonds that result in exceptions to the octet rule, as explained in the text.

The octet rule is a useful guideline, but it has numerous exceptions. Boron, for example, has only three valence electrons it can share ($\cdot\dot{B}\cdot$) and thus often forms compounds in which it has only three covalent bonds and six electrons, such as BF_3. Exceptions to the octet rule are also seen with elements in the third row of the periodic table and below because these elements have vacant *d* orbitals that can be used for bonding. Phosphorus sometimes forms five covalent bonds (using 10 bonding electrons); sulfur sometimes forms four or six covalent bonds (using 8 and 12 bonding electrons, respectively); and chlorine, bromine, and iodine sometimes form three, five, or seven covalent bonds, respectively. Phosphorus and sulfur, for example, form molecules such as PCl_5, SF_4, and SF_6.

BF_3
Boron trifluoride
(6 valence electrons on B)



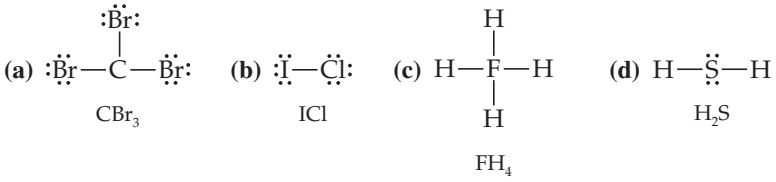
PCl_5
Phosphorus pentachloride
(10 valence electrons on P)



SF_6
Sulfur hexafluoride
(12 valence electrons on S)

Worked Example 4.1 Molecular Compounds: Octet Rule and Covalent Bonds

Using Figure 4.3, tell whether the following molecules are likely to exist.



ANALYSIS Count the number of covalent bonds formed by each element and see if the numbers correspond to those shown in Figure 4.3.

SOLUTION

(a) No. Carbon needs four covalent bonds to achieve a complete valence-shell octet but has only three in CBr_3.

(b) Yes. Both iodine and chlorine have achieved a complete octet by forming one covalent bond in ICl.

(c) No. Fluorine only needs one covalent bond to achieve an octet. It cannot form more than one covalent bond because it is in the second period and does not have valence *d* orbitals to use for bonding.

(d) Yes. Sulfur, which is in group 6A like oxygen, can achieve a complete valence-shell octet by forming two covalent bonds.

Worked Example 4.2 Molecular Compounds: Electron-Dot Symbols

Using electron-dot symbols, show the reaction between one hydrogen atom and one fluorine atom.

ANALYSIS The electron-dot symbols show the valence electrons for the hydrogen and fluorine atoms. A covalent bond is formed by the sharing of unpaired valence electrons between the two atoms so that each atom now has the electron configuration of a noble gas (helium in the case of hydrogen and neon in the case of fluorine).

SOLUTION

Draw the electron-dot symbols for the H and F atoms, showing the covalent bond as a shared electron pair.

Worked Example 4.3 Molecular Compounds: Predicting Number of Bonds

What are likely formulas for the following molecules?

(a) $SiH_2Cl_?$ **(b)** $HBr_?$ **(c)** $PBr_?$

ANALYSIS The numbers of covalent bonds needed to achieve a complete valence-shell octet for each element should be as indicated in Figure 4.3.

SOLUTION

(a) Silicon typically forms four bonds: SiH_2Cl_2

(b) Hydrogen forms only one bond: HBr

(c) Phosphorus typically forms three bonds: PBr_3

PROBLEM 4.2

How many covalent bonds are formed by each atom in the following molecules? Draw molecules using the electron-dot symbols and lines to show the covalent bonds.

(a) PH_3 **(b)** H_2Se **(c)** HCl **(d)** SiF_4

PROBLEM 4.3

What are likely formulas for the following molecules?

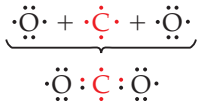
(a) $CH_2Cl_?$ **(b)** $BH_?$ **(c)** $NI_?$ **(d)** $SiCl_?$

4.3 Multiple Covalent Bonds

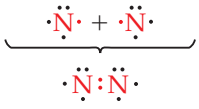
Learning Objective:

- Use the octet rule to determine when multiple covalent bonds (double and triple) will appear between two atoms.

The bonding in some molecules cannot be explained by the sharing of only two electrons between atoms. For example, the carbon and oxygen atoms in carbon dioxide (CO_2) and the nitrogen atoms in the N_2 molecule cannot have electron octets if only two electrons are shared:



UNSTABLE—Carbon has only 6 electrons; each oxygen has only 7.



UNSTABLE—Each nitrogen has only 6 electrons.

The only way the atoms in CO_2 and N_2 can have outer-shell electron octets is by sharing *more* than two electrons, resulting in the formation of *multiple* covalent bonds between two atoms. Only if the carbon atom shares four electrons with each oxygen atom do all atoms in CO_2 have electron octets, and only if the two nitrogen atoms share six electrons do both have electron octets. A bond formed by sharing two electrons (one pair) is a **single bond,** a bond formed by sharing four electrons (two pairs) is a **double bond,** and a bond formed by sharing six electrons (three pairs) is a **triple bond.** As you might expect, sharing more than two electrons increases the attractive forces between the two atoms and pulls them closer together. Hence, the bond length decreases in the order single bond > double bond > triple bond. Just as a single bond is represented by a single line between atoms, a double bond is represented by two lines between atoms and a triple bond by three lines:

Single bond A covalent bond formed by sharing one electron pair.

Double bond A covalent bond formed by sharing two electron pairs.

Triple bond A covalent bond formed by sharing three electron pairs.

:Ö: :C: :Ö: *or* :Ö=C=Ö:

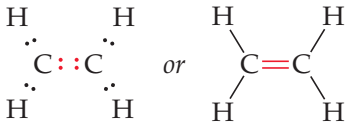
:N⋮⋮N: *or* :N≡N:

The carbon atom in CO_2 has two double bonds ($4e^-$ each) for a total of eight electrons. Each oxygen atom also has a complete octet: a double bond ($4e^-$) plus two sets of **lone pairs.** Similarly, formation of a triple bond in N_2 allows each nitrogen to obtain a complete octet: six electrons from the triple bond plus a lone pair.

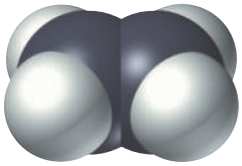
Lone pair A pair of electrons that is not used for bonding.

Carbon, nitrogen, and oxygen are the elements most often present in multiple bonds. Carbon and nitrogen form both double and triple bonds; oxygen forms double bonds. Multiple covalent bonding is particularly common in *organic* molecules, which consist predominantly of the element carbon. For example, ethene, a simple compound used commercially to induce ripening in fruit, has the formula C_2H_4. The only way for the two carbon atoms to have octets is for them to share four electrons in a carbon–carbon double bond.

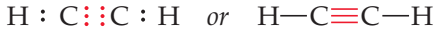
LOOKING AHEAD In Chapters 12–18, we will explore the diverse chemistry of organic compounds containing multiple bonds between carbons and other atoms.



Ethene—the carbon atoms share 4 electrons in a double bond.



Another example, ethyne, the gas used in welding, has the formula C_2H_2. To achieve octets, the two carbons share six electrons in a carbon–carbon triple bond.

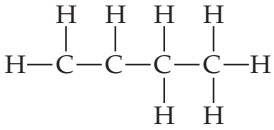


Ethyne—the carbon atoms share 6 electrons in a triple bond.

Note that in compounds with multiple bonds like ethene and ethyne, each carbon atom still forms a total of four covalent bonds.

Worked Example 4.4 Molecular Compounds: Multiple Bonds

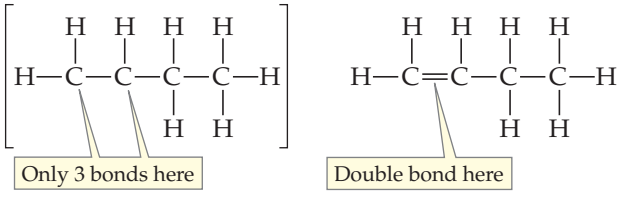
The compound 1-butene contains a multiple bond between two carbon atoms. In the following representation, however, only the connections between atoms are shown; the multiple bond is not specifically indicated. Identify the position of the multiple bond.



1-Butene

ANALYSIS Look for two adjacent atoms that appear to have fewer than the typical number of covalent bonds and connect those atoms by a double or triple bond. Refer to Figure 4.3 to see how many bonds will typically be formed by hydrogen and carbon atoms in order to achieve a complete octet of valence-shell electrons.

SOLUTION

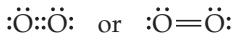


Worked Example 4.5 Multiple Bonds: Electron-Dot and Line Structures

Draw the oxygen molecule by (a) using the electron-dot symbols and (b) by using lines rather than dots to indicate covalent bonds.

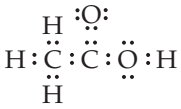
ANALYSIS Each oxygen atom has six valence electrons and will tend to form two covalent bonds to reach an octet. Thus, each oxygen atom will need to share four electrons to form a double bond.

SOLUTION



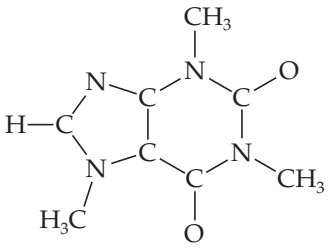
PROBLEM 4.4

Acetic acid, an organic constituent of vinegar, can be drawn using electron-dot symbols as shown next. How many outer-shell electrons are associated with each atom? Draw the structure using lines rather than dots to indicate covalent bonds.



PROBLEM 4.5

Identify the positions of all double bonds in caffeine, a stimulant found in coffee and many soft drinks and as an additive in several over-the-counter drugs, such as aspirin.



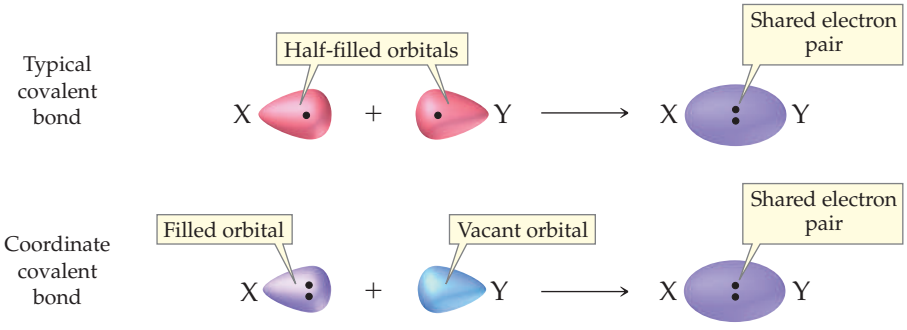
4.4 Coordinate Covalent Bonds

Learning Objective:

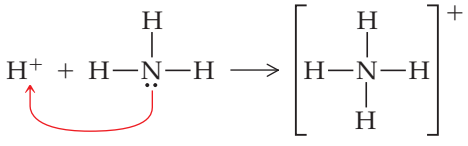
- Identify coordinate covalent bonds in a molecule or polyatomic ion.

Coordinate covalent bond The covalent bond that forms when both electrons are donated by the same atom.

In the covalent bonds we have seen thus far, the shared electrons have come from different atoms. That is, the bonds result from the overlap of two singly occupied valence orbitals, one from each atom. Sometimes, though, a bond is formed by the overlap of a filled orbital on one atom with a vacant orbital on another atom so that both electrons come from the *same* atom. The bond that results in this case is called a **coordinate covalent bond.**



The ammonium ion, NH_4^+, is an example of a species with a coordinate covalent bond. When ammonia (NH_3) reacts in water solution with a hydrogen ion, H^+, the nitrogen atom donates two electrons from a filled valence orbital to form a coordinate covalent bond to the hydrogen ion which, due to the loss of its electron, has a vacant 1*s* orbital.



Once formed, a coordinate covalent bond contains two shared electrons and is no different from any other covalent bond. All four covalent bonds in NH_4^+ are identical.

Note, however, that formation of a coordinate covalent bond often results in unusual bonding patterns, such as an N atom with four covalent bonds rather than the usual three, or an oxygen atom with three bonds rather than the usual two (H_3O^+). An entire class of substances is based on the ability of transition metals to form coordinate covalent bonds with nonmetals. Called *coordination compounds,* many of these substances have important roles in living organisms. For example, toxic metals can be removed from the bloodstream by the formation of water-soluble coordination compounds.

We will see in Chapter 19 that essential metal ions are held in enzyme molecules by coordinate covalent bonds.

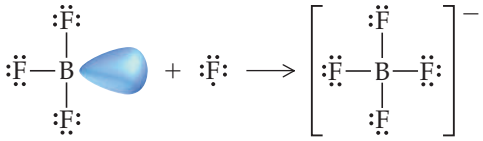
Worked Example 4.6 Coordinate Covalent Bonds

Boron typically only forms three covalent bonds but can achieve a complete octet by forming coordinate covalent bonds. Illustrate the formation of BF_4^- by the reaction between BF_3 and F^-.

ANALYSIS A coordinate covalent bond is formed when a pair of electrons from one atom occupies an empty orbital on another atom.

SOLUTION

The reaction between BF_3 and F^- can be represented as follows:



In this molecule, a coordinate covalent bond is formed when a pair of electrons from a filled valence orbital on the F^- ion occupies an empty valence orbital on the B atom in BF_3. As a result, the B atom now has four covalent bonds, three of which we would expect based on Figure 4.3.

PROBLEM 4.6

The BF_3 molecule can also react with NH_3 by formation of a coordinate covalent bond. Show the reaction and identify the coordinate covalent bond that is formed.

4.5 Characteristics of Molecular Compounds

Learning Objective:

- Distinguish structures, compositions, and properties of molecular compounds from those of ionic compounds.

We saw in Section 3.10 that ionic compounds have high melting and boiling points because the attractive forces between oppositely charged ions are so strong that the ions are held tightly together. But molecules are neutral, so there is no strong electrostatic attraction between molecules. There are, however, several weaker forces between molecules, called *intermolecular forces,* which we will look at in more detail in Chapter 8.

When intermolecular forces are very weak, molecules of a substance are so weakly attracted to one another that the substance is a gas at ordinary temperatures. If the forces are somewhat stronger, the molecules are pulled together into a liquid; and if the forces are still stronger, the substance becomes a molecular solid. Even so, the melting points and boiling points of molecular solids are usually lower than those of ionic solids because the intermolecular forces between molecules are weaker than the electrostatic attractive forces between ions.

In addition to having lower melting points and boiling points, molecular compounds differ from ionic compounds in other ways as well. Most molecular compounds are insoluble in water, for instance, because they have little attraction to the strongly polar water molecules. In addition, they do not conduct electricity when melted because they have no charged particles. Table 4.1 provides a comparison of the properties of ionic and molecular compounds.

Table 4.1 A Comparison of Ionic and Molecular Compounds

Ionic Compounds	Molecular Compounds
Smallest components are ions (eg., Na^+, Cl^-)	Smallest components are molecules (e.g., CO_2, H_2O)
Usually composed of metals combined with nonmetals	Usually composed of nonmetals combined with nonmetals
Crystalline solids	Gases, liquids, or low-melting-point solids
High melting points (e.g., NaCl = 1074 K)	Low melting points (H_2O = 273 K)
High boiling points (above 973 K) (e.g., NaCl = 1686 K)	Low boiling points (e.g., H_2O = 373 K; CH_3CH_2OH = 349 K)
Conduct electricity when molten or dissolved in water	Do not conduct electricity
Many are water soluble	Relatively few are water soluble
Not soluble in organic liquids	Many are soluble in organic liquids

PROBLEM 4.7

Aluminum chloride ($AlCl_3$) has a melting point of 463 K (190 °C), whereas aluminum oxide (Al_2O_3) has a melting point of 2343 K (2070 °C). Explain why the melting points of the two compounds are so different.

4.6 Molecular Formulas and Lewis Structures

Learning Objective:

- Interpret molecular formulas and draw Lewis structures for molecules.

Molecular formula A formula that shows the numbers and kinds of atoms in one molecule of a compound.

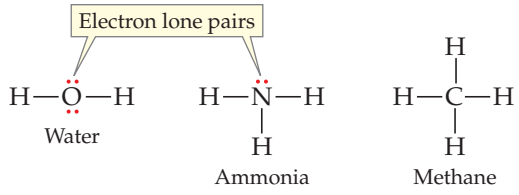
Structural formula A molecular representation that shows the connections among atoms by using lines to represent covalent bonds.

Lewis structure A molecular representation that shows both the connections among atoms and the locations of lone-pair valence electrons.

Formulas such as H_2O, NH_3, and CH_4, which show the numbers and kinds of atoms in one molecule of a compound, are called **molecular formulas.** Though important, molecular formulas are limited in their use because they do not provide information about how the atoms in a given molecule are connected.

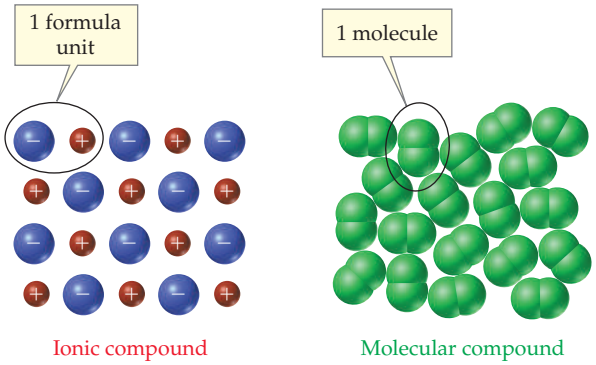
Much more useful are **structural formulas,** which use lines to show how atoms are connected, and **Lewis structures,** which show both the connections among atoms and the placement of unshared valence electrons. In a water molecule, for instance, the oxygen atom shares two electron pairs in covalent bonds with two hydrogen atoms and has two other pairs of valence electrons that are not shared in bonds. Such unshared pairs of valence electrons are called lone pairs. In an ammonia molecule, three electron pairs are used in bonding, and there is one lone pair. In methane, all four electron pairs are bonding.

Lewis structures



Note how a molecular formula differs from an ionic formula described previously in Section 3.9. A *molecular* formula gives the number of atoms that are combined in one molecule of a compound, whereas an *ionic* formula gives only a ratio of ions (Figure 4.4). The formula C_2H_4 for ethene, for example, says that every ethene molecule consists of two carbon atoms and four hydrogen atoms. The formula NaCl for

sodium chloride, however, says only that there are equal numbers of Na^+ and Cl^- ions in the crystal; the formula says nothing about how the ions interact with one another.



▲ **Figure 4.4**
The distinction between ionic and molecular compounds.
In ionic compounds, the smallest particle is an ion. In molecular compounds, the smallest particle is a molecule.

4.7 Drawing Lewis Structures

Learning Objective:

- Draw Lewis structures for molecules using their molecular formula and the octet rule.

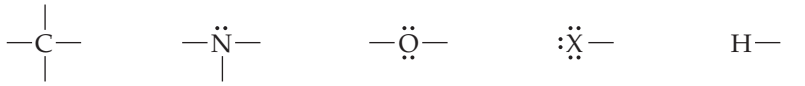
To draw a Lewis structure, you first need to know the connections among atoms. Sometimes the connections are obvious. Water, for example, can only be H—O—H because only oxygen can be in the middle and form two covalent bonds. Other times, you will have to be told how the atoms are connected.

Two approaches are used for drawing Lewis structures once the connections are known. The first is particularly useful for organic molecules like those found in living organisms because the atoms follow common bonding patterns. The second approach is a more general, stepwise procedure that works for all molecules.

Lewis Structures for Molecules Containing C, N, O, X (Halogen), and H

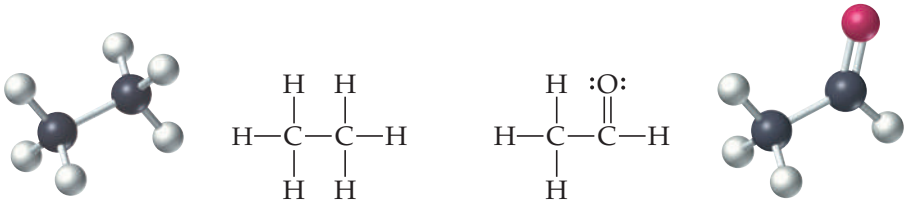
As summarized in Figure 4.3, carbon, nitrogen, oxygen, halogen, and hydrogen atoms usually maintain consistent bonding patterns in order to achieve a valence-shell octet:

- C forms four covalent bonds and often bonds to other carbon atoms.
- N forms three covalent bonds and has one lone pair of electrons.
- O forms two covalent bonds and has two lone pairs of electrons.
- Halogens (X = F, Cl, Br, I) form one covalent bond and have three lone pairs of electrons.
- H forms one covalent bond.



Relying on these common bonding patterns simplifies the writing of Lewis structures. In ethane (C_2H_6), a constituent of natural gas, for example, three of the four covalent bonds of each carbon atom are used in bonds to hydrogen, and the fourth is a carbon–carbon bond. There is no other arrangement in which all eight atoms can have their usual bonding patterns. In ethanal (C_2H_4O), a substance used in

manufacturing perfumes, dyes, and plastics, one carbon has three bonds to hydrogen, whereas the other has one bond to hydrogen and a double bond to oxygen.



Ethane, CH_3CH_3 Ethanal, CH_3CHO

Condensed structure A molecular representation in which bonds are not specifically shown but rather are understood by the order in which atoms are written.

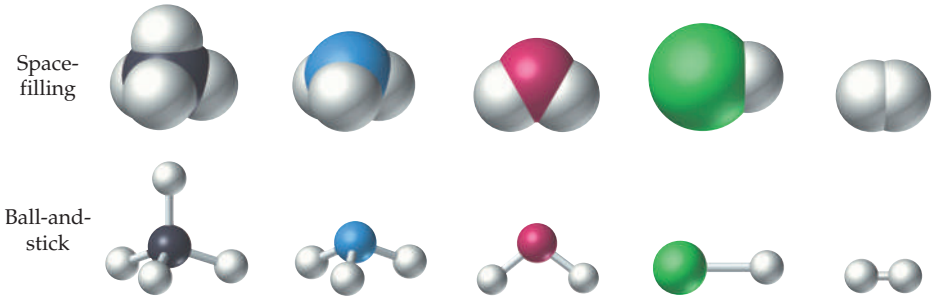
Because Lewis structures are awkward for larger organic molecules, ethane is more frequently written as a **condensed structure** in which the bonds are not specifically shown. In its condensed form, ethane is CH_3CH_3, meaning that each carbon atom has three hydrogen atoms bonded to it (CH_3) and the two (CH_3) units are bonded to each other. In the same way, ethanal can be written as CH_3CHO. Note that neither the lone-pair electrons nor the C═O double bond in ethanal is shown explicitly. You will get a lot more practice with such condensed structures in later chapters.

Condensed structures are used extensively to represent molecular structures in organic chemistry (Chapters 12–17).

Many of the computer-generated pictures we will be using from now on will be *ball-and-stick models* rather than the space-filling models used previously. Space-filling models are more realistic, but ball-and-stick models do a better job of showing connections and molecular geometry. All models, regardless of type, use a consistent color such as that presented in Table 4.2

Table 4.2 Molecular Models Color Code

Element	Color
H	White/ivory
C	Black
O	Red
N	Blue
S	Yellow
F	Light green
Cl	Dark green
Br	Brownish red
I	Purple



A General Method for Drawing Lewis Structures

A Lewis structure can be drawn for any molecule or polyatomic ion by following a five-step procedure. Take PCl_3, for example, a substance in which three chlorine atoms surround the central phosphorus atom.

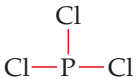
STEP 1: Find the total number of valence electrons of all atoms in the molecule or ion. In PCl_3, for example, phosphorus (group 5A) has five valence electrons and chlorine (group 7A) has seven valence electrons, giving a total of 26:

$$P + (3 \times Cl) = PCl_3$$
$$5e^- + (3 \times 7e^-) = 26e^-$$

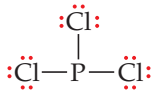
For a polyatomic ion, add one electron for each negative charge or subtract one for each positive charge. In OH^-, the total is eight electrons (six from oxygen, one from hydrogen, plus one for the negative charge). In NH_4^+, the total is eight (five from nitrogen, one from each of four hydrogens, minus one for the positive charge).

STEP 2: Draw a line between each pair of connected atoms to represent the two electrons in a covalent bond. Remember that elements in the second row of the periodic table form the number of bonds discussed earlier in this section, whereas elements in the third row and beyond can use more than eight electrons and form more than the "usual" number of bonds (Figure 4.3). A particularly common pattern is that an atom

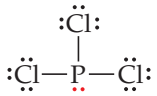
in the third row (or beyond) occurs as the central atom in a cluster. In PCl_3, for example, the phosphorus atom is in the center with the three chlorine atoms bonded to it:



STEP 3: Using the remaining electrons, add lone pairs so that each atom connected to the central atom (except H) gets an octet. In PCl_3, six of the 26 valence electrons were used to make the covalent bonds. From the remaining 20 electrons, each Cl atom needs three lone pairs to complete the octet:



STEP 4: Place any remaining electrons in lone pairs on the central atom. In PCl_3, we have used 24 of the 26 available electrons—six in three single bonds and 18 in the three lone pairs on each chlorine atom. This leaves two electrons for one lone pair on phosphorus:



STEP 5: If the central atom does not yet have an octet after all electrons have been assigned, take a lone pair from a neighboring atom and form a multiple bond to the central atom. In PCl_3, each atom has an octet, all 26 available electrons have been used, and the Lewis structure is finished.

Worked Examples 4.7–4.9 show how to deal with cases where this fifth step is needed.

Worked Example 4.7 Multiple Bonds: Electron Dots and Valence Electrons

Draw a Lewis structure for the toxic gas hydrogen cyanide, HCN. The atoms are connected in the order shown in the preceding sentence.

ANALYSIS Follow the procedure outlined in the text.

SOLUTION

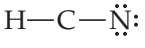
STEP 1: Find the total number of valence electrons.

$$H = 1, C = 4, N = 5 \quad \text{Total number of valence electrons} = 10$$

STEP 2: Draw a line between each pair of connected atoms to represent bonding electron pairs.

$$H—C—N \quad 2 \text{ bonds} = 4 \text{ electrons, } 6 \text{ electrons remaining}$$

STEP 3: Add lone pairs so that each atom (except H) has a complete octet.



STEP 4: All valence electrons have been used, and so Step 4 is not needed. H and N have filled valence shells but C does not.

STEP 5: If the central atom (C in this case) does not yet have an octet, use lone pairs from a neighboring atom (N) to form multiple bonds. This results in a triple bond between the C and N atoms, as shown in the following electron-dot and ball-and-stick representations:

We can check the structure by noting that all 10 valence electrons have been used (in four covalent bonds and one lone pair) and that each atom has the expected number of bonds (one bond for H, three for N, and four for C).

Worked Example 4.8 Lewis Structures: Location of Multiple Bonds

Draw a Lewis structure for vinyl chloride, C_2H_3Cl, a substance used in making polyvinyl chloride, or PVC, plastic.

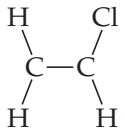
ANALYSIS Since H and Cl form only one bond each, the carbon atoms must be bonded to each other, with the remaining atoms bonded to the carbons. With only four atoms available to bond with them, the carbon atoms cannot have four covalent bonds each unless they are joined by a double bond.

SOLUTION

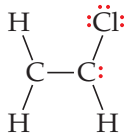
STEP 1: The total number of valence electrons is 18, four from each of the two C atoms, one from each of the three H atoms, and seven from the Cl atom.

STEP 2: Place the two C atoms in the center and divide the four other atoms between them.

The five bonds account for 10 valence electrons with eight remaining.

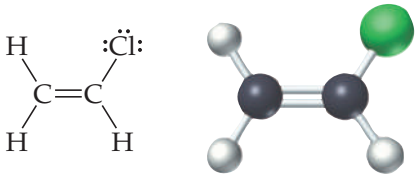


STEP 3: Place six of the remaining valence electrons around the Cl atom so that it has a complete octet and place the remaining two valence electrons on one of the C atoms (either C, it does not matter).



When all the valence electrons are distributed, the C atoms still do not have a complete octet; they each need four bonds but have only three.

STEP 5: The lone pair of electrons on the C atom can be used to form a double bond between the C atoms, giving each a total of four bonds (eight electrons). Placement of the double bond yields the Lewis structure and ball-and-stick model for vinyl chloride shown next.



All 18 valence electrons are accounted for in six covalent bonds and three lone pairs, and each atom has the expected number of bonds.

Worked Example 4.9 Lewis Structures: Octet Rule and Multiple Bonds

Draw a Lewis structure for sulfur dioxide, SO_2. The connections are O—S—O.

ANALYSIS Follow the procedure outlined in the text.

SOLUTION

STEP 1: The total number of valence electrons is 18, six from each atom.

$$S + (2 \times O) = SO_2$$
$$6e^- + (2 + 6e^-) = 18e^-$$

STEP 2: O—S—O Two covalent bonds use four valence electrons.

STEP 3: :Ö—S—Ö: Adding three lone pairs to each oxygen atom to give each an octet uses 12 additional valence electrons.

STEP 4: :Ö—S—Ö: The remaining two valence electrons are placed on sulfur, but sulfur still does not have an octet.

STEP 5: Moving one lone pair from a neighboring oxygen to form a double bond with the central sulfur gives sulfur an octet. It does not matter on which side the S=O bond is written.

:Ö—S=Ö:

NOTE: The Lewis structure for SO_2 includes a single bond to one O and a double bond to the other O. It doesn't matter which O has the double bond—both structures are equally acceptable. In reality, however, the S—O bonds in this molecule are actually closer to 1.5, an average between the two possible structures we could draw. This is an example of resonance structures or different Lewis structures that could be used to represent the same molecule.

PROBLEM 4.8

Methanamine, CH_5N, is responsible for the characteristic odor of decaying fish. Draw a Lewis structure of methanamine.

PROBLEM 4.9

Add lone pairs where appropriate to the following structures:

(a) H—C(H)(H)—O—H **(b)** N≡C—C(H)(H)—H **(c)** Cl—N(Cl)—Cl

PROBLEM 4.10

Draw Lewis structures for the following:

(a) Phosgene, $COCl_2$, a poisonous gas
(b) Hypochlorite ion, ClO^-, present in many swimming pool chemicals
(c) Hydrogen peroxide, H_2O_2
(d) Sulfur dichloride, SCl_2

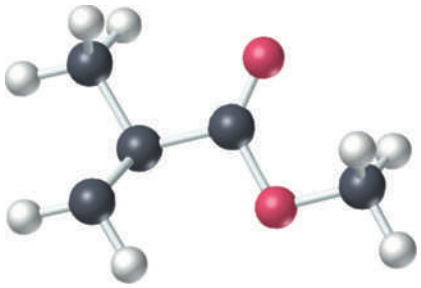
PROBLEM 4.11

Draw a Lewis structure for nitric acid, HNO_3. The nitrogen atom is in the center, and the hydrogen atom is bonded to an oxygen atom.

KEY CONCEPT PROBLEM 4.12

The molecular model shown here is a representation of methyl methacrylate, a starting material used to prepare Lucite plastic. Only the connections between atoms are shown; multiple bonds are not indicated.

(a) What is the molecular formula of methyl methacrylate?
(b) Using the octet rule and bonding patterns from Figure 4.3 indicate the likely positions of the multiple bonds and lone pairs in methyl methacrylate.



Because resonance structures don't always represent the true nature of the covalent bonds in compounds, chemists sometimes use different methods to represent bonding in molecules with resonance structures. Aromatic compounds, a class of organic compounds discussed in Section 13.8, are an important example of resonance structures in which the bonding patterns are represented using a "ring" of electrons rather than double bonds.

CHEMISTRY IN ACTION

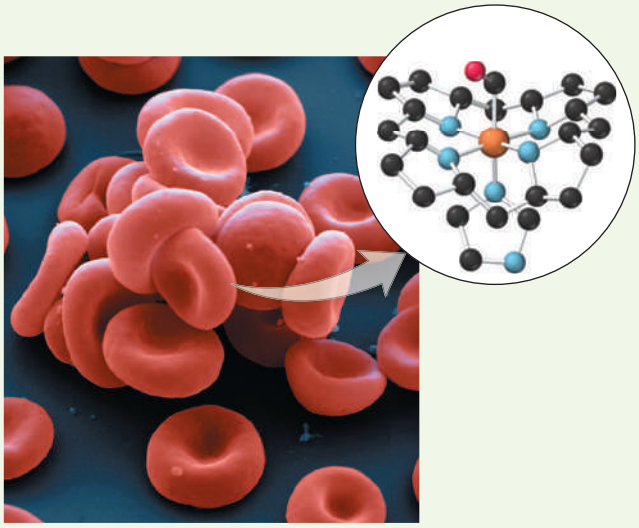
CO and NO: Pollutants or Miracle Molecules?

Carbon monoxide (CO) is a killer; everyone knows that. It is a colorless, odorless, and highly poisonous gas whose inhalation can lead to death by asphyxiation. Many accidental deaths and even suicides are reported every year around the world. Nitric oxide (NO) is formed in combustion engines and reacts with oxygen to form nitrogen dioxide (NO_2), the reddish-brown gas associated with urban smog. What most people do not know, however, is that our bodies cannot function without these molecules. A startling discovery made in 1992 showed that CO and NO are key chemical messengers in the body, used by cells to regulate critical metabolic processes.

The toxicity of CO in moderate concentration is due to its ability to bind to hemoglobin molecules in the blood, thereby preventing the hemoglobin from carrying oxygen to tissues. The high reactivity of NO leads to the formation of compounds that are toxic irritants. However, low concentrations of CO and NO are produced in cells throughout the body. Both CO and NO are highly soluble in water and can diffuse from one cell to another, where they stimulate production of a substance called *guanylyl cyclase*. Guanylyl cyclase, in turn, controls the production of another substance called *cyclic guanosine monophosphate*, which regulates many cellular functions.

Levels of CO production are particularly high in certain regions of the brain, including those associated with long-term memory. Evidence from experiments with rat brains suggests that a special kind of cell in the brain's hippocampus is signaled by transfer of a molecular messenger from a neighboring cell. The receiving cell responds back to the signaling cell by releasing CO, which causes still more messenger molecules to be sent. After several rounds of this back-and-forth communication, the receiving cell undergoes some sort of change that becomes a memory. When CO production is blocked, possibly in response to a medical condition or exposure to certain toxic metals, long-term memories are no longer stored, and those memories that previously existed are erased. When CO production is stimulated, however, memories are again laid down.

NO controls a seemingly limitless range of functions in the body. The immune system uses NO to fight infections and tumors. It is also used to transmit messages between nerve cells and is associated with the processes involved in learning and memory, sleeping, and depression. Its most advertised role, however, is as a *vasodilator,* a substance that allows blood vessels to relax and dilate. This discovery led to the development of a new class of drugs that stimulate production of enzymes called nitric oxide synthases (NOSs). These drugs can be used to treat conditions from erectile dysfunction (Viagra) to hypertension. Given the importance of NO in the fields of neuroscience, physiology, and immunology, it is not surprising that it was named "Molecule of the Year" in 1992.



▲ Carbon monoxide (CO) in the air can be toxic because it can bind to hemoglobin and interfere with oxygen transport. But CO also plays an important role in many cellular functions, including signal transmission.

CIA Problem 4.1 The CO molecule is highly reactive and will bind to the Fe^{2+} ion in hemoglobin and interfere with O_2 transport. What type of bond is formed between the CO molecule and the Fe^{2+} ion?

CIA Problem 4.2 Draw the Lewis dot structures for the molecules CO and NO. What is different about these structures compared with the general examples we have seen so far? How could these Lewis structures provide insight into the high chemical reactivity of these molecules?

PROBLEM 4.13

Molecular oxygen (O_2) is relatively stable, whereas ozone (O_3) is a very reactive compound. Draw a Lewis dot structure for ozone. Based on this structure and the bonding patterns in Figure 4.3, explain why ozone is so reactive.

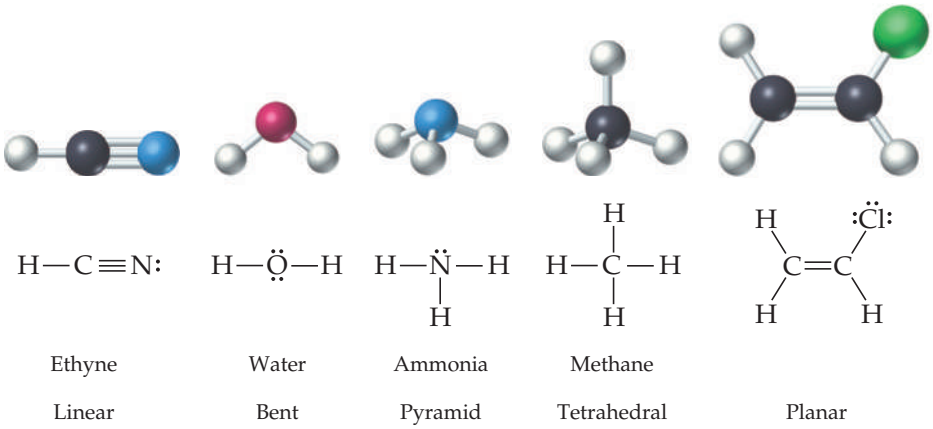
4.8 The Shapes of Molecules

Learning Objective:

- Use Lewis structures to predict molecular geometry.

Look again at the computer-generated drawings of molecules introduced in the preceding section and compiled in Figure 4.5, and you will find that the molecules are shown

with specific shapes. Ethyne is *linear,* water is *bent,* ammonia is *pyramid-shaped,* methane is *tetrahedral,* and ethene chloride is flat, or *planar.* What determines such shapes? Why, for example, are the three atoms in water connected at an angle of 104.5° rather than in a straight line? Like so many other properties, molecular shapes are related to the numbers and locations of the valence electrons around atoms.



◂ Figure 4.5
Examples of the molecular geometries for molecules with two, three, and four valence electron charge clouds.

Molecular shapes can be predicted by noting how many bonds and electron pairs surround individual atoms and applying what is called the **valence-shell electron-pair repulsion (VSEPR) model.** The basic idea of the VSEPR model is that the constantly moving valence electrons in bonds and lone pairs make up negatively charged clouds of electrons, which electrically repel one another. The clouds therefore tend to keep as far apart as possible, causing molecules to assume specific shapes. There are three steps to applying the VSEPR model:

Valence-shell electron-pair repulsion (VSEPR) model A method for predicting molecular shape by noting how many electron charge clouds surround atoms and assuming that the clouds orient as far away from one another as possible.

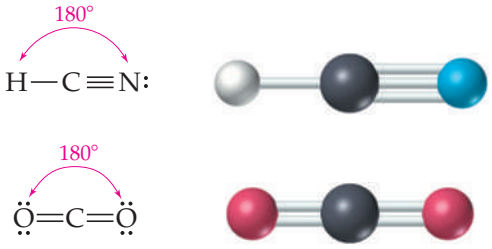
STEP 1: Draw a Lewis structure of the molecule, and identify the atom whose geometry is of interest. In a simple molecule like PCl_3 or CO_2, this is usually the central atom because it will determine the molecular geometry. In more complex molecules, the geometry around specific atoms will vary depending on the dot structure.

STEP 2: Count the number of electron charge clouds surrounding the atom of interest. The number of charge clouds is simply the total number of lone pairs plus connections to other atoms. It does not matter whether a connection is a single bond or a multiple bond because we are interested only in the *number* of charge clouds, not in how many electrons each cloud contains. The carbon atom in carbon dioxide, for instance, has two double bonds to oxygen $(O{=}C{=}O)$, and thus has two charge clouds.

STEP 3: Predict molecular shape by assuming that the charge clouds orient in space so that they are as far away from one another as possible. How they achieve this favorable orientation depends on how many bonds and lone pairs there are, as summarized in Table 4.3.

If there are only two charge clouds, as occurs on the central atom of CO_2 (two double bonds) and HCN (one single bond and one triple bond), the clouds are farthest apart when they point in opposite directions. Thus, both HCN and CO_2 are linear molecules, with **bond angles** of 180°.

Bond angle The angle formed by three adjacent atoms in a molecule.



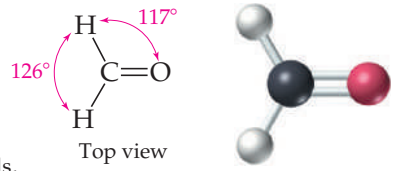
These molecules, with two bonding e⁻ clouds, are **linear,** with bond angles of 180°.

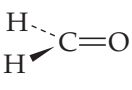
Table 4.3 Molecular Geometry Around Atoms with 2, 3, and 4 Charge Clouds

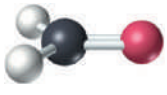
Number of Bonds	Number of Lone Pairs	Total Number of Charge Clouds	Molecular Geometry	Example
2	0	2	Linear	O=C=O
3	0	3	Trigonal planar	H, H, C=O
2	1		Bent	O, O, S
4	0	4	Tetrahedral	H, H, C, H, H
3	1		Pyramidal	H, H, N, H
2	2		Bent	H, O, H

When there are three charge clouds, as occurs on the central atom in formaldehyde (two single bonds and one double bond) and SO_2 (one single bond, one double bond, and one lone pair), the clouds will be farthest apart if they lie in a plane and point to the corners of an equilateral triangle. Thus, a formaldehyde molecule is trigonal planar, with all bond angles near 120°. Similarly, an SO_2 molecule has a trigonal planar arrangement of its three electron clouds, but one point of the triangle is occupied by a lone pair. As a result, the connection between the three atoms is therefore bent rather than linear as in CO_2, with an O—S—O bond angle of approximately 120°.

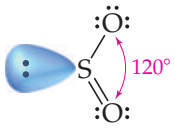
A formaldehyde molecule, with three bonding e^- clouds, is **trigonal planar** with bond angles of roughly 120°.

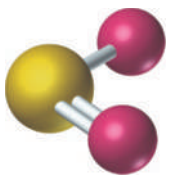


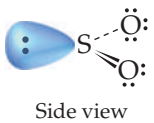




An SO_2 molecule, with two bonding e^- clouds and one nonbonding lone pair, is **bent** with a bond angle of roughly 120°.



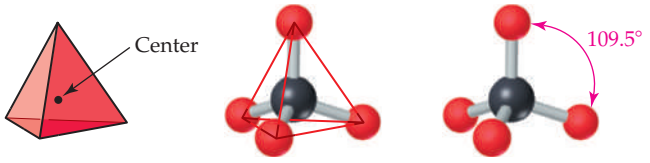




Note how the three-dimensional shapes of molecules like formaldehyde and SO_2 are shown. Solid lines are assumed to be in the plane of the paper, a dashed line recedes behind the plane of the paper away from the viewer, and a dark wedged line protrudes out of the paper toward the viewer. This standard method for showing three-dimensionality will be used throughout the rest of the book.

When there are four charge clouds, as occurs on the central atom in CH_4 (four single bonds), NH_3 (three single bonds and one lone pair), and H_2O (two single bonds and two lone pairs), the clouds can be farthest apart when they extend to the corners of a *regular tetrahedron*. As illustrated in Figure 4.6, a **regular tetrahedron** is a geometric solid whose four identical faces are equilateral triangles. The central atom is at the center of the tetrahedron, the charge clouds point to the corners, and the angle between lines drawn from the center to any two corners is 109.5°.

Regular tetrahedron A geometric figure with four identical triangular faces.



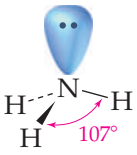
A regular tetrahedron (a) (b) A tetrahedral molecule (c)

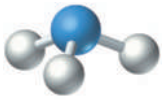
▲ **Figure 4.6**
The tetrahedral geometry of an atom surrounded by four charge clouds.
The atom is located at the center of the regular tetrahedron, and the four charge clouds point toward the corners. The bond angle between the center and any two corners is 109.5°.

Because valence-shell electron octets are so common, a great many molecules have geometries based on the tetrahedron. In methane (CH_4), for example, the carbon atom has tetrahedral geometry with H—C—H bond angles of exactly 109.5°. In ammonia (NH_3), the nitrogen atom has a tetrahedral arrangement of its four charge clouds, but one corner of the tetrahedron is occupied by a lone pair, resulting in an overall pyramidal shape for the molecule. Similarly, water, which has two corners of the tetrahedron occupied by lone pairs, has an overall bent shape.

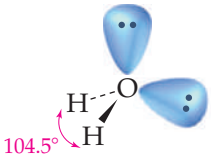
A methane molecule, with four bonding e^- clouds, is **tetrahedral** with bond angles of 109.5°.

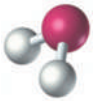
An ammonia molecule, with three bonding e^- clouds and one lone pair, is **pyramidal** with bond angles of 107°.





A water molecule, with two bonding e^- clouds and two lone pairs is **bent** with a bond angle of 104.5°.



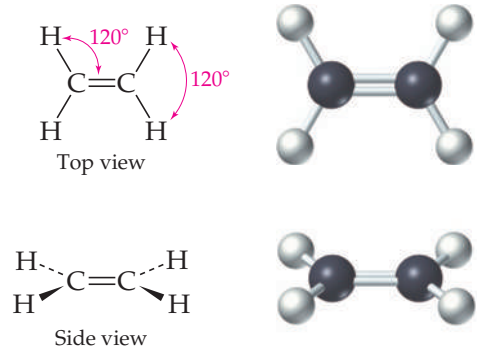


Note that the H—N—H bond angle in ammonia (107°) and the H—O—H bond angle in water (104.5°) are close to, but not exactly equal to, the ideal 109.5° tetrahedral value. The angles are diminished somewhat from their ideal value because the lone-pair charge clouds repel other electron clouds strongly and compress the rest of the molecule.

The geometry around atoms in larger molecules also derives from the shapes shown in Table 4.3. For example, each of the two carbon atoms in ethene $(H_2C{=}CH_2)$ has three charge clouds, giving rise to trigonal planar geometry. It turns out that the

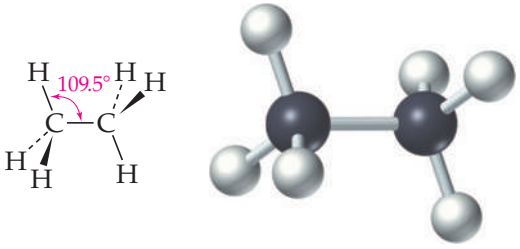
molecule as a whole is also planar, with H—C—C and H—C—H bond angles of approximately 120°.

The ethene molecule (three bonding e⁻ clouds on each carbon atom), is **planar,** with bond angles of 120°.



Carbon atoms bonded to four other atoms are each at the center of a tetrahedron, as shown here for ethane, $H_3C—CH_3$.

The ethane molecule (4 bonding e⁻ clouds) has **tetrahedral** carbon atoms, with bond angles of 109.5°.



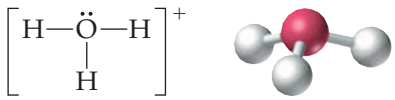
Worked Example 4.10 Lewis Structures: Molecular Shape

What shape would you expect for the hydronium ion, H_3O^+?

ANALYSIS Draw the Lewis structure for the molecular ion, and count the number of charge clouds around the central oxygen atom; imagine the clouds orienting as far away from one another as possible.

SOLUTION

The Lewis structure for the hydronium ion shows that the oxygen atom has four charge clouds (three single bonds and one lone pair). The hydronium ion is therefore pyramidal with bond angles of approximately 109.5°.



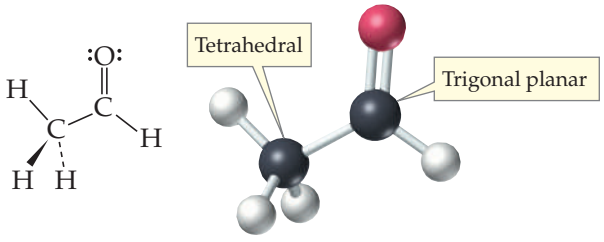
Worked Example 4.11 Lewis Structures: Charge Cloud Geometry

Predict the geometry around each of the carbon atoms in an ethanal molecule, CH_3CHO.

ANALYSIS Draw the Lewis structure and identify the number of charge clouds around each of the central carbon atoms.

SOLUTION

The Lewis structure of ethanal shows that the CH_3 carbon has four charge clouds (four single bonds) and the CHO carbon atom has three charge clouds (two single bonds, one double bond). Table 4.3 indicates that the CH_3 carbon is tetrahedral, but the CHO carbon is trigonal planar.



CHEMISTRY IN ACTION

VERY Big Molecules

How big can a molecule be? The answer is very, very big. The really big molecules in our bodies and in many items we buy are all polymers. Like a string of beads, a polymer is formed of many repeating units connected in a long chain. Each "bead" in the chain comes from a simple molecule that has formed chemical bonds at both ends, linking it to other molecules. The repeating units can be the same:

–a–a–a–a–a–a–a–a–a–a–a–a–

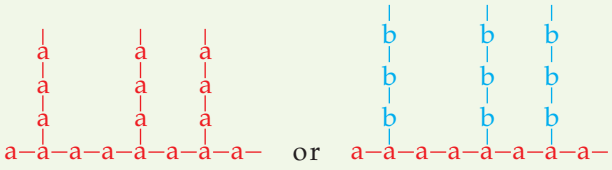
or they can be different. If different, they can be connected in an ordered pattern:

–a–b–a–b–a–b–a–b–a–b–a–b–

or in a random pattern:

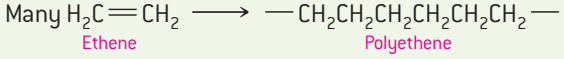
–a–b–b–a–b–a–a–a–b–a–b–b–

Furthermore, the polymer chains can have branches, and the branches can have either the same repeating unit as the main chain or a different one:



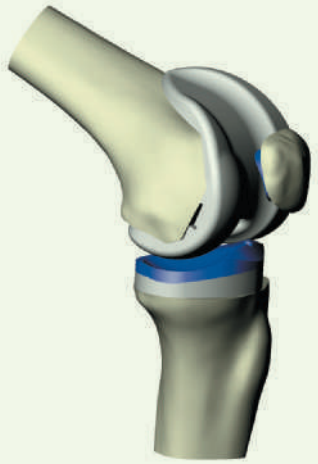
Still other possible variations include complex, three-dimensional networks of "cross-linked" chains. The rubber used in tires, for example, contains polymer chains connected by cross-linking atoms of sulfur to impart greater rigidity.

We all use synthetic polymers every day—we usually call them "plastics." Common synthetic polymers are made by connecting up to several hundred thousand smaller molecules together, producing giant polymer molecules with masses up to several million atomic mass units. Polyethene, for example, is made by combining as many as 50,000 ethene molecules to give a polymer with repeating units.



The product is used in such items as chairs, toys, drain pipes, milk bottles, and packaging films. Other examples of polymers include the nylon used in clothing and pantyhose, molded hardware (nuts and bolts), and the Kevlar used in bulletproof vests.

Nature began to exploit the extraordinary variety of polymer properties long before humans did. In fact, despite great progress in recent years, there is still much to be learned about the polymers in living things. Carbohydrates and proteins are polymers, as are the giant molecules of deoxyribonucleic acid (DNA) that govern many cellular processes, including reproduction, in all organisms. Nature's polymer molecules, though, are more complex than any that chemists have yet created.



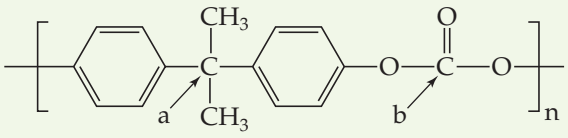
▲ The ultrahigh molecular weight polyethene (UHMWPE) used as a lubricating interface in this artificial knee is made from the same basic polymer used for milk jugs and plastic shopping bags.

Polymers also find diverse applications in the fields of health and medicine, depending on their chemical and physical properties. Some polymers are absorbed or broken down by the body (i.e. are biodegradable) and are used as sutures or adhesives, for support of internal organs or tissue, or for controlled delivery of drugs. Other polymers are stable or inert and can retain their integrity for years. For example, Teflon and ultrahigh molecular weight polyethene (UHMWPE) are highly durable low-friction polymer coatings used as lubricating interfaces in artificial joints.

Carbohydrates are polymers composed of sugar molecules linked together in long chains (Chapter 20), whereas proteins are polymers of smaller molecules called amino acids (Chapter 18). DNA is a polymer of repeating nucleotide subunits, which is discussed in Chapter 26.

CIA Problem 4.3 Find the structure of Teflon (polytetrafluoroethylene). How is it similar to the structure of polyethene, and how is it different?

CIA Problem 4.4 Polycarbonate, also known as plexiglass, has the basic repeating unit shown in the following figure. What is the geometry of the electron clouds for the carbon atoms labeled "a" and "b" in this structure?



PROBLEM 4.14

Boron typically only forms three covalent bonds because it only has three valence electrons but can form coordinate covalent bonds. Draw the Lewis structure for BF_4^- and predict the molecular shape of the ion.

PROBLEM 4.15

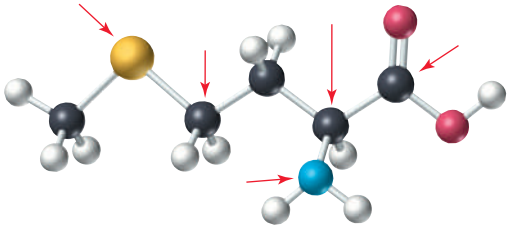
Predict shapes for the organic molecules chloroform, $CHCl_3$, and 1,1-dichloroethene, $Cl_2C{=}CH_2$.

PROBLEM 4.16

Selenium and sulfur are in the same chemical family as oxygen. Hydrogen selenide (H_2Se) and hydrogen sulfide (H_2S) are both toxic gases having terrible odors. Draw Lewis structures and identify the shape of these compounds.

KEY CONCEPT PROBLEM 4.17

Draw a structure corresponding to the molecular model of the amino acid methionine shown here, and describe the geometry around the indicated atoms. Refer to the color key in Table 4.2.



Methionine

4.9 Polar Covalent Bonds and Electronegativity

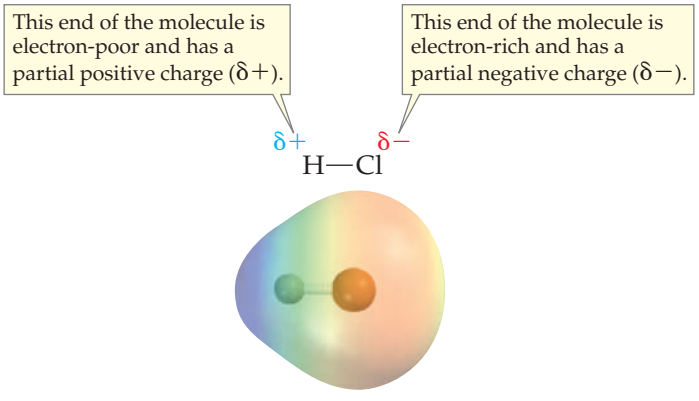
Learning Objective:

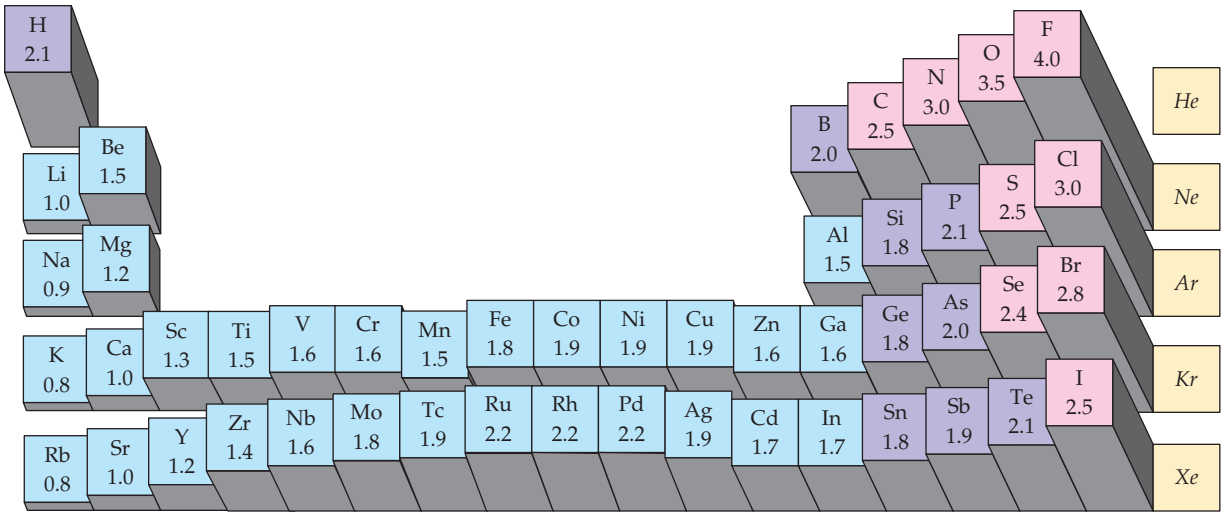
- Distinguish between polar covalent, nonpolar covalent, and ionic bonds using electronegativity.

Polar covalent bond A bond in which the electrons are attracted more strongly by one atom than by the other.

Electrons in a covalent bond occupy the region between the bonded atoms. If the atoms are identical, as in H_2 and Cl_2, the electrons are attracted equally to both atoms and are shared equally. If the atoms are *not* identical, however, as in HCl, the bonding electrons are attracted more strongly by one atom than by the other and are shared unequally. Such bonds are said to be **polar covalent bonds.** In hydrogen chloride, for example, electrons spend more time near the chlorine atom than near the hydrogen atom. Although the molecule as a whole is neutral, the chlorine is more negative than the hydrogen, resulting in *partial* charges on the atoms. These partial charges are represented by placing a $\delta-$ (Greek lowercase *delta*) on the more negative atom and a $\delta+$ on the more positive atom.

A particularly helpful way of visualizing this unequal distribution of bonding electrons is to look at what is called an *electrostatic potential map,* which uses color to portray the calculated electron distribution in a molecule. In HCl, for example, the electron-poor hydrogen is blue and the electron-rich chlorine is reddish-yellow.





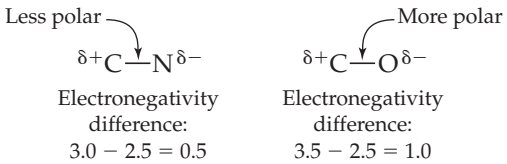
▲ **Figure 4.7**

Electronegativities of several main group and transition metal elements.
Reactive nonmetals at the top right of the periodic table are the most electronegative, and metals at the lower left are the least electronegative. The noble gases are not assigned values.

The ability of an atom to attract electrons in a covalent bond is called the atom's **electronegativity.** Fluorine, the most electronegative element, is assigned a value of four, and less electronegative atoms are assigned lower values, as shown in Figure 4.7. Metallic elements on the left side of the periodic table attract electrons only weakly and have lower electronegativities, whereas the halogens and other reactive nonmetal elements on the upper right side of the table attract electrons strongly and have higher electronegativities. Note in Figure 4.7 that electronegativity generally decreases going down the periodic table within a group.

Electronegativity The ability of an atom to attract electrons in a covalent bond.

Comparing the electronegativities of bonded atoms makes it possible to compare the polarities of bonds and to predict the occurrence of ionic bonding. Both oxygen (electronegativity 3.5) and nitrogen (3.0), for instance, are more electronegative than carbon (2.5). As a result, both C—O and C—N bonds are polar, with carbon at the positive end. The larger difference in electronegativity values shows that the C—O bond is the more polar of the two.



The values given in Figure 4.7 indicate that carbon and hydrogen have similar electronegativities. As a result, C—H bonds are nonpolar. We will see in Chapters 12–25 how this fact helps explain the properties of organic and biological compounds, all of which have carbon and hydrogen as their principal constituents.

As a rule of thumb, electronegativity differences of less than 0.5 (such as C—H) result in nonpolar covalent bonds, differences up to 1.9 (such as N—H and O—H) indicate increasingly polar covalent bonds, and differences of two or more indicate ionic bonds. The electronegativity differences show, for example, that the bond between carbon and fluorine is highly polar covalent, the bond between sodium and chlorine is largely ionic, and the bond between rubidium and fluorine is almost completely ionic.

Electronegativity Difference		Type of Bond
0—0.4	~	Covalent
0.5 —1.9	~	Polar covalent
2.0 and above	~	Ionic

	$^{\delta+}C—F^{\delta-}$	Na^+Cl^-	Rb^+F^-
Electronegativity difference:	1.5	2.1	3.2

The partial charges associated with each end of the bond result in a **dipole,** meaning "two poles," similar to the "+" and "–" ends of a magnet. The larger the dipole associated with a bond, the more polar it is. Note, though, that there is no sharp dividing line between polar covalent and ionic bonds; most bonds fall somewhere between two extremes.

Dipole A difference in charge (+ or –) associated with one end of a covalent bond compared with the other or one end of a molecule compared with another.

Worked Example 4.12 Electronegativity: Ionic, Nonpolar, and Polar Covalent Bonds

Predict whether each of the bonds between the following atoms would be ionic, polar covalent, or nonpolar covalent. If polar covalent, which atom would carry the partial positive and negative charges?

(a) C and Br **(b)** Li and Cl **(c)** N and H **(d)** Si and I

ANALYSIS Compare the electronegativity values for the atoms and classify the nature of the bonding based on the electronegativity difference.

SOLUTION

(a) The electronegativity for C is 2.5 and for Br is 2.8, and the difference is 0.3, indicating nonpolar covalent bonding would occur between these atoms.

(b) The electronegativity for Li is 1.0 and for Cl is 3.0, and the difference is 2.0, indicating that ionic bonding would occur between these atoms.

(c) The electronegativity for N is 3.0 and for H is 2.5, and the difference is 0.5. Bonding would be polar covalent, with N $= \delta-$ and H $= \delta+$.

(d) The electronegativity for Si is 1.8 and for I is 2.5, and the difference is 0.7. Bonding would be polar covalent, with I $= \delta-$, and Si $= \delta+$.

PROBLEM 4.18

The elements H, N, O, P, and S are commonly bonded to carbon in organic compounds. Arrange these elements in order of increasing electronegativity.

PROBLEM 4.19

Use electronegativity differences to classify bonds between the following pairs of atoms as ionic, nonpolar covalent, or polar covalent. For those that are polar, use the symbols $\delta+$ and $\delta-$ to identify the location of the partial charges on the polar covalent bond.

(a) I and Cl **(b)** Li and O

(c) Br and Br **(d)** P and Br

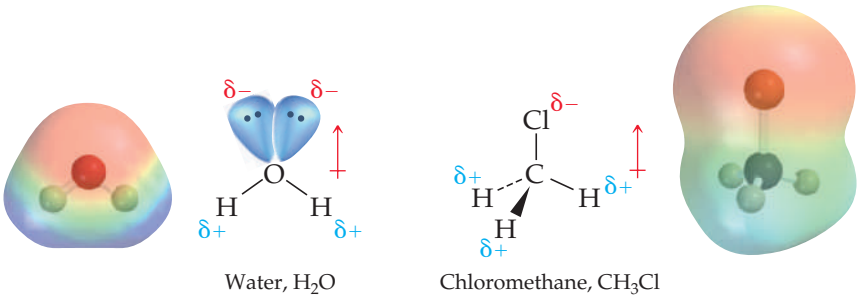
4.10 Polar Molecules

Learning Objective:

- Predict polarity of molecules using electronegativity and molecular geometry (VSEPR).

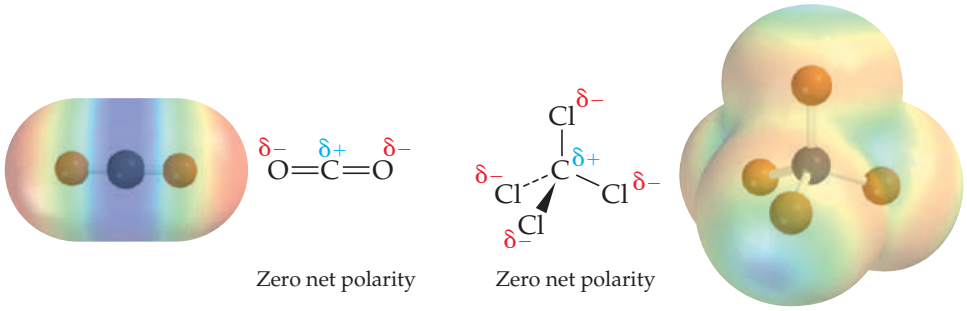
Just as individual bonds can be polar, entire *molecules* can be polar if electrons are attracted more strongly to one part of the molecule than to another. Molecular polarity is due to the sum of all individual bond polarities and lone-pair contributions in the molecule and is often represented by an arrow pointing in the direction that electrons are displaced. The arrow is pointed at the negative end and is crossed at the positive end to resemble a plus sign, $(\delta+) \leftrightarrow (\delta-)$.

Molecular polarity depends on the shape of the molecule as well as the presence of polar covalent bonds and lone pairs. In water, for example, electrons are displaced away from the less electronegative hydrogen atoms toward the more electronegative oxygen atom so that the net polarity points between the two O—H bonds. In chloromethane, CH_3Cl, electrons are attracted from the carbon/hydrogen part of the molecule toward the electronegative chlorine atom so that the net polarity points along the C—Cl bond. Electrostatic potential maps show these polarities clearly, with electron-poor regions in blue and electron-rich regions in red.



Water, H_2O Chloromethane, CH_3Cl

Furthermore, just because a molecule has polar covalent bonds, it does not mean that the molecule is necessarily polar overall. Carbon dioxide (CO_2) and tetrachloromethane (CCl_4) molecules, for instance, have no net polarity because their symmetrical shapes cause the individual C═O and C—Cl bond polarities to cancel.



Zero net polarity Zero net polarity

Polarity has a dramatic effect on the physical properties of molecules, particularly on melting points, boiling points, and solubilities. We will see numerous examples of such effects in subsequent chapters.

The unique properties of water, which will be discussed in Chapter 8, result from its polarity and molecular geometry.

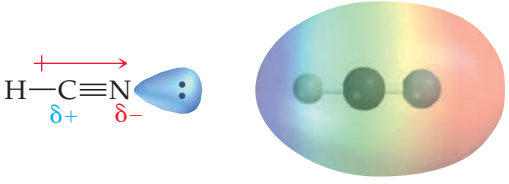
Worked Example 4.13 Electronegativity: Polar Bonds and Polar Molecules

Look at the structures of (a) hydrogen cyanide (HCN) and (b) vinyl chloride $(H_2C{=}CHCl)$, described in Worked Examples 4.6 and 4.7; decide whether or not the molecules are polar, and show the direction of net polarity in each.

ANALYSIS Draw a Lewis structure for each molecule to find its shape, and identify any polar bonds using the electronegativity values in Figure 4.7. Then, decide on net polarity by adding the individual contributions.

SOLUTION

(a) The carbon atom in hydrogen cyanide has two charge clouds, making HCN a linear molecule. The C—H bond is relatively nonpolar, but the C≡N bonding electrons are pulled toward the electronegative nitrogen atom. In addition, a lone pair protrudes from nitrogen. Thus, the molecule has a net polarity.



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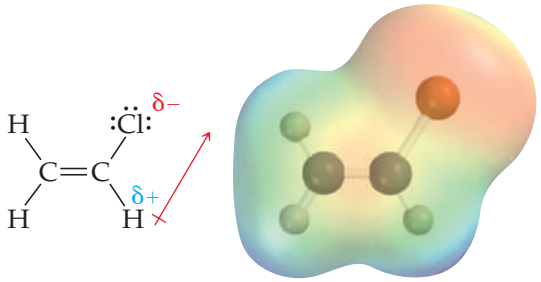
(b) Vinyl chloride, like ethene, is a planar molecule. The C—H and C═C bonds are nonpolar, but the C—Cl bonding electrons are displaced toward the electronegative chlorine. Thus, the molecule has a net polarity.



PROBLEM 4.20

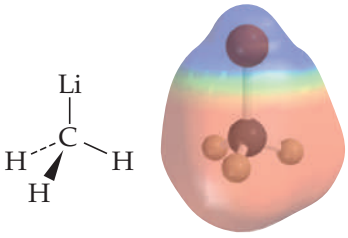
Look at the molecular shape of formaldehyde (CH_2O) described on page 152, decide whether or not the molecule is polar, and show the direction of net polarity.

PROBLEM 4.21

Draw a Lewis structure for dimethyl ether (CH_3OCH_3), predict its shape, and tell whether or not the molecule is polar.

KEY CONCEPT PROBLEM 4.22

From this electrostatic potential map of methyllithium, identify the direction of net polarity in the molecule. Explain this polarity based on electronegativity values.



Methyllithium

HANDS-ON CHEMISTRY 4.1

Visualization of molecules can help us to understand their properties. Chemists typically do this with model kits or computer simulations, but we can approximate this by using toothpicks and gum drops or some other small, colored soft candy. We will let the toothpicks represent covalent bonds and the gum drops represent atoms of different elements. Try to find gum drops or candies with colors that match the color codes in Table 4.2.

a. We will start by building a methane molecule (CH_4). Take two tooth picks and one carbon atom (black gumdrop) and arrange them on the table like the figure to the right (in margin) to approximate a bond angle of 109.5°. Repeat this process twice more until you have your central C atom (black gumdrop) with four bonds oriented similarly to the tetrahedral methane molecule reproduced here.

Finally, add white gum drops to the end of each of the four toothpicks to represent H atoms. Examine your methane model from various directions and orientations. Is it symmetrical? Refer to the electronegativity differences in Figure 4.7. Are the covalent bonds polar or nonpolar?

b. Now replace two of the H atoms with chlorine (green gum drops). Are the C—Cl bonds polar? Which end of each covalent bond is negative? Orient your molecule on the table top so that both Cl atoms are on the same side. Now look at the molecule as a whole. Where are the partial negative charges ($\delta-$) in the molecule? Is one side of the molecule more negative than the other? Is this molecule polar?

c. Now replace all four H atoms with Cl atoms, and answer the same questions as in Part b.

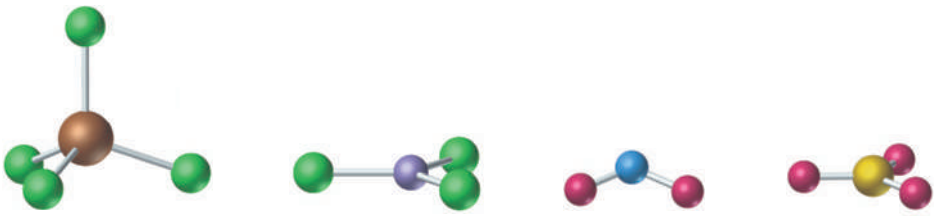
4.11 Naming Binary Molecular Compounds

Learning Objective:

- Name binary molecular compounds.

When two different elements combine, they form what is called a **binary compound.** The formulas of binary molecular compounds are usually written with the less electronegative element first. Thus, metals are always written before nonmetals, and a nonmetal farther left on the periodic table generally comes before a nonmetal farther right. For example,

Binary compound A compound formed by combination of two different elements.



$TiCl_4$ BCl_3 NO_2 SO_3

as we learned in Section 3.8, the formulas of ionic compounds indicate the number of anions and cations necessary for a neutral formula unit, which depends on the charge on each of the ions. With molecular compounds, however, many combinations of atoms are possible, since nonmetals are capable of forming multiple covalent bonds. When naming binary molecular compounds, therefore, we must identify exactly how many atoms of each element are included in the molecular formula. The names of binary molecular compounds are assigned in two steps, using the prefixes listed in Table 4.4 to indicate the number of atoms of each element combined.

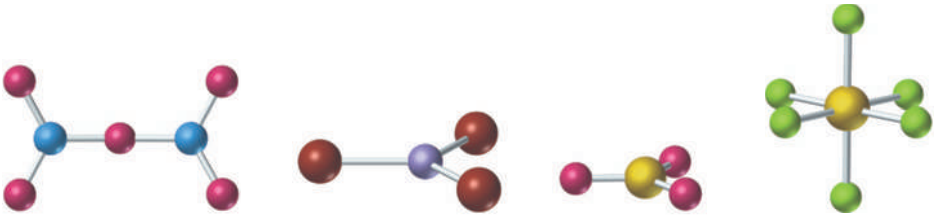
Table 4.4 Numerical Prefixes Used in Chemical Names

Number	Prefix
1	mono-
2	di-
3	tri-
4	tetra-
5	penta-
6	hexa-
7	hepta-
8	octa-
9	nona-
10	deca-

STEP 1: Name the first element in the formula, using a prefix if needed to indicate the number of atoms.

STEP 2: Name the second element in the formula, and modify by adding the *-ide* suffix as when naming anions (Section 3.5). Include numerical prefixes as appropriate.

The prefix *mono-,* meaning one, is omitted except where needed to distinguish between two different compounds with the same elements. For example, the two oxides of carbon are named carbon *mon*oxide for CO and carbon *di*oxide for CO_2. (Note that when the element name begins with a vowel, the last letter in the numerical prefix (if an "o" or an "a") is often deleted. For instance, we say *mon*oxide instead of *mono*oxide, and *pent*oxide instead of *penta*oxide.) Some examples follow:



N_2O_5 — *Di*nitrogen *pent*oxide

BBr_3 — Boron *tri*bromide

SO_3 — Sulfur *tri*oxide

SF_6 — Sulfur *hexa*fluoride

Naming of molecular compounds can get complicated when more than two elements are present. This is particularly true for *organic compounds,* a class of molecular compounds composed largely of carbon (see examples in the Chemistry in Action on the following page). The rules for naming these compounds will be discussed in later chapters.

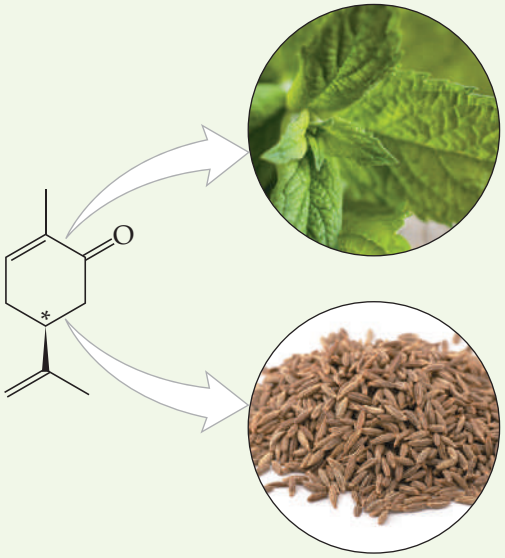
CHEMISTRY IN ACTION

Damascenone by Any Other Name Would Smell as Sweet

What's in a name? According to Shakespeare's *Romeo and Juliet*, a rose by any other name would smell as sweet. Chemical names, however, often provoke less favorable responses: "It's unpronounceable;" "It's too complicated;" "It must be something bad."

But why are chemical names so complicated? The reason is obvious once you realize that there are more than 19 *million* known chemical compounds. The full name of a chemical compound has to include enough information to tell chemists the composition and structure of the compound. It is as if every person on earth had to have his or her own unique name that described height, hair color, and other identifying characteristics in sufficient detail to distinguish him or her from every other person. Consider, also, that subtle differences in structure can result in significant differences in chemical or physical properties. Geraniol, for example, is used as a flavor additive in the food industry, whereas citronellol is used in perfumes and insect repellants, such as citronella candles. The common names for these substances are easier to remember, but their *chemical* names give us precise information about their structural differences and similarities. Geraniol also known as *3,7-dimethylocta-2,6-dien-1-ol* differs from citronellol (or *3,7-dimethyloct-6-en-1-ol*) by only one double bond.

The three-dimensional orientation of atoms in a molecule is also important and must be reflected in the chemical name. As we saw in our chapter opener, many drugs and other biochemically active compounds exist in two forms that have identical molecular formulas but differ in the orientation of side groups around a single carbon atom—a property known as chirality that will be explored further in Chapters 14 and 20. L-Dopa, for example, is used to treat Parkinson's disease, whereas its counterpart (D-Dopa) has been linked to granulocytopenia, an immune system disorder. Similarly, one form of thalidomide is effective in treating morning sickness, whereas the other form causes birth defects. We learned at the beginning of the chapter that dextromethorphan is a cough suppressant in common over-the-counter remedies, whereas its counterpart, levomethorphan, is a highly addictive opiate.

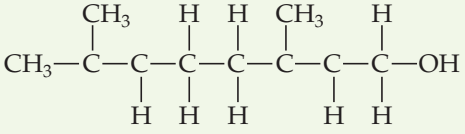


▲ The different aromas of L-carvone (spearmint) and D-carvone (cumin) result from variations in the 3-dimensional orientation of bonds around one carbon in carvone (indicated in the figure with a *).

Even carvone, one of the compounds that contribute to the aroma of roses, exists in multiple forms; L-carvone is perceived by smell receptors in the nose as spearmint, whereas D-carvone evokes the savory aroma of caraway or cumin. Molecular structure determines chemical behavior and biological activity, and the chemical name must specify that structure precisely—including the presence and location of multiple bonds and three-dimensional orientation.

CIA Problem 4.5 Why are many chemical names so complex?

CIA Problem 4.6 Geraniol, one of the components of rose oil has the basic structure represented here. Draw the structural formula for geraniol to include any multiple bonds, and then write the condensed structure for geraniol.



Worked Example 4.14 Naming Molecular Compounds

Name the following compounds:

(a) N_2O_3 **(b)** $GeCl_4$ **(c)** PCl_5

SOLUTION

(a) The first element is N (nitrogen) and there are two N atoms = *di*nitrogen; the second element is O (oxygen), which is modified with the *-ide* suffix. There are three O atoms = *tri*oxide. Put all of the elements together to get the molecule's name: Dinitrogen trioxide.

(b) Ge = germanium; Cl = chlorine, which is modified to chlor*ide*. There are four Cl atoms = *tetra*chloride; Germanium tetrachloride.

(c) P = Phosphorus; Cl = chlor*ide*. There are five Cl atoms = Phosphorus pentachloride.

Worked Example 4.15 Writing Formulas for Molecular Compounds

Write molecular formulas for the following compounds:

(a) Nitrogen triiodide **(b)** Silicon tetrachloride **(c)** Carbon disulfide

SOLUTION

(a) The first element is nitrogen (N), the "tri" prefix indicates "3," and iodide is derived from iodine (I) = NI_3

(b) Silicon is Si, "tetra" = 4, and chloride is derived from chlorine (Cl) = $SiCl_4$

(c) Carbon is C, "di" = 2, and sulfide is derived from sulfur (S) = CS_2

PROBLEM 4.23

Name the following compounds:

(a) S_2Cl_2 **(b)** ICl **(c)** ICl_3

PROBLEM 4.24

Write formulas for the following compounds:

(a) Selenium tetrafluoride

(b) Diphosphorus pentoxide

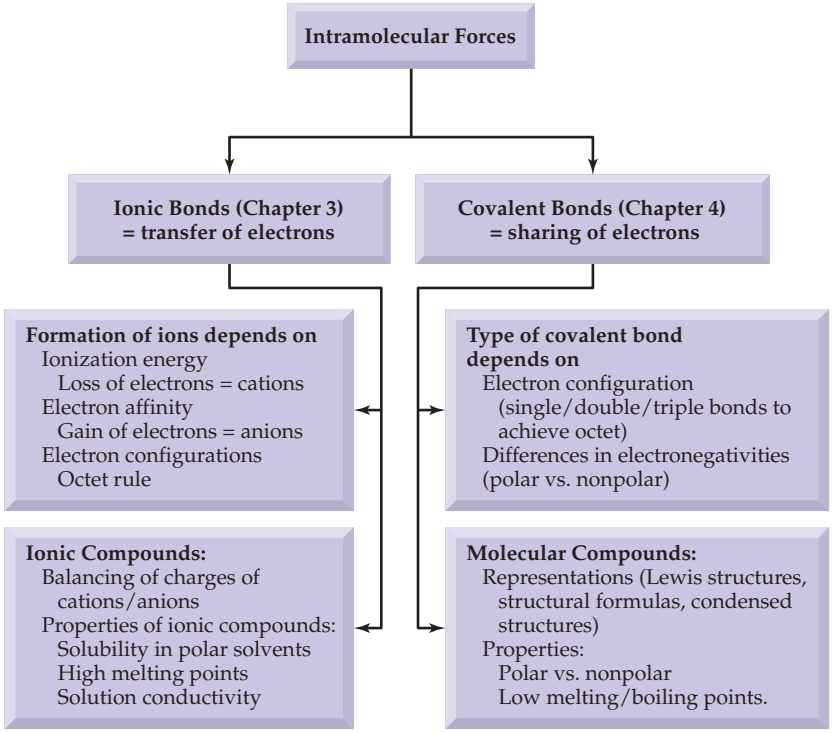
(c) Bromine trifluoride

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Describe the nature of covalent bonds and how they are formed.** A covalent bond is formed by the sharing of electrons between atoms, and typically occurs when a singly occupied valence orbital on one atom overlaps a singly occupied valence orbital on another atom. The two electrons occupy both overlapping orbitals and belong to both atoms, thereby bonding the atoms together *(see Problems 31, 34, 100, and 103)*.
- **Differentiate between ionic and covalent bonds.** A covalent bond is formed by the sharing of electrons between atoms rather than by the complete transfer of electrons from one atom to another *(see Problems 31, 34, 100, and 103)*.
- **Predict the number of covalent bonds an atom will form based on its position in the periodic table.** Depending on the number of valence electrons, different atoms form different numbers of covalent bonds. In general, an atom shares enough electrons to reach a noble gas configuration. Hydrogen, for instance, forms one covalent bond because it needs to share one more electron to achieve the helium configuration $1s^2$ Carbon and other group 4A elements form four covalent bonds because they need to share four more electrons to reach an octet. In the same way, nitrogen and other group 5A elements form three covalent bonds, oxygen and other group 6A elements form two covalent bonds, and halogens (group 7A elements) form one covalent bond *(see Problems 36, 37, 40, 49, 85, 88, 89, and 103)*.
- **Use the octet rule to determine when multiple covalent bonds (double and triple) will appear between two atoms.** The atoms in some molecules can satisfy the octet rule by sharing two electrons to form a single bond (such as C—C). In other molecules, some atoms have to share more than one pair of electrons to satisfy the octet rule. Atoms that share four electrons are joined by a double bond (such as O═O), and atoms that share six electrons are joined by a triple bond (such as N≡N) *(see Problems 27–29, 33, 46, 49, and 98)*.
- **Identify coordinate covalent bonds in a molecule or polyatomic ion.** Alternatively, electron sharing can occur when a filled orbital containing an unshared, lone pair of electrons on one atom overlaps a vacant orbital on another atom to form a coordinate covalent bond *(see Problems 32, 38, 39, 42, 43, 89, and 90)*.
- **Distinguish structures, compositions, and properties of molecular compounds from those of ionic compounds.** A group of atoms held together by covalent bonds or shared electron pairs is called a molecule. Molecular compounds can be gases, liquids, or low-melting solids. They usually have lower melting points and boiling points than ionic compounds, many are water insoluble, and they do not conduct electricity when melted or dissolved. By contrast, ionic compounds are formed by the transfer of electrons between atoms to form ions, which are held together by electrostatic attractions, or ionic bonds. Ionic compounds tend to be solids with high-melting point and are conductive when dissolved in solution *(see Problems 27, 29, 41, 44, 45, 53, 54, 100, and 103)*.
- **Interpret molecular formulas and draw Lewis structures for molecules.** Formulas such as H_2O, NH_3, and CH_4, which show the numbers and kinds of atoms in a molecule, are called molecular formulas. More useful are Lewis structures, which show how atoms are connected in molecules. Covalent bonds are indicated as lines between atoms, and valence electron lone pairs are shown as dots *(see Problems 30, 46, 52, 55–62, and 97)*.
- **Draw Lewis structures for molecules using their molecular formula and the octet rule.** Lewis structures are drawn by counting the total number of valence electrons in a molecule or polyatomic ion and then placing shared pairs (bonding) and lone pairs (nonbonding) so that all electrons are accounted for *(see Problems 28, 35, 42, 43, 46–52, 55–62, 85, 86, 90, 93–96, 98, 99, 101, and 102)*.

- **Use Lewis structures to predict molecular geometry.** Molecules have specific shapes that depend on the number of electron charge clouds (bonds and lone pairs) surrounding the various atoms. These shapes can often be predicted using the VSEPR model. Atoms with two electron charge clouds adopt linear geometry, atoms with three charge clouds adopt trigonal planar geometry, and atoms with four charge clouds adopt tetrahedral geometry *(see Problems 25–27, 29, 63–68, 86, 87, 90, 93, and 99)*.
- **Distinguish between polar covalent, nonpolar covalent, and ionic bonds using electronegativity.** Bonds between atoms are polar covalent if the bonding electrons are not shared equally between the atoms. The ability of an atom to attract electrons in a covalent bond is the atom's electronegativity and is highest for reactive nonmetal elements on the upper right of the periodic table and lowest for metals on the lower left. Comparing electronegativities allows prediction of whether a given bond is polar covalent, nonpolar covalent, or ionic *(see Problems 34, 69–76, 86, 89, 92, and 100)*.
- **Predict polarity of molecules using electronegativity and molecular geometry (VSEPR).** Just as individual bonds can be polar, entire molecules can be polar if electrons are attracted more strongly to one part of the molecule than to another. Molecular polarity is due to the sum of all individual bond polarities and lone-pair contributions in the molecule *(see Problems 30, 34, 77–80, 87, and 91)*.
- **Name binary molecular compounds.** When naming binary molecular compound, the less electronegative element (further to the left or further down in the periodic table) is named first. The name of the more electronegative element is modified by adding the *-ide* suffix and is then added to the compound name. Numerical prefixes are added as needed to indicate the number of each type of atom. For example, NO_2 is *nitrogen dioxide (see Problems 81–84, and 92)*.

CONCEPT MAP: ELECTROSTATIC FORCES



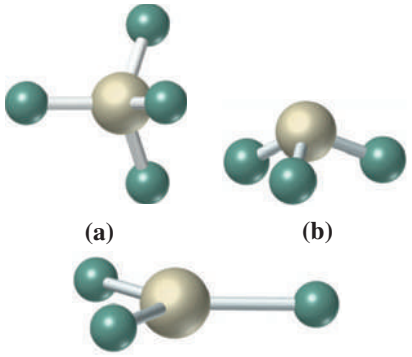
▲ **Figure 4.8 Concept Map.** As you can see from the concept map, the electronic structure of atoms discussed in Chapter 2 plays a critical role in the formation of ionic compounds (Chapter 3) or molecular compounds (Chapter 4). Furthermore, the nature of the attractive forces between particles (intermolecular versus intramolecular) plays a role in the physical and chemical behavior of substances discussed in later chapters.

KEY WORDS

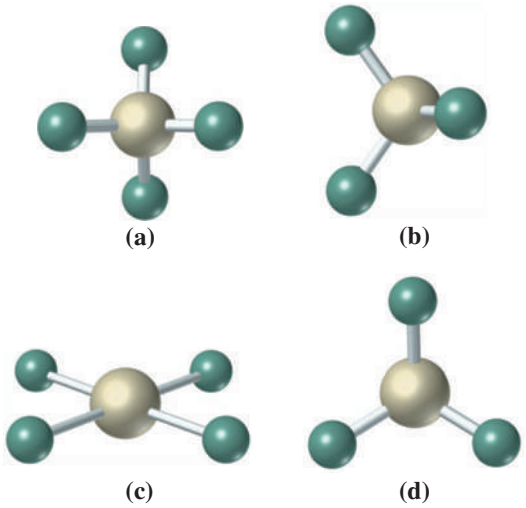
Binary compound, *p. 161*
Bond angle, *p. 151*
Bond length, *p. 136*
Condensed structure, *p. 146*
Coordinate covalent bond, *p. 142*
Covalent bond, *p. 135*
Dipole, *p. 157*
Double bond, *p. 140*
Electronegativity, *p. 157*
Lewis structure, *p. 144*
Lone pair, *p. 140*
Molecular compound, *p. 137*
Molecular formula, *p. 144*
Molecule, *p. 135*
Polar covalent bond, *p. 156*
Regular tetrahedron, *p. 153*
Single bond, *p. 140*
Structural formula, *p. 144*
Triple bond, *p. 140*
Valence-shell electron-pair repulsion (VSEPR) model, *p. 151*

UNDERSTANDING KEY CONCEPTS

4.25 What is the geometry around the central atom in the following molecular models? (There are no "hidden" atoms; all atoms in each model are visible.)



4.26 Three of the following molecular models have a tetrahedral central atom and one does not. Which is the odd one? (Note: Not all atoms and/or lone pairs may be visible in the models.)

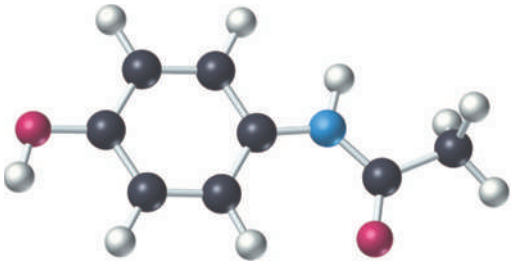


4.27 The ball-and-stick molecular model shown here is a representation of acetaminophen, the active ingredient in over-the-counter headache remedies such as Tylenol. The lines indicate only the connections between atoms not whether the bonds are single, double, or triple (red = O, gray = C, blue = N, ivory = H).

(a) What is the molecular formula of acetaminophen?

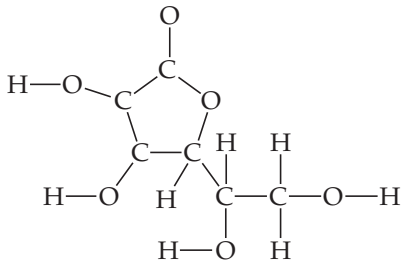
(b) Indicate the positions of the multiple bonds in acetaminophen.

(c) What is the geometry around each carbon and each nitrogen?



Acetaminophen

4.28 The atom-to-atom connections in vitamin C (ascorbic acid) are as shown here. Convert this skeletal drawing to a Lewis electron-dot structure for vitamin C by showing the positions of any multiple bonds and lone pairs of electrons.



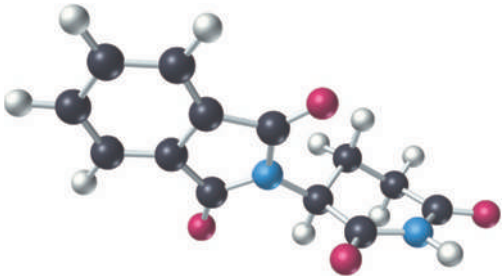
Vitamin C

4.29 The ball-and-stick molecular model shown here is a representation of thalidomide, a drug that has been approved for treating leprosy but causes severe birth defects when taken by expectant mothers. The lines indicate only the connections between atoms and not whether the bonds are single, double, or triple (red = O, gray = C, blue = N, ivory = H).

(a) What is the molecular formula of thalidomide?

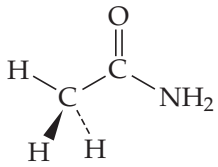
(b) Indicate the positions of the multiple bonds in thalidomide.

(c) What is the geometry around each carbon and each nitrogen?

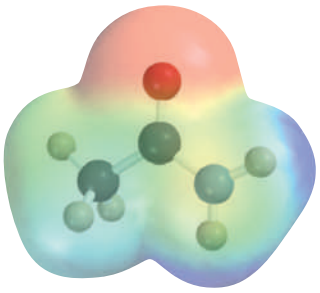


Thalidomide

4.30 Show the position of any electron lone pairs in this structure of acetamide, and indicate the electron-rich and electron-poor regions.



Acetamide



ADDITIONAL PROBLEMS

COVALENT BONDS AND MOLECULAR COMPOUNDS (SECTIONS 4.1–4.5)

4.31 What is a covalent bond, and how does it differ from an ionic bond?

4.32 What is a coordinate covalent bond, and how does it differ from a covalent bond?

4.33 When are multiple bonds formed between atoms and why?

4.34 Identify the bonds formed between the following pairs of atoms as either covalent or ionic.

(a) Aluminum and bromine

(b) Carbon and fluorine

(c) Cesium and iodine

(d) Zinc and fluorine

(e) Lithium and chlorine

4.35 Write electron-dot symbols to show the number of covalent bonds and the lone pairs of electrons in the molecules that are formed by reactions between the atoms in Problem 4.34.

4.36 Look up tellurium $(Z = 52)$ in the periodic table and predict how many covalent bonds it is likely to form. Explain.

4.37 Look up antimony in the periodic table $(Z = 51)$. How many covalent bonds would you expect it to form? Based on this information, which of the following antimony compounds is covalent and which is ionic: $SbCl_3$ or $SbCl_5$?

4.38 Which of the following contains a coordinate covalent bond? (Hint: How many covalent bonds would you expect the central atom (underlined) to form?)

(a) $\underline{Pb}Cl_2$ **(b)** $\underline{Cu}(NH_3)_4^{2+}$ **(c)** $\underline{N}H_4^+$

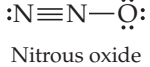
4.39 Which of the following contains a coordinate covalent bond? (Hint: How many covalent bonds would you expect the central atom (underlined) to form?)

(a) $H_2\underline{O}$ **(b)** $\underline{B}F_4^-$ **(c)** $H_3\underline{O}^+$

4.40 Tin forms both an ionic compound and a covalent compound with chlorine. The ionic compound is $SnCl_2$. Is the covalent compound more likely to be $SnCl_3$, $SnCl_4$, or $SnCl_5$? Explain.

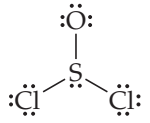
4.41 A compound of gallium with chlorine has a melting point of 350 K (77 °C) and a boiling point of 474 K (201 °C). Is the compound ionic or covalent? What is a likely formula?

4.42 Nitrous oxide, N_2O, has the following structure. Which bond in N_2O is a coordinate covalent bond? Explain.



Nitrous oxide

4.43 Thionyl chloride, $SOCl_2$, has the following structure. Which bond in $SOCl_2$ is a coordinate covalent bond?



Thionyl chloride

STRUCTURAL FORMULAS (SECTION 4.6)

4.44 Distinguish between the following:

(a) A molecular formula and a structural formula

(b) A structural formula and a condensed structure

(c) A lone pair and a shared pair of electrons

4.45 Assume that you are given samples of two white crystalline compounds, one of them ionic and the other one covalent. Describe how you might tell which is which.

4.46 Determine the total number of valence electrons in the following molecules. If the molecule contains multiple bonds, indicate where the multiple bonds are located and whether they are double or triple bonds.

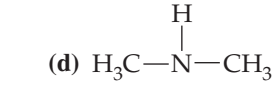
(a) N_2 **(b)** NOCl

(c) CH_3CH_2CHO **(d)** OF_2

4.47 Add lone pairs where appropriate to the following structures:

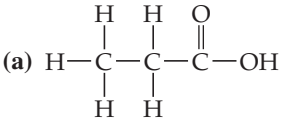
(a) $C{\equiv}O$ **(b)** CH_3SH

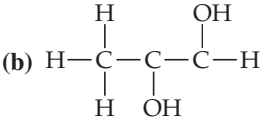
(c) 

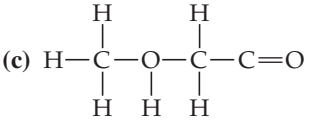
(d) 

4.48 If a research paper appeared reporting the structure of a new molecule with formula C_2H_8, most chemists would be highly skeptical. Why?

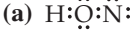
4.49 Consider the following possible structural formulas for $C_3H_6O_2$. If a structure is not reasonable, explain what changes could be made to convert it to a reasonable structure.

(a) 

(b) 

(c) 

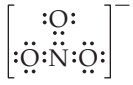
4.50 Convert the following Lewis structures into structural formulas in which lines replace the bonding electrons. Include the lone pairs.

(a) 

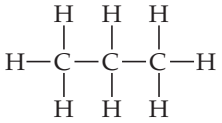
(b)

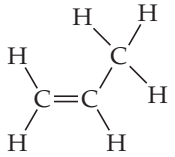
(c) 

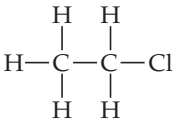
4.51 Convert the following Lewis structure for the nitrate ion into a line structure that includes the lone pairs. Why does the nitrate ion have a −1 charge?



4.52 Convert the following structural formulas into condensed structures.

(a)


(b)


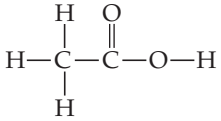
(c)


4.53 Expand the following condensed structures into the correct structural formulas.

(a) $CH_3CH_2COCH(CH_3)_2$ **(b)** $CH_3CH_2COOCH_3$

(c) $CH_3CH_2OCH_2Cl$

4.54 Acetic acid is the major organic constituent of vinegar. Convert the following structural formula of acetic acid into a condensed structure similar to those shown in Problem 4.53.



DRAWING LEWIS STRUCTURES (SECTION 4.7)

4.55 Draw a Lewis structure for the following molecules:

(a) SF_6 **(b)** $AlCl_3$

(c) CS_2 **(d)** SeF_4

(e) $BeCl_2$ (Note: This molecule does not follow the octet rule.)

(f) N_2O_4

4.56 Draw a Lewis structure for the following molecules:

(a) Nitrous acid, HNO_2 (H is bonded to an O atom)

(b) Sulfur trioxide, SO_3

(c) Ethanal, CH_3CHO

4.57 Ethanol, or "grain alcohol," has the formula C_2H_6O and contains an O—H bond. Propose a structure for ethanol that is consistent with common bonding patterns.

4.58 Dimethyl ether has the same molecular formula as ethanol (Problem 4.57) but very different properties. Propose a structure for dimethyl ether in which the oxygen is bonded to two carbons.

4.59 Tetrachloroethylene, C_2Cl_4, is used commercially as a dry-cleaning solvent. Propose a structure for tetrachloroethene based on the common bonding patterns expected in organic molecules. What kind of carbon–carbon bond is present?

4.60 Draw a Lewis structure for hydroxylamine, NH_2OH.

4.61 The carbonate ion, CO_3^{2-}, contains a double bond. Draw a Lewis structure for the ion and show why it has a charge of −2.

4.62 Draw a Lewis structure for the following polyatomic ions:

(a) Formate, HCO_2^-

(b) Sulfite, SO_3^{2-}

(c) Thiocyanate, SCN^-

(d) Phosphate, PO_4^{3+}

(e) Chlorite, ClO_2^- (Chlorine is the central atom.)

MOLECULAR GEOMETRY (SECTION 4.8)

4.63 Predict the geometry and bond angles around atom A for molecules with the general formulas AB_3 and AB_2E, where B represents another atom and E represents an electron pair.

4.64 Predict the geometry and bond angles around atom A for molecules with the general formulas AB_4, AB_3E, and AB_2E_2, where B represents another atom and E represents an electron pair.

4.65 Sketch the three-dimensional shape of the following molecules:

(a) Methanamine, CH_3NH_2

(b) Iodoform, CHI_3

(c) Ozone, O_3

(d) Phosphorus pentachloride, PCl_5

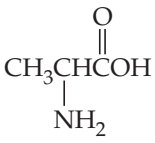
(e) Chloric acid, $HClO_3$

4.66 Predict the three-dimensional shape of the following molecules:

(a) SiF_4 **(b)** CF_2Cl_2 **(c)** SO_3

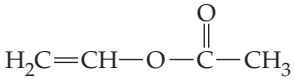
(d) BBr_3 **(e)** NF_3

4.67 Predict the geometry around each carbon atom in the amino acid alanine.



Alanine

4.68 Predict the geometry around each carbon atom in vinyl acetate, a precursor of the polyvinyl alcohol polymer used in automobile safety glass.



Vinyl acetate

POLARITY OF BONDS AND MOLECULES (SECTIONS 4.9 AND 4.10)

4.69 Where in the periodic table are the most electronegative elements found, and where are the least electronegative elements found?

4.70 Using Figure 4.7, predict the electronegativity of the yet-undiscovered element with $Z = 119$.

4.71 Look at the periodic table, and then order the following elements according to increasing electronegativity: K, Si, Be, O, B.

4.72 Look at the periodic table, and then order the following elements according to decreasing electronegativity: C, Ca, Cs, Cl, Cu.

4.73 Which of the following bonds are polar? If a bond is polar, identify the negative and positive ends of each bond by using $\delta+$ and $\delta-$.

(a) I—Br **(b)** O—H
(c) C—F **(d)** N—C
(e) C—C

4.74 Which of the following bonds are polar? If a bond is polar, identify the negative and positive ends of each bond by using $\delta+$ and $\delta-$.

(a) O—Cl **(b)** N—Cl
(c) P—H **(d)** C—I
(e) C—O

4.75 Based on electronegativity differences, would you expect bonds between the following pairs of atoms to be largely ionic or largely covalent?

(a) Be and F **(b)** Ca and Cl
(c) O and H **(d)** Be and Br

4.76 Arrange the following molecules in order of the increasing polarity of their bonds:

(a) HCl **(b)** PH_3
(c) H_2O **(d)** CF_4

4.77 Ammonia, NH_3, and phosphorus trihydride, PH_3, both have trigonal pyramid geometry. Which one is more polar? Explain.

4.78 Decide whether each of the compounds listed in Problem 4.76 is polar, and show the direction of polarity.

4.79 Carbon dioxide is a nonpolar molecule, whereas sulfur dioxide is polar. Draw Lewis structures for each of these molecules to explain this observation.

4.80 Water (H_2O) is more polar than hydrogen sulfide (H_2S). Explain.

NAMES AND FORMULAS OF MOLECULAR COMPOUNDS (SECTION 4.11)

4.81 Name the following binary compounds:

(a) PI_3 **(b)** $AsCl_3$ **(c)** P_4S_3
(d) Al_2F_6 **(e)** N_2O_5 **(f)** $AsCl_5$

4.82 Name the following compounds:

(a) SeO_2 **(b)** XeO_4
(c) N_2S_5 **(d)** P_3Se_4

4.83 Write formulas for the following compounds:

(a) Nitrogen dioxide **(b)** Sulfur hexafluoride
(c) Bromine triiodide **(d)** Dinitrogen trioxide
(e) Nitrogen triiodide **(f)** Iodine heptafluoride

4.84 Write formulas for the following compounds:

(a) Silicon tetrachloride
(b) Sodium hydride
(c) Antimony pentafluoride
(d) Osmium tetroxide

CONCEPTUAL PROBLEMS

4.85 The discovery in the 1960s that xenon and fluorine react to form a molecular compound was a surprise to most chemists, because it had been thought that noble gases could not form bonds.

(a) Why was it thought that noble gases could not form bonds?
(b) Draw a Lewis structure of XeF_4 in which Xe is the central atom. How many electron clouds are there on the central atom?
(c) What type of bonds are the Xe—F bonds? Explain.

4.86 Acetone, a common solvent used in some nail polish removers, has the molecular formula C_3H_6O and contains a carbon–oxygen double bond.

(a) Propose two Lewis structures for acetone.
(b) What is the geometry around the carbon atoms in each of the structures?
(c) Which of the bonds in each structure are polar?

4.87 Draw the structural formulas for two compounds having the molecular formula C_2H_4O. What is the molecular geometry around the carbon atoms in each of these molecules? Would these molecules be polar or nonpolar? (Hint: There is one double bond.)

4.88 The following formulas are unlikely to be correct. What is wrong with each?

(a) CCl_3 **(b)** N_2H_5
(c) H_3S **(d)** C_2OS

4.89 Which of the following compounds contain ionic bonds? Which contain covalent bonds? Which contain coordinate covalent bonds? (A compound may contain more than one type of bond.)

(a) $BaCl_2$ **(b)** $Ca(NO_3)_2$
(c) BCl_4^- **(d)** $TiBr_4$

4.90 The phosphonium ion, PH_4^+, is formed by reaction of phosphine, PH_3, with an acid.

(a) Draw the Lewis structure of the phosphonium ion.
(b) Predict its molecular geometry.
(c) Describe how a fourth hydrogen can be added to PH_3.
(d) Explain why the ion has a +1 charge.

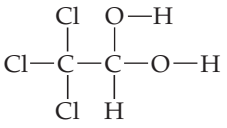
4.91 Compare the trend in electronegativity seen in Figure 4.7 (p. 157) with the trend in electron affinity shown in Figure 3.2 (p. 113). What similarities do you see? What differences? Explain.

4.92 Name the following compounds. Be sure to determine whether the compound is ionic or covalent so that you use the proper rules.

(a) $CaCl_2$ **(b)** $TeCl_2$
(c) BF_3 **(d)** $MgSO_4$
(e) K_2O **(f)** FeF_3
(g) PF_3

4.93 The sulfite ion (SO_3^{2-}) and sulfur trioxide (SO_3) have the same chemical formulas but different molecular geometries. Draw the Lewis dot structures and identify the molecular geometry of each.

4.94 Draw a Lewis structure for chloral hydrate, known in detective novels as "knockout drops." Indicate all lone pairs.

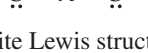


Chloral hydrate

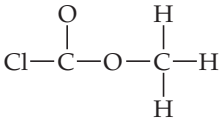
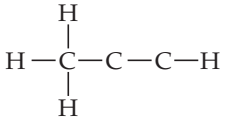
4.95 The dichromate ion, $Cr_2O_7^{2-}$, has neither Cr—Cr nor O—O bonds. Draw a Lewis structure.

4.96 Oxalic acid, $H_2C_2O_4$, is a substance found in uncooked spinach leaves and other greens that can be poisonous at high concentrations (e.g., in raw rhubarb leaves). If oxalic acid has a C—C single bond and the H atoms are both connected to O atoms, draw its Lewis structure.

4.97 Identify the fourth row elements represented by "X" in the following compounds.

(a)  **(b)** 

4.98 Write Lewis structures for molecules with the following connections, showing the positions of any multiple bonds and lone pairs of electrons.

(a)  **(b)** 

4.99 Electron-pair repulsion influences the shapes of polyatomic ions in the same way it influences neutral molecules. Draw electron-dot symbols and predict the shape of the ammonium ion, NH_4^+, the sulfate ion, SO_4^{2-}, and the phosphite ion, PO_3^{3-}.

GROUP PROBLEMS

4.100 Which of the following elements would you expect to form (i) diatomic molecules, (ii) mainly covalent bonds, (iii) mainly ionic bonds, and (iv) both covalent and ionic bonds? (More than one answer may apply; remember that some nonmetals can form ionic bonds with metals.) Explain your answers.

(a) Oxygen **(b)** Potassium

(c) Phosphorus **(d)** Iodine

(e) Hydrogen **(f)** Cesium

4.101 Hydrazine is a substance used to make rocket fuel. Look up the formula and propose a structure for hydrazine.

4.102 Dimethyl sulfoxide, also known as DMSO, is an important organic solvent often used for drug delivery since it readily penetrates the skin. Look up the formula for DMSO and write the Lewis dot structure. (Hint: There are no C—C bonds in the molecule.)

4.103 Titanium forms both molecular and ionic compounds with nonmetals, as, for example, $TiBr_4$ and TiO_2. Look up the melting points for these two compounds and use the information to identify which is ionic and which is molecular. Explain your answer in terms of electronegativities of the atoms involved in each compound.

5

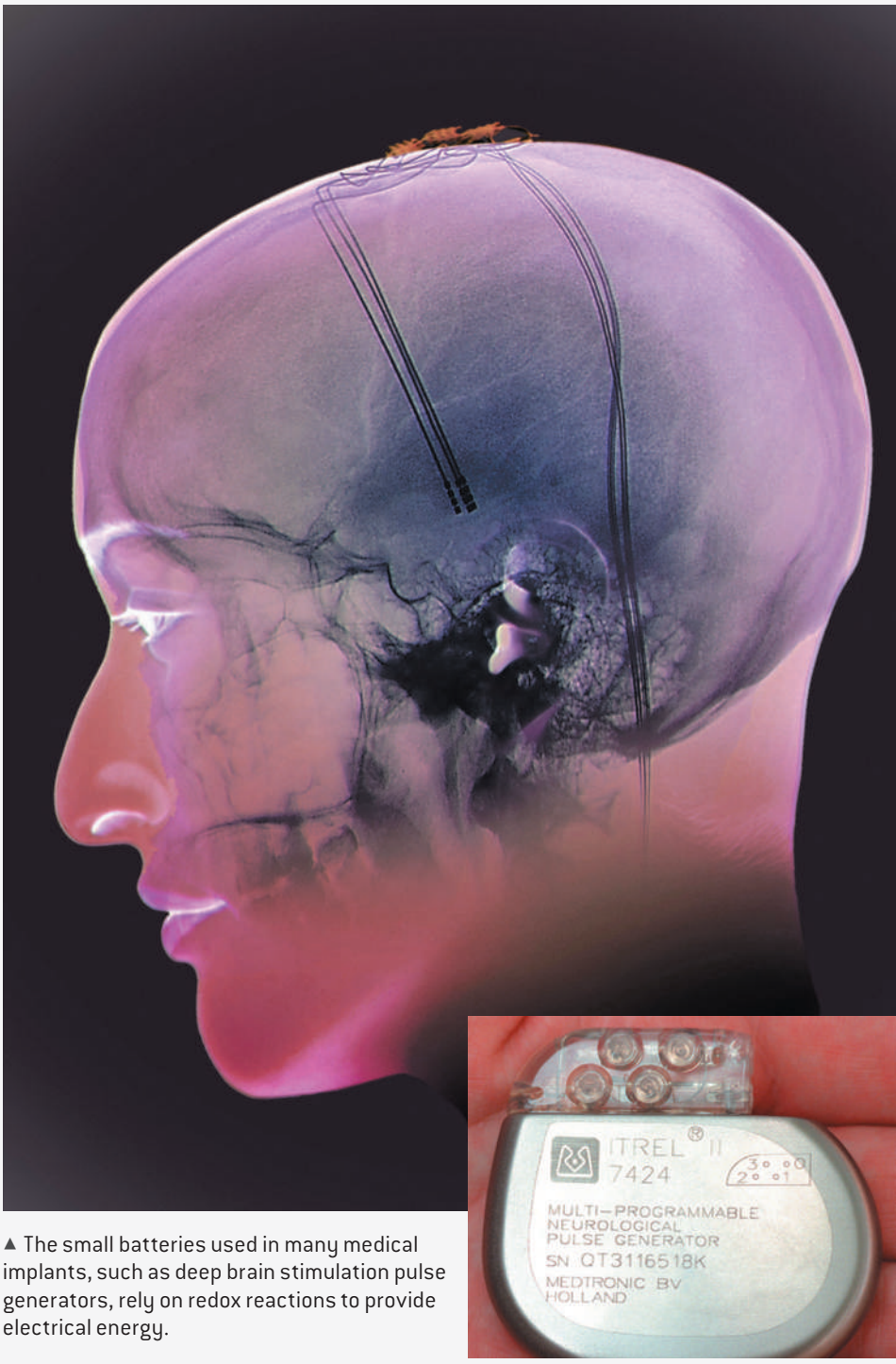
Classification and Balancing of Chemical Reactions

CONTENTS

CONCEPTS TO REVIEW

A. Periodic Properties and Ion Formation (Section 3.4)

B. H^+ and OH^- Ions: An Introduction to Acids and Bases (Section 3.11)



▲ The small batteries used in many medical implants, such as deep brain stimulation pulse generators, rely on redox reactions to provide electrical energy.

Advances in microelectronics made way for the development of small electronic devices for medical applications, such as pacemakers and insulin pumps. One of the more promising medical techniques involves "deep brain stimulation," in which a microdevice, called an implantable pulse generator (or IPG), provides electrical impulses to specific parts of the brain to either stimulate hormone production or inhibit abnormal nerve signals. This technique is used to treat conditions ranging from Parkinsons disease to Tourette's syndrome to clinical depression. What IPGs, pacemakers, and other electronic medical implants have in common is that they use small rechargeable

batteries that use chemical reactions to generate the electricity needed to power the devices, as explained in the Chemistry in Action feature on page 184.

The study of how and why chemical reactions happen is a major part of chemistry, providing information that is both fascinating and practical. In this chapter, we will begin to look at chemical reactions, starting with a discussion of how to represent them in writing. We will then examine how to balance reactions and how to recognize different types or classes of chemical reactions.

5.1 Chemical Equations

Learning Objective:

- Understand the law of conservation of mass and how it applies to chemical equations.

One way to view chemical reactions is to think of them as "recipes." Like recipes, all the "ingredients" in a chemical equation and their relative amounts are given, as well as the amount of product that is produced. Take, for example, a recipe for making s'mores, a concoction of chocolate, marshmallows, and graham crackers:

$$\text{Graham crackers} + \text{Roasted marshmallows} + \text{Chocolate bars} \longrightarrow \text{S'mores}$$

This recipe, however, is simply a list of ingredients and gives no indication of the relative amounts of each ingredient, or how many s'mores we would obtain. A more detailed recipe would be

$$2\ \text{Graham crackers} + 1\ \text{Roasted marshmallow} + \tfrac{1}{4}\ \text{Chocolate bar} \longrightarrow 1\ \text{S'more}$$

In this case, the relative amounts of each ingredient are given, as well as the amount of the final product.

Let us extend this analogy to a typical chemical reaction. When sodium hydrogen carbonate, also known as baking soda, is heated in the range 323–373 K, sodium carbonate, water, and carbon dioxide are produced. In words, we might write the reaction as

$$\text{Sodium hydrogen carbonate} \xrightarrow{\text{Heat}} \text{Sodium carbonate} + \text{Water} + \text{Carbon dioxide}$$

Just as in the recipe, the starting materials and final products are listed. Replacing the chemical names with formulas converts the word description of this reaction into a **chemical equation:**

Chemical equation An expression in which symbols and formulas are used to represent a chemical reaction.

$$\underbrace{2\,NaHCO_3}_{\text{Reactant}} \xrightarrow{\text{Heat}} \underbrace{Na_2CO_3 + H_2O + CO_2}_{\text{Products}}$$

To review the information regarding chemical reactions from Chapter 1, let us look at how this equation is written. The **reactants** are written on the left, the **products** are written on the right, and an arrow is placed between them to indicate a chemical change. Conditions necessary for the reaction to occur—heat in this particular instance—are often specified above the arrow. The substances that take part in chemical reactions may be solids, liquids, or gases, or they may be dissolved in a solvent. Ionic compounds, in particular, frequently undergo reactions in *aqueous solution*—that is, when they are dissolved in water. This information can be added to an equation by placing the appropriate abbreviations after the formulas:

Reactant A substance that undergoes change in a chemical reaction and is written on the left side of the reaction arrow in a chemical equation.

Product A substance that is formed in a chemical reaction and is written on the right side of the reaction arrow in a chemical equation.

(s)	(l)	(g)	(aq)
Solid	Liquid	Gas	Aqueous solution

Why is the number 2 placed before $NaHCO_3$ in the equation? The 2 is necessary because of a fundamental law of nature called the **law of conservation of mass,** which states that matter can neither be created nor destroyed in a chemical reaction.

Law of conservation of mass Matter is neither created nor destroyed in chemical reactions.

The bonds between atoms in the reactants are rearranged to form new compounds in chemical reactions, but none of the atoms disappear and no new ones are formed.

Balanced equation A chemical equation in which the numbers and kinds of atoms are the same on both sides of the reaction arrow.

Coefficient A number placed in front of a formula to balance a chemical equation.

As a consequence, chemical equations must be **balanced equations,** meaning that *the numbers and kinds of atoms must be the same on both sides of the reaction arrow.*

The numbers placed in front of formulas to balance equations are called **coefficients,** and they multiply all the atoms in a formula. Thus, the symbol "2 $NaHCO_3$" indicates two units of sodium hydrogen carbonate (reactant), which contain 2 Na atoms, 2 H atoms, 2 C atoms, and 6 O atoms ($2 \times 3 = 6$, the coefficient times the subscript for O). Count the numbers of atoms on the right side of the equation to convince yourself that it is indeed balanced.

Thus, the decomposition of solid sodium hydrogen carbonate can be written as

$$2\,NaHCO_3(s) \xrightarrow[\text{Heat}]{} Na_2CO_3(s) + H_2O(l) + CO_2(g)$$

5.2 Balancing Chemical Equations

Learning Objective:

- Balance chemical equations.

Just as a recipe indicates the appropriate amounts of each ingredient needed to make a given dish, a balanced chemical equation indicates the appropriate amounts of reactants needed to generate a given amount of product. Although balancing chemical equations often involves some trial and error, most reactions can be balanced by the following four-step approach:

STEP 1: Write an unbalanced equation, using the correct formulas for all given reactants and products. For example, hydrogen and oxygen must be written as H_2 and O_2, rather than as H and O, since we know that both elements exist as diatomic molecules. Remember that *the subscripts in chemical formulas cannot be changed in balancing an equation because doing so would change the identity of the substances in the reaction.*

STEP 2: Add appropriate coefficients to balance the numbers of atoms of each element. It helps to begin with elements that appear in only one compound or formula on each side of the equation, leaving elements that exist in elemental forms, such as oxygen and hydrogen, until last. For example, in the reaction of sulfuric acid with sodium hydroxide to give sodium sulfate and water, we might balance sodium first. We could do this by adding a coefficient of 2 for NaOH:

$$H_2SO_4 + NaOH \longrightarrow Na_2SO_4 + H_2O \quad \text{(Unbalanced)}$$

$$H_2SO_4 + 2\,NaOH \longrightarrow Na_2SO_4 + H_2O \quad \text{(Balanced for Na)}$$

Add this coefficient . . . . . to balance these 2 Na.

If a polyatomic ion appears on both sides of an equation, it can be treated as a single unit. For example, the sulfate ion (SO_4^{2-}) in our example is balanced because there is one on the left and one on the right:

$$H_2SO_4 + 2\,NaOH \longrightarrow Na_2SO_4 + H_2O \quad \text{(Balanced for Na and sulfate)}$$

One sulfate here . . . . . and one here.

At this point, the equation can be balanced for H and O by adding a coefficient of 2 for H_2O:

$$H_2SO_4 + 2\,NaOH \longrightarrow Na_2SO_4 + 2\,H_2O \quad \text{(Completely balanced)}$$

4 H and 2 O here. . . . . 4 H and 2 O here.

STEP 3: Check the equation to make sure the numbers and kinds of atoms on both sides of the equation are the same.

STEP 4: Make sure the coefficients are reduced to their lowest whole-number values.
For example, the equation

$$2\,H_2SO_4 + 4\,NaOH \longrightarrow 2\,Na_2SO_4 + 4\,H_2O$$

is balanced but can be simplified by dividing all coefficients by 2:

$$H_2SO_4 + 2\,NaOH \longrightarrow Na_2SO_4 + 2\,H_2O$$

Worked Example 5.1 Balancing Chemical Equations

Write a balanced chemical equation for the Haber process, an important industrial reaction in which elemental nitrogen and hydrogen combine to form ammonia.

SOLUTION

STEP 1: Write an unbalanced equation, using the correct formulas for all reactants and products.

$$N_2(g) + H_2(g) \longrightarrow NH_3(g)$$

By examination, we see that only two elements, N and H, need to be balanced. Both these elements exist in nature as diatomic gases, as indicated on the reactant side of the unbalanced equation.

STEP 2: Add appropriate coefficients to balance the numbers of atoms of each element. Remember that the subscript 2 in N_2 and H_2 indicates that these are diatomic molecules (i.e., 2 N atoms or 2 H atoms per molecule). Since there are 2 nitrogen atoms on the left, we must add a coefficient of 2 in front of the NH_3 on the right side of the equation to balance the equation with respect to N:

$$N_2(g) + H_2(g) \longrightarrow 2\,NH_3(g)$$

Now we see that there are 2 H atoms on the left but 6 H atoms on the right. We can balance the equation with respect to hydrogen by adding a coefficient of 3 in front of the $H_2(g)$ on the left side:

$$N_2(g) + 3\,H_2(g) \longrightarrow 2\,NH_3(g)$$

STEP 3: Check the equation to make sure the numbers and kinds of atoms on both sides of the equation are the same.

On the left: $(1 \times 2)\,N = 2\,N \quad (3 \times 2)\,H = 6\,H$

On the right: $(2 \times 1)\,N = 2\,N \quad (2 \times 3)\,H = 6\,H$

STEP 4: Make sure the coefficients are reduced to their lowest whole-number values. In this case, the coefficients already represent the lowest whole-number values.

Worked Example 5.2 Balancing Chemical Equations

Natural gas (methane, CH_4) burns in oxygen to yield water and carbon dioxide (CO_2). Write a balanced equation for the reaction.

SOLUTION

STEP 1: Write the unbalanced equation, using correct formulas for all substances:

$$CH_4 + O_2 \longrightarrow CO_2 + H_2O \quad (\text{Unbalanced})$$

STEP 2: Since carbon appears in one formula on each side of the arrow, let us begin with that element. In fact, there is only 1 carbon atom in each formula, so the equation is already balanced for that element. Next, note that there are 4 hydrogen atoms on the left (in CH_4) and only 2 on the right (in H_2O). Placing a coefficient of 2 before H_2O gives the same number of hydrogen atoms on both sides:

$$CH_4 + O_2 \longrightarrow CO_2 + 2\,H_2O \quad (\text{Balanced for C and H})$$

—continued on next page

—continued from previous page

Finally, look at the number of oxygen atoms. There are 2 on the left (in O_2) but 4 on the right (2 in CO_2 and 1 in each H_2O). If we place a 2 before the O_2, the number of oxygen atoms will be the same on both sides, but the numbers of other elements will not change:

$$CH_4 + 2\,O_2 \longrightarrow CO_2 + 2\,H_2O \quad \text{(Balanced for C, H, and O)}$$

STEP 3: Check to be sure the numbers of atoms on both sides are the same.

On the left: 1 C 4 H (2×2) O = 4 O

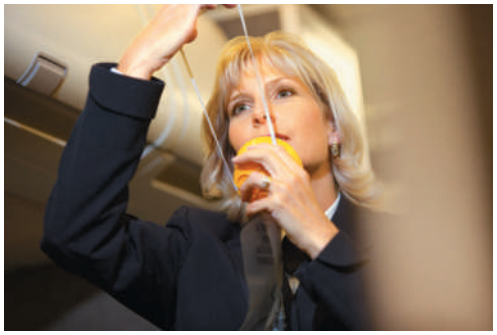
On the right: 1 C (2×2) H = 4 H 2 O + 2 O = 4 O

From CO_2 From 2 H_2O

STEP 4: Make sure the coefficients are reduced to their lowest whole-number values. In this case, the answer is already correct.

Worked Example 5.3 Balancing Chemical Equations

Sodium chlorate $(NaClO_3)$ decomposes when heated to yield sodium chloride and oxygen, a reaction used to provide oxygen for the emergency breathing masks in airliners. Write a balanced equation for this reaction.



▲The oxygen in emergency breathing masks comes from heating sodium chlorate.

SOLUTION

STEP 1: The unbalanced equation is

$$NaClO_3 \longrightarrow NaCl + O_2$$

STEP 2: Both the Na and the Cl are already balanced, with only one atom of each on the left and right sides of the equation. There are 3 O atoms on the left but only 2 on the right. The O atoms can be balanced by placing a coefficient of 1½ in front of O_2 on the right side of the equation:

$$NaClO_3 \longrightarrow NaCl + 1\tfrac{1}{2}\,O_2$$

STEP 3: Checking to make sure the same number of atoms of each type occurs on both sides of the equation, we see 1 atom each of Na and Cl on both sides and 3 O atoms on both sides.

STEP 4: In this case, obtaining all coefficients in their smallest whole-number values requires that we multiply all coefficients by 2 to obtain:

$$2\,NaClO_3 \longrightarrow 2\,NaCl + 3\,O_2$$

Checking gives

On the left: 2 Na 2 Cl (2×3) O = 6 O

On the right: 2 Na 2 Cl (3×2) O = 6 O

PROBLEM 5.1

Ozone (O_3) is formed in the earth's upper atmosphere by the action of solar radiation on oxygen molecules (O_2). Write a balanced equation for the formation of ozone from oxygen.

PROBLEM 5.2

Balance the following equations:

(a) $Ca(OH)_2 + HCl \longrightarrow CaCl_2 + H_2O$

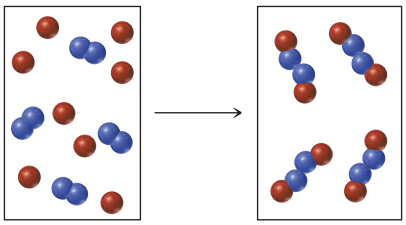
(b) $Al + O_2 \longrightarrow Al_2O_3$

(c) $CH_3CH_3 + O_2 \longrightarrow CO_2 + H_2O$

(d) $AgNO_3 + MgCl_2 \longrightarrow AgCl + Mg(NO_3)_2$

KEY CONCEPT PROBLEM 5.3

The following diagram represents the reaction of A (red spheres) with B_2 (blue spheres). Write a balanced equation for the reaction.



HANDS-ON CHEMISTRY 5.1

Look up a recipe for your favorite cookies. Using the list of ingredients and the expected yield (number of cookies), write a balanced equation to represent this process. Also, think about the units used to indicate the amount of each substance (teaspoon, cup, or gram). What units would you use if all the ingredients had to be measured in the same unit?

5.3 Precipitation Reactions and Solubility Guidelines

Learning Objective:

- Apply solubility rules to predict if a precipitation reaction will occur, and write the appropriate balanced reaction.

One of the best ways to understand any subject is to look for patterns that help us categorize large amounts of information. When learning about chemical reactions, for instance, it is helpful to group the reactions of ionic compounds into three general classes: *precipitation reactions, acid-base neutralization reactions,* and *oxidation-reduction reactions.* We will study each of these three reaction classes in more detail in the next three sections, beginning here with precipitation reactions.

Precipitation reactions are processes in which an insoluble solid called a **precipitate** forms when reactants are combined in aqueous solution. Most precipitations take place when the anions and cations of two ionic compounds change partners. For example, an aqueous solution of lead(II) nitrate reacts with an aqueous solution of potassium iodide to yield an aqueous solution of potassium nitrate plus an insoluble yellow precipitate of lead iodide:

$$Pb(NO_3)_2\,(aq) + 2\,KI(aq) \longrightarrow 2\,KNO_3(aq) + PbI_2(s)$$

To predict whether a precipitation reaction will occur upon mixing aqueous solutions of two ionic compounds, you must know the **solubilities** of the potential products—how much of each compound will dissolve in a given amount of solvent at a given temperature. If a substance has a low solubility in water, then it is likely to precipitate from an aqueous solution. If a substance has a high solubility in water, then no precipitate will form.

Solubility is a complex matter, and it is not always possible to make correct predictions. As a rule of thumb, though, the following solubility guidelines for ionic compounds are useful.

Precipitate An insoluble solid that forms in solution during a chemical reaction.

Solubility The amount of a compound that will dissolve in a given amount of solvent at a given temperature.

▲ Reaction of aqueous $Pb(NO_3)_2$ with aqueous KI gives a yellow precipitate of PbI_2.

General Rules on Solubility

RULE 1: **A compound is probably soluble if it contains one of the following cations:**

- Group 1A cation: Li^+, Na^+, K^+, Rb^+, Cs^+
- Ammonium ion: NH_4^+

CHEMISTRY IN ACTION

Kidney Stones: A Problem in Solubility

One of the major pathways in the body for the breakdown of the nucleic acids—deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)—is by conversion to a substance called *uric acid*, $C_5H_4N_4O_3$, so named because it was first isolated from urine in 1776. Most people excrete about 0.5 g of uric acid every day in the form of sodium urate, the salt that results from an acid-base reaction of uric acid. Unfortunately, the amount of sodium urate that dissolves in water (or urine) is fairly low—only about 0.07 mg/mL at the normal body temperature of 37 °C (310.15 K). When too much sodium urate is produced or mechanisms for its elimination fail, its concentration in blood and urine rises, and the excess sometimes precipitates in the joints to cause gout (see the Chemistry in Action in Chapter 25, p. 804) and in the kidneys as kidney stones.

▲ The limited solubility of uric acid and calcium oxalate can result in the formation of kidney stones measuring ~0.5 cm in diameter.

RULE 2: A compound is probably soluble if it contains one of the following anions:

- Halide: Cl^-, Br^-, and I^- except Ag^+, Hg_2^{2+}, and Pb^{2+} compounds
- Nitrate (NO_3^-), perchlorate (ClO_4^-), acetate $(CH_3CO_2^-)$, and sulfate (SO_4^{2-}) except Ba^{2+}, Hg_2^{2+}, and Pb^{2+} sulfates

If a compound does *not* contain at least one of the ions listed above, it is probably *not* soluble. Thus, Na_2CO_3 is soluble because it contains a group 1A cation, and $CaCl_2$ is soluble because it contains a halide anion. The compound $CaCO_3$, however, is probably *insoluble* because it contains none of the ions listed above. These same guidelines are presented in table form in Table 5.1.

Table 5.1 General Solubility Guidelines for Ionic Compounds in Water

Soluble	Exceptions
Ammonium compounds (NH_4^+)	None
Lithium compounds (Li^+)	None
Sodium compounds (Na^+)	None
Potassium compounds (K^+)	None
Nitrates (NO_3^-)	None
Perchlorates (ClO_4^-)	None
Acetates $(CH_3CO_2^-)$	None
Chlorides (Cl^-)	Ag^+, Hg_2^{2+}, and Pb^{2+} compounds
Bromides (Br^-)	Ag^+, Hg_2^{2+}, and Pb^{2+} compounds
Iodides (I^-)	Ag^+, Hg_2^{2+}, and Pb^{2+} compounds
Sulfates (SO_4^{2-})	Ba^{2+}, Hg_2^{2+}, and Pb^{2+} compounds

Let us try a problem. What will happen if aqueous solutions of sodium nitrate $(NaNO_3)$ and potassium sulfate (K_2SO_4) are mixed? To answer this question, look at the guidelines to find the solubilities of the two possible products, Na_2SO_4 and KNO_3. Because both have group 1A cations (Na^+ and K^+), both are water-soluble and no precipitation will occur. If aqueous solutions of silver nitrate $(AgNO_3)$ and sodium

Kidney stones are small crystals that precipitate in the kidney. Although often quite small, kidney stones cause excruciating pain when they pass through the ureter, the duct that carries urine from the kidney to the bladder. In some cases, complete blockage of the ureter occurs. Treatment or prevention of kidney stones depends on the underlying cause and the composition of the stones. The most common type of kidney stones consists of calcium oxalate, an insoluble ionic compound. High dietary intake of supplemental calcium by postmenopausal women is linked to increased incidents of kidney stones. Also, high intake of dietary oxalates, found in rhubarb, spinach, blueberries, and chocolate, can contribute to kidney stone formation.

Sodium urate–based kidney stones are linked to high dietary intake of animal protein, especially in foods such as liver, sardines, and shellfish. Drugs such as allopurinol can lower production of sodium urate by inhibiting the action of an enzyme called *xanthine oxidase,* thereby blocking a step in nucleic acid metabolism. In addition to dietary modification, kidney stones can be avoided by avoiding dehydration (i.e., increasing daily water consumption) and increasing dietary intake of citrates.

CIA Problem 5.1 Many kidney stones are formed by precipitation of oxalate by calcium. Show the balanced chemical equation for the precipitation of calcium oxalate, starting with calcium chloride ($CaCl_2$) and sodium oxalate ($Na_2C_2O_4$).

CIA Problem 5.2 Uric acid is formed in the body by the metabolism of purines. The reaction can be represented as $C_5H_4N_4$ (purine) + O_2 ⟶ $C_5H_4N_4O_3$ (uric acid).

(a) Balance the reaction.
(b) What type of reaction is this?

carbonate (Na_2CO_3) are mixed, however, the guidelines predict that a precipitate of insoluble silver carbonate (Ag_2CO_3) will form.

$$2\,AgNO_3(aq) + Na_2CO_3(aq) \longrightarrow Ag_2CO_3(s) + 2\,NaNO_3(aq)$$

Worked Example 5.4 Chemical Reactions: Solubility Rules

Will a precipitation reaction occur when aqueous solutions of $CdCl_2$ and $(NH_4)_2S$ are mixed?

SOLUTION

Identify the two potential products, and predict the solubility of each using the guidelines in the text. In this instance, $CdCl_2$ and $(NH_4)_2S$ might give CdS and NH_4Cl. Since the guidelines predict that CdS is insoluble, a precipitation reaction will occur:

$$CdCl_2(aq) + (NH_4)_2S(aq) \longrightarrow CdS(s) + 2NH_4Cl(aq)$$

PROBLEM 5.4

Predict the solubility of the following compounds:

(a) $CdCO_3$ **(b)** Na_2S **(c)** $PbSO_4$ **(d)** $(NH_4)_3PO_4$ **(e)** Hg_2Cl_2

PROBLEM 5.5

Predict whether a precipitation reaction will occur in the following situations. If a precipitation reaction occurs, write the balanced chemical equation for the reaction.

(a) $NiCl_2(aq) + (NH_4)_2S(aq) \longrightarrow$ **(b)** $AgNO_3(aq) + CaBr_2(aq) \longrightarrow$

5.4 Acids, Bases, and Neutralization Reactions

Learning Objective:

- Predict the products of an acid-base neutralization reaction.

Acid-base neutralization reactions are processes in which an acid reacts with a base to yield water plus an ionic compound called a **salt.** We will look at both acids and bases in more detail in Chapter 10, but you might recall from Chapter 3 that we previously defined acids as compounds that produce H^+ ions and bases as compounds that produce OH^- ions when dissolved in water. Thus, a neutralization reaction removes H^+

Salt An ionic compound formed from reaction of an acid with a base.

CONCEPTS TO REVIEW See Section 3.11 for more discussion of acids and bases.

and OH^- ions from solution and yields neutral H_2O. The reaction between hydrochloric acid and sodium hydroxide is a typical example:

$$HCl(aq) + NaOH(aq) \longrightarrow H_2O(l) + NaCl(aq)$$

Neutralization reaction The reaction of an acid with a base.

When acids and bases are mixed in the correct proportion, both acidic and basic properties disappear because of a **neutralization reaction.** The most common kind of neutralization reaction occurs between an acid (generalized as HA) and a metal hydroxide (generalized as MOH) to yield water and a salt. The H^+ ion from the acid combines with the OH^- ion from the base to give neutral H_2O, whereas the anion from the acid (A^-) combines with the cation from the base (M^+) to give the salt.

A neutralization reaction: $HA(aq) + MOH(aq) \longrightarrow H_2O(l) + MA(aq)$

Acid Base Water A salt

Note that in the example involving HCl and NaOH, the "salt" produced is sodium chloride or common table salt. In a general sense, however, *any* ionic compound produced in an acid-base reaction is also called a salt. Other examples include potassium nitrate (KNO_3), magnesium bromide $(MgBr_2)$, and sodium sulfate (Na_2SO_4).

Another kind of neutralization reaction occurs between an acid and a carbonate (or hydrogen carbonate) to yield water, a salt, and carbon dioxide. Hydrochloric acid reacts with potassium carbonate, for example, to give H_2O, KCl, and CO_2:

$$2\,HCl(aq) + K_2CO_3(aq) \longrightarrow H_2O(l) + 2\,KCl(aq) + CO_2(g)$$

LOOKING AHEAD Acids and bases are enormously important in biological chemistry. We will see in Chapter 18, for instance, how acids and bases affect the structure and properties of proteins.

The reaction occurs because the carbonate ion (CO_3^{2-}) reacts initially with H^+ to yield H_2CO_3, which is unstable and immediately decomposes to give CO_2 plus H_2O.

Worked Example 5.5 Chemical Reactions: Acid-Base Neutralization

Write an equation for the neutralization reaction of aqueous HBr and aqueous $Ba(OH)_2$.

SOLUTION

The reaction of HBr with $Ba(OH)_2$ involves the combination of a proton (H^+) from the acid with OH^- from the base to yield water and a salt $(BaBr_2)$.

$$2\,HBr(aq) + Ba(OH)_2(aq) \longrightarrow 2\,H_2O(l) + BaBr_2(aq)$$

PROBLEM 5.6

Write and balance equations for the following acid-base neutralization reactions:

(a) $CsOH(aq) + H_2SO_4(aq) \longrightarrow$

(b) $Ca(OH)_2(aq) + CH_3CO_2H(aq) \longrightarrow$

(c) $NaHCO_3(aq) + HBr(aq) \longrightarrow$

HANDS-ON CHEMISTRY 5.2

Pour one-fourth cup of vinegar (containing acetic acid!) into a large glass and fill the glass half-way with water.

1. Carefully waft the vapor above the solution to your nose. Can you smell the characteristic aroma of the vinegar/acetic acid?
2. Carefully add one antacid tablet (TUMS, Rolaids) or a teaspoon of baking soda (sodium hydrogen carbonate) to the glass. What do you observe, and how is this evidence of a neutralization reaction? When the reaction stops, can you still smell the aroma of vinegar? If you add another antacid tablet, is there any further reaction?

5.5 Redox Reactions

Learning Objective:

- Recognize redox reactions, and identify the species being oxidized and reduced.

Oxidation-reduction (redox) reaction A reaction in which electrons are transferred from one atom to another.

Oxidation-reduction (redox) reactions, the third and final category of reactions that we will discuss in this chapter, are more complex than precipitation and neutralization reactions. Redox reactions are processes in which electrons are transferred between reaction partners (atoms, molecules, ions). As a result of this transfer, the number of electrons assigned to individual atoms in the various reactants change. Look at the following examples and see if you can tell how they qualify as redox reactions. Copper metal reacts with aqueous silver nitrate to form silver metal and aqueous copper(II) nitrate; iron rusts in air to form iron(III) oxide; the zinc metal container on the outside of a battery reacts with manganese dioxide and ammonium chloride inside the battery to generate electricity and give aqueous zinc chloride plus manganese(III) oxide. Although these and many thousands of other reactions appear unrelated, all are examples of redox reactions.

$$Cu(s) + 2\,AgNO_3(aq) \longrightarrow 2\,Ag(s) + Cu(NO_3)_2(aq)$$

$$2\,Fe(s) + 3\,O_2(g) \longrightarrow Fe_2O_3(s)$$

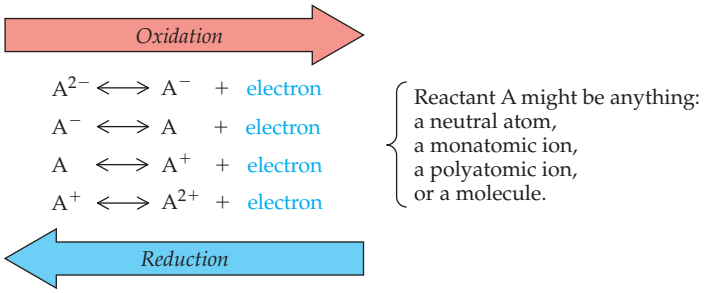
$$Zn(s) + 2\,MnO_2(s) + 2\,NH_4Cl(s) \longrightarrow ZnCl_2(aq) + Mn_2O_3(s) + 2\,NH_3(aq) + H_2O(l)$$

Oxidation The loss of one or more electrons by an atom.

Reduction The gain of one or more electrons by an atom.

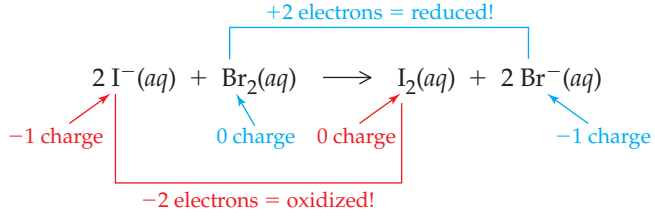
Historically, the word *oxidation* referred to the combination of an element with oxygen to yield an oxide, and the word *reduction* referred to the removal of oxygen from an oxide to yield the element. Today, though, the words have taken on a much broader meaning. An **oxidation** is now defined as the loss of one or more electrons by an atom, and a **reduction** is the gain of one or more electrons. Thus, an oxidation-reduction reaction, or redox reaction, is one in which *electrons are transferred from one atom to another.*

Fundamentally, all reactions involving covalent compounds are classified as redox reactions, because electrons are rearranged as bonds are broken and new bonds are formed. The discussion here, however, will focus mainly on reactions involving ionic substances.

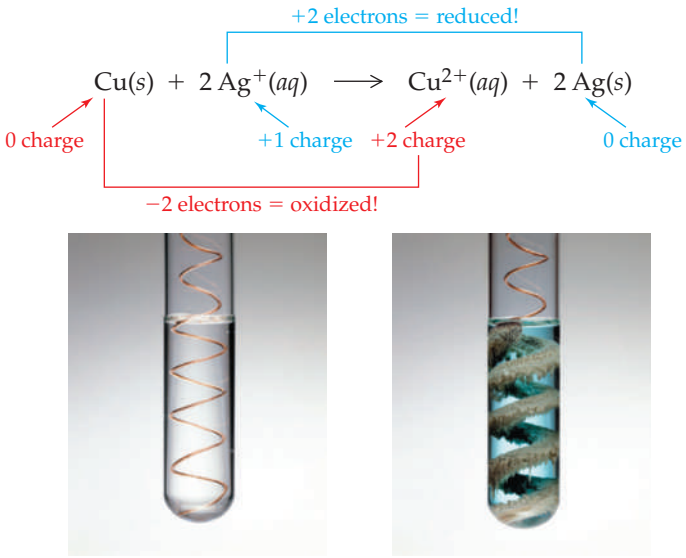


Take the reaction of copper with aqueous Ag^+ as an example, as shown in Figure 5.1. Copper metal gives an electron to each of two Ag^+ ions, forming Cu^{2+} and silver metal. Copper is oxidized in the process, and Ag^+ is reduced. You can follow the transfer of the electrons by noting that the charge on the copper increases from 0 to +2 when it loses two electrons, whereas the charge on Ag^+ decreases from +1 to 0 when it gains an electron.

Similarly, in the reaction of aqueous iodide ion with bromine, iodide ion gives an electron to bromine, forming iodine and bromide ion. Iodide ion is oxidized as its charge increases from −1 to 0, and bromine is reduced as its charge decreases from 0 to −1.



As these examples show, oxidation and reduction always occur together. Whenever one substance loses an electron (is oxidized), another substance must gain that electron (be reduced). The substance that gives up an electron and causes the reduction—the



▶ Figure 5.1
The copper wire reacts with aqueous Ag^+ ion and becomes coated with metallic silver. At the same time, copper(II) ions go into solution, producing the blue color.

Reducing agent A reactant that causes a reduction in another reactant by giving up electron to it.

Oxidizing agent A reactant that causes an oxidation by taking electrons from another reactant.

copper atom in the reaction of Cu with Ag^+ and the iodide ion in the reaction of I^- with Br_2—is called a **reducing agent.** The substance that gains an electron and causes the oxidation—the silver ion in the reaction of Cu with Ag^+ and the bromine molecule in the reaction of I^- with Br_2—is called an **oxidizing agent.** The charge on the reducing agent increases during the reaction, and the charge on the oxidizing agent decreases.

Reducing agent	Loses one or more electrons Causes reduction Undergoes oxidation Becomes more positive (less negative) (May gain oxygen atoms)
Oxidizing agent	Gains one or more electrons Causes oxidation Undergoes reduction Becomes more negative (less positive) (May lose oxygen atoms)

Among the simplest of redox processes is the reaction of an element, usually a metal, with an aqueous cation to yield a different element and a different ion. Iron metal reacts with aqueous copper(II) ion, for example, to give iron(II) ion and copper metal. Similarly, magnesium metal reacts with aqueous acid to yield magnesium ion and hydrogen gas. In both cases, the reactant element (Fe or Mg) is oxidized, and the reactant ion (Cu^{2+} or H^+) is reduced.

$$Fe(s) + Cu^{2+}(aq) \longrightarrow Fe^{2+}(aq) + Cu(s)$$
$$Mg(s) + 2\,H^+(aq) \longrightarrow Mg^{2+}(aq) + H_2(g)$$

The reaction of a metal with water or aqueous acid (H^+) to release H_2 gas is a particularly important process. As you might expect based on the periodic properties discussed in Section 3.4, the alkali metals and alkaline earth metals (on the left side of the periodic table) are the most powerful reducing agents (electron donors), so powerful that they even react with pure water, in which the concentration of H^+ is very low. This is due in part to the fact that alkali metals and alkaline earth metals have low ionization energies. Ionization energy, which is a measure of how easily an element will lose an electron, tends to decrease as we move to the left and down in the periodic table. Thus, metals toward the middle of the periodic table, such as iron and chromium, have higher ionization energies and do not lose electrons as readily; they react only with aqueous

acids but not with water. Those metals near the bottom right of the periodic table, such as platinum and gold, react with neither aqueous acid nor water. At the other extreme from the alkali metals, the reactive nonmetals at the top right of the periodic table have the highest ionization energies and are extremely weak reducing agents but powerful oxidizing agents (electron acceptors). This is, again, predictable based on the periodic property of electron affinity (Section 3.4), which becomes more energetically favored as we move up and to the right in the periodic table.

The relationship between formation of ions and ionization energy/electronegativity was discussed in Chapter 3.

We can make a few generalizations about the redox behavior of metals and nonmetals.

1. In reactions involving metals and nonmetals, metals tend to lose electrons while nonmetals tend to gain electrons. The number of electrons lost or gained can often be predicted based on the position of the element in the periodic table. (Section 3.3)
2. In reactions involving nonmetals, the "more metallic" element (farther down and/or to the left in the periodic table) tends to lose electrons, and the "less metallic" element (up and/or to the right) tends to gain electrons.

   Redox reactions involve almost every element in the periodic table, and they occur in a vast number of processes throughout nature, biology, and industry. Here are just a few examples:

   - *Corrosion* is the deterioration of a metal by oxidation, such as the rusting of iron in moist air. The economic consequences of rusting are enormous: it has been estimated that up to one-fourth of the iron produced in the United States is used to replace bridges, buildings, and other structures that have been destroyed by corrosion.
   - *Combustion* is the burning of a fuel by rapid oxidation with oxygen in air. Gasoline, fuel oil, natural gas, wood, paper, and other organic compounds of carbon and hydrogen are the most common fuels that burn in air. Even some metals, though, will burn in air. Magnesium and calcium are examples.

$$\underset{\text{Methane}\ (\text{natural gas})}{CH_4(g)} + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(l)$$

$$2\,Mg(s) + O_2(g) \longrightarrow 2\,MgO(s)$$

   - *Respiration* is the process of breathing and using oxygen for the many biological redox reactions that provide the energy required by living organisms. We will see in Chapters 21 and 22 that in the respiration process, energy is released from food molecules slowly and in complex, multistep pathways, but that the overall result is similar to that of the simpler combustion reactions. For example, the simple sugar glucose $(C_6H_{12}O_6)$ reacts with O_2 to give CO_2 and H_2O according to the following equation:

$$\underset{\text{Glucose}\ (\text{a carbohydrate})}{C_6H_{12}O_6} + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + \text{Energy}$$

   - *Bleaching* makes use of redox reactions to decolorize or lighten colored materials. Dark hair is bleached to turn it blond, clothes are bleached to remove stains, wood pulp is bleached to make white paper, and so on. The oxidizing agent used depends on the situation: hydrogen peroxide (H_2O_2) is used for hair, sodium hypochlorite (NaOCl) for clothes, and elemental chlorine for wood pulp, but the principle is always the same. In all cases, colored organic materials are destroyed by reaction with strong oxidizing agents.
   - *Metallurgy,* the science of extracting and purifying metals from their ores, makes use of numerous redox processes. Worldwide, approximately 800 million tons of iron are produced each year by reduction of the mineral hematite, Fe_2O_3, with carbon monoxide.

Worked Example 5.6 Chemical Reactions: Redox Reactions

For the following reactions, indicate which atom is oxidized and which is reduced, based on the definitions provided in this section. Identify the oxidizing and reducing agents.

(a) $Cu(s) + Pt^{2+}(aq) \longrightarrow Cu^{2+}(aq) + Pt(s)$

(b) $2\,Mg(s) + CO_2(g) \longrightarrow 2\,MgO(s) + C(s)$

ANALYSIS The definitions for oxidation include a loss of electrons, an increase in charge, and a gain of oxygen atoms; reduction is defined as a gain of electrons, a decrease in charge, and a loss of oxygen atoms.

SOLUTION

(a) In this reaction, the charge on the Cu atom increases from 0 to 2+. This corresponds to a loss of two electrons. The Cu is therefore oxidized and acts as the reducing agent. Conversely, the Pt^{2+} ion undergoes a decrease in charge from 2+ to 0, corresponding to a gain of two electrons for the Pt^{2+} ion. The Pt^{2+} is reduced and acts as the oxidizing agent.

(b) In this case, the gain or loss of oxygen atoms is the easiest way to identify which atoms are oxidized and reduced. The Mg atom is gaining oxygen to form MgO; therefore, the Mg is being oxidized and acts as the reducing agent. The C atom in CO_2 is losing oxygen. Therefore, the C atom in CO_2 is being reduced, and so CO_2 acts as the oxidizing agent.

Worked Example 5.7 Chemical Reactions: Identifying Oxidizing/Reducing Agents

For the respiration and metallurgy examples discussed previously, identify the atoms being oxidized and reduced, and label the oxidizing and reducing agents.

ANALYSIS Again, using the definitions of oxidation and reduction provided in this section, we can determine which atom(s) are gaining/losing electrons or gaining/losing oxygen atoms.

SOLUTION

Respiration: $C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O$

Because the charge associated with the individual atoms is not evident, we will use the definition of oxidation/reduction as the gaining/losing of oxygen atoms. In this reaction, there is only one reactant besides oxygen $(C_6H_{12}O_6)$, so we must determine *which* atom in the compound is changing. The ratio of carbon to oxygen in $C_6H_{12}O_4$ is 1:1, whereas the ratio in CO_2 is 1:2. Therefore, the C atoms are gaining oxygen and are oxidized; the $C_6H_{12}O_{16}$ is the reducing agent and O_2 is the oxidizing agent. Note that the ratio of hydrogen to oxygen in $C_6H_{12}O_6$ and in H_2O is 2:1. The H atoms are neither oxidized nor reduced.

Metallurgy: $Fe_2O_3(s) + 3\,CO(g) \longrightarrow 2\,Fe(s) + 3\,CO_2(g)$

The Fe_2O_3 is losing oxygen to form Fe(*s*); it is being reduced and acts as the oxidizing agent. In contrast, the CO is gaining oxygen to form CO_2; it is being oxidized and acts as the reducing agent.

Worked Example 5.8 Chemical Reactions: Identifying Redox Reactions

For the following reactions, identify the atom(s) being oxidized and reduced:

(a) $2\,Al(s) + 3\,Cl_2(g) \longrightarrow 2\,AlCl_3(s)$

(b) $C(s) + 2\,Cl_2(g) \longrightarrow CCl_4(l)$

ANALYSIS Again, there is no obvious increase or decrease in charge to indicate a gain or loss of electrons. Also, the reactions do not involve a gain or loss of oxygen. We can, however, evaluate the reactions in terms of the typical behavior of metals and nonmetals in reactions.

SOLUTION

(a) In this case, we have the reaction of a metal (Al) with a nonmetal (Cl_2). Because metals tend to lose electrons and nonmetals tend to gain electrons, we can assume that the Al atom is oxidized (loses electrons) and the Cl_2 is reduced (gains electrons).

(b) The carbon atom is the less electronegative element (farther to the left) and is less likely to gain an electron. The more electronegative element (Cl) will tend to gain electrons (be reduced).

Worked Example 5.9 Classifying Chemical Reactions

Classify the following as a precipitation, an acid-base neutralization, or a redox reaction.

(a) $Ca(OH)_2(aq) + 2\,HBr(aq) \longrightarrow 2\,H_2O(l) + CaBr_2(aq)$

(b) $Pb(ClO_4)_2(aq) + 2\,NaCl(aq) \longrightarrow PbCl_2(s) + 2\,NaClO_4(aq)$

(c) $2\,AgNO_3(aq) + Cu(s) \longrightarrow 2\,Ag(s) + Cu(NO_3)_2(aq)$

ANALYSIS One way to identify the class of reaction is to examine the products that form and match them with the descriptions for the types of reactions provided in this section. By a process of elimination, we can readily identify the appropriate reaction classification.

SOLUTION

(a) The products of this reaction are water and an ionic compound, or salt ($CaBr_2$). This is consistent with the description of an acid-base neutralization reaction.

(b) This reaction involves two aqueous reactants, $Pb(ClO_4)_2$ and NaCl, which combine to form a solid product, $PbCl_2$. This is consistent with a precipitation reaction.

(c) The products of this reaction are a solid, $Ag(s)$, and an aqueous ionic compound, $Cu(NO_3)_2$. This does not match the description of a neutralization reaction, which would form *water* and an ionic compound. One of the products *is* a solid, but the reactants are not both aqueous compounds; one of the reactants is *also* a solid (Cu). Therefore, this reaction would not be classified as a precipitation reaction. By the process of elimination, then, it must be a redox reaction.

PROBLEM 5.7

Classify each of the following as a precipitation, an acid-base neutralization, or a redox reaction.

(a) $AgNO_3(aq) + KCl(aq) \longrightarrow AgCl(s) + KNO_3(aq)$

(b) $2\,Al(s) + 3\,Br_2(l) \longrightarrow 2\,AlBr_3(s)$

(c) $Ca(OH)_2(aq) + 2\,HNO_3(aq) \longrightarrow 2\,H_2O(l) + Ca(NO_3)_2(aq)$

PROBLEM 5.8

Identify the oxidized reactant, the reduced reactant, the oxidizing agent, and the reducing agent in the following reactions:

(a) $Fe(s) + Cu^{2+}(aq) \longrightarrow Fe^{2+}(aq) + Cu(s)$

(b) $Mg(s) + Cl_2(g) \longrightarrow MgCl_2(s)$

(c) $2\,Al(s) + Cr_2O_3(s) \longrightarrow 2\,Cr(s) + Al_2O_3(s)$

PROBLEM 5.9

Potassium, a silvery metal, reacts with bromine, a corrosive, reddish liquid, to yield potassium bromide, a white solid. Write the balanced equation, and identify the oxidizing and reducing agents.

CHEMISTRY IN ACTION

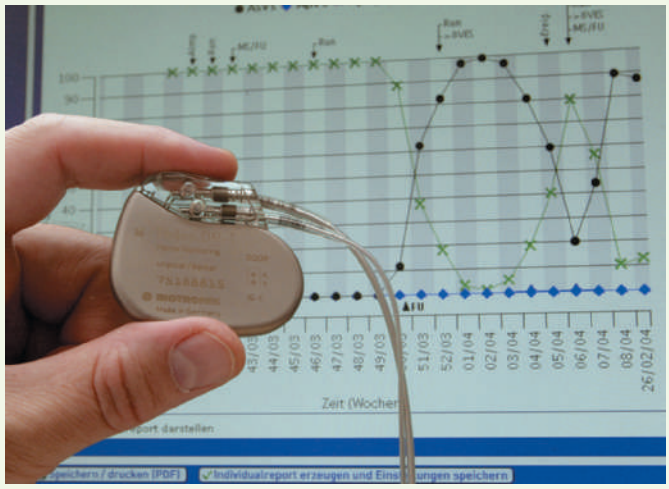
Batteries

A patient suffering from congestive heart failure receives an artificial mechanical heart, whereas another heart patient with arrythmia may receive a pacemaker or an implantable cardioverter defibrillator. A disabled veteran suffering from posttraumatic stress disorder (PTSD) receives a brain implant to monitor and control brain impulses affecting mood, whereas another patient uses a similar implant to send electrical impulses to control tremors associated with Parkinson's disease. A deaf person receives a cochlear implant to stimulate auditory sensation, whereas a patient experiencing vertigo associated with Meniere's disease may use a similar device to maintain equilibrium. What do all these scenarios have in common? They all utilize electronic implants that are powered by small batteries.

It is hard to imagine life without batteries: no cars (they do not start very easily without their batteries!), no flashlights, no hearing aids, no laptops, no radios, no cell phones, nor thousands of other things. Modern society could not exist without batteries.

Although they come in many types and sizes, all batteries work using redox reactions. In a typical redox reaction carried out in the laboratory—say, the reaction of zinc metal with Ag^+ to yield Zn^{2+} and silver metal—the reactants are simply mixed in a flask and electrons are transferred by direct contact between the reactants. In a battery, however, the two reactants are kept in separate compartments and the electrons are transferred through a wire running between them.

The common household battery used for flashlights and radios is the *dry cell,* developed in 1866. One reactant is a can of zinc metal, and the other is a paste of solid manganese dioxide. A graphite rod sticks into the MnO_2 paste to provide electrical contact, and a moist paste of ammonium chloride separates the two reactants. If the zinc can and the graphite rod are connected by a wire, zinc sends electrons flowing through the wire toward the MnO_2 in a redox reaction. The resultant electrical current can then be used to power a lightbulb or a radio. The accompanying figure shows a cutaway view of a dry-cell battery.



▲ This battery-powered pacemaker can run for 8 to 12 years, relaying cardiological data directly to doctors to monitor patients remotely.

$$Zn(s) + 2\,MnO_2(s) + 2\,NH_4Cl(s) \longrightarrow ZnCl_2(aq) + Mn_2O_3(s) + 2\,NH_3(aq) + H_2O(l)$$

Closely related to the dry-cell battery is the familiar *alkaline* battery, in which the ammonium chloride paste is replaced

5.6 Recognizing Redox Reactions

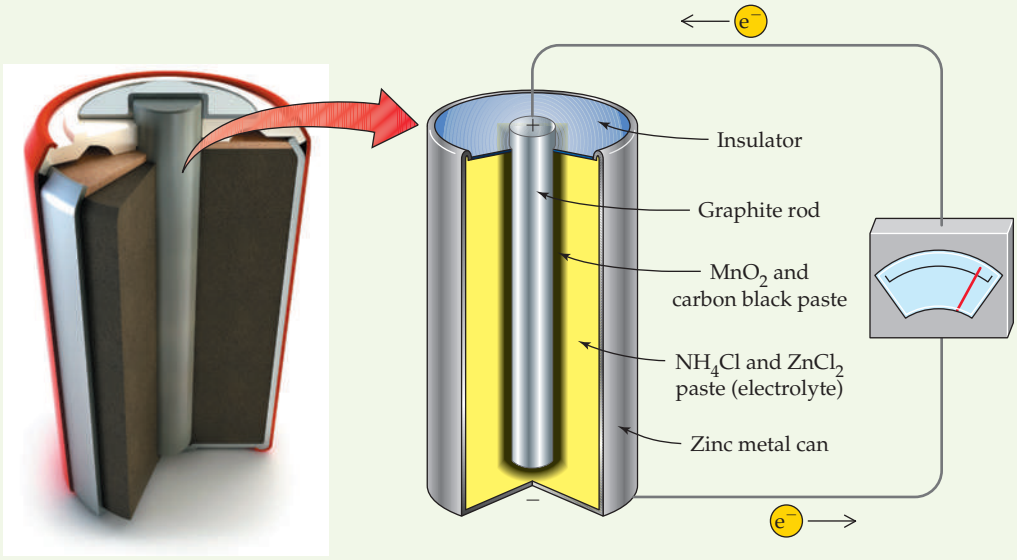
Learning Objective:

- Determine the oxidation number of an atom in a compound.

How can you tell when a redox reaction is taking place? When ions are involved, it is simply a matter of determining whether there is a change in the charges. For reactions involving metals and nonmetals, we can predict the gain or loss of electrons as discussed previously. When molecular substances are involved, though, it is not as obvious. Is the combining of sulfur with oxygen a redox reaction? If so, which partner is the oxidizing agent and which is the reducing agent?

$$S(s) + O_2(g) \longrightarrow SO_2(g)$$

One way to evaluate this reaction is in terms of the oxygen gain by sulfur, indicating that S atoms are oxidized and O atoms are reduced. But can we also look at this reaction in terms of the gain or loss of electrons by the S and O atoms? Because oxygen is more electronegative than sulfur, the oxygen atoms in SO_2 attract the electrons in the S—O bonds more strongly than sulfur does, giving the oxygen atoms a larger share of the electrons than sulfur. By extending the ideas of oxidation and reduction to an



▲ A dry-cell battery. The cutaway view shows the two reactants that make up the redox reaction.

by an alkaline, or basic, paste of NaOH or KOH. The alkaline battery has a longer life than the standard dry-cell battery because the zinc container corrodes less easily under basic conditions. The redox reaction is

$$Zn(s) + 2\,MnO_2(s) \longrightarrow ZnO(aq) + Mn_2O_3(s)$$

The batteries used in implanted medical devices such as pacemakers must be small, corrosion-resistant, reliable, and able to last up to 10 years. Nearly all pacemakers being implanted today—about 750,000 each year—use titanium-encased, lithium–iodine batteries, whose redox reaction is

$$2\,Li(s) + I_2(s) \longrightarrow 2\,LiI(aq)$$

CIA Problem 5.3 The rechargeable NiCd battery uses the following reaction:

$$2\,NiO(OH) + Cd + 2\,H_2O \longrightarrow 2\,Ni(OH)_2 + Cd(OH)_2$$

Which reactant is being oxidized and which is being reduced in this reaction?

CIA Problem 5.4 The redox reaction that provides energy for the lithium is

$$2\,Li(s) + I_2(s) \longrightarrow 2\,LiI(aq)$$

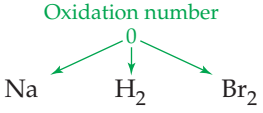
Identify which reactant is being oxidized and which is being reduced in this reaction.

increase or decrease in electron *sharing* instead of complete electron *transfer,* we can say that the sulfur atom is oxidized in its reaction with oxygen because it loses a share in some electrons, whereas the oxygen atoms are reduced because they gain a share in some electrons.

A formal system has been devised for keeping track of changes in electron sharing, and thus for determining whether atoms are oxidized or reduced in reactions. To each atom in a substance, we assign a value called an **oxidation number** (or *oxidation state*), which indicates whether the atom is neutral, electron-rich, or electron-poor. By comparing the oxidation number of an atom before and after a reaction, we can tell whether the atom has gained or lost shares in electrons. Note that *oxidation numbers do not necessarily imply ionic charges.* They are simply a convenient device for keeping track of electrons in redox reactions.

The rules for assigning oxidation numbers are straightforward:

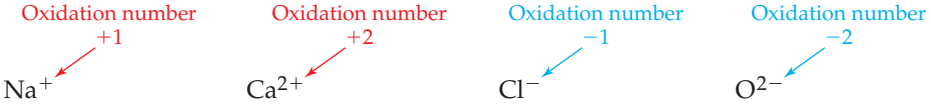
- **An atom in its elemental state has an oxidation number of 0.**



◀◀ Electronegativity, or the propensity of an atom in a covalent bond to attract electrons, was introduced in Section 4.9.

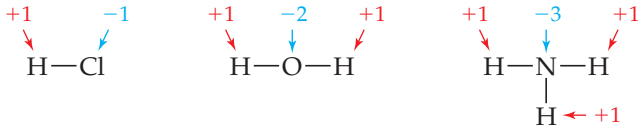
Oxidation number A number that indicates whether an atom is neutral, electron-rich, or electron-poor.

- **A monatomic ion has an oxidation number equal to its charge.**

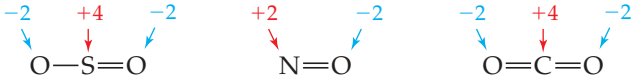


- **In a molecular compound, an atom usually has the same oxidation number it would have if it were a monatomic ion.** Recall from Chapters 3 and 4 that the less electronegative elements (hydrogen and metals) on the left side of the periodic table tend to form cations, and the more electronegative elements (oxygen, nitrogen, and the halogens) near the top right of the periodic table tend to form anions. Hydrogen and metals, therefore, have positive oxidation numbers in most compounds, whereas reactive nonmetals generally have negative oxidation numbers. Hydrogen is usually +1, oxygen is usually −2, nitrogen is usually −3, and halogens are usually −1.

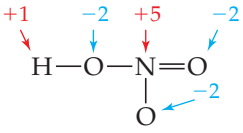
Review the Important Points about Ion Formation and the Periodic Table listed in Section 3.3.



For compounds with more than one nonmetal element, such as SO_2, NO, or CO_2, the more electronegative element—oxygen in these examples—has a negative oxidation number and the less electronegative element has a positive oxidation number. Thus, in answer to the question posed at the beginning of this section, combining sulfur with oxygen to form SO_2 is a redox reaction because the oxidation number of sulfur increases from 0 to +4 and that of oxygen decreases from 0 to −2.



- **The sum of the oxidation numbers in a neutral compound is 0.** Using this rule, the oxidation number of any atom in a compound can be found if the oxidation numbers of the other atoms are known. In the SO_2 example just mentioned, each of the two O atoms has an oxidation number of −2, so the S atom must have an oxidation number of +4. In HNO_3, the H atom has an oxidation number of +1 and the strongly electronegative O atom has an oxidation number of −2, so the N atom must have an oxidation number of +5. In a polyatomic ion, the sum of the oxidation numbers equals the charge on the ion.



Total = 1 + 5 + 3(−2) = 0

Worked Examples 5.10 and 5.11 show further instances of assigning and using oxidation numbers.

Worked Example 5.10 Redox Reactions: Oxidation Numbers

What is the oxidation number of the titanium atom in $TiCl_4$? Name the compound using a Roman numeral (Sections 3.5 and 3.9).

SOLUTION

Chlorine, a reactive nonmetal, is more electronegative than titanium and has an oxidation number of −1. Because there are four chlorine atoms in $TiCl_4$, the oxidation number of titanium must be +4. The compound is named titanium(IV) chloride. Note that the Roman numeral IV in the name of this molecular compound refers to the oxidation number +4 rather than to a true ionic charge.

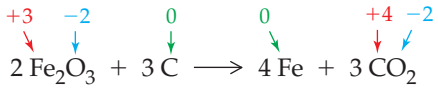
Worked Example 5.11 Redox Reactions: Identifying Redox Reactions

Use oxidation numbers to show that the production of iron metal from its ore (Fe_2O_3) by reaction with charcoal (C) is a redox reaction. Which reactant has been oxidized, and which has been reduced? Which reactant is the oxidizing agent, and which is the reducing agent?

$$2\,Fe_2O_3(s) + 3\,C(s) \longrightarrow 4\,Fe(s) + 3\,CO_2(g)$$

SOLUTION

The idea is to assign oxidation numbers to both reactants and products and see if there has been a change. In the production of iron from Fe_2O_3, the oxidation number of Fe changes from +3 to 0, and the oxidation number of C changes from 0 to +4. Iron has thus been reduced (decrease in oxidation number), and carbon has been oxidized (increase in oxidation number). Oxygen is neither oxidized nor reduced because its oxidation number does not change. Carbon is the reducing agent, and Fe_2O_3 is the oxidizing agent.



PROBLEM 5.10

What are the oxidation numbers of the metal atoms in the following compounds? Name each, using the oxidation number as a Roman numeral.

(a) VCl_3 **(b)** $SnCl_4$ **(c)** CrO_3
(d) $Cu(NO_3)_2$ **(e)** $NiSO_4$

PROBLEM 5.11

Assign an oxidation number to each atom in the reactants and products shown here to determine which of the following reactions are redox reactions:

(a) $Na_2S(aq) + NiCl_2(aq) \longrightarrow 2\,NaCl(aq) + NiS(s)$
(b) $2\,Na(s) + 2\,H_2O(l) \longrightarrow 2\,NaOH(aq) + H_2(g)$
(c) $C(s) + O_2(g) \longrightarrow CO_2(g)$
(d) $2\,CO(g) + O_2(g) \longrightarrow 2\,CO_2(g)$
(e) $CuO(s) + 2\,HCl(aq) \longrightarrow CuCl_2(aq) + H_2O(l)$
(f) $2\,MnO_4^-(aq) + 5\,SO_2(g) + 2\,H_2O(l) \longrightarrow 2\,Mn^{2+}(aq) + 5\,SO_4^{2-}(aq) + 4\,H^+(aq)$

PROBLEM 5.12

For each of the reactions you identified as redox reactions in Problem 5.11, identify the oxidizing agent and the reducing agent.

5.7 Net Ionic Equations

Learning Objective:

- For ionic reactions, write the molecular, ionic, and net ionic reactions, and identify spectator ions.

In the equations we have been writing up to this point, all the substances involved in reactions have been written using their full formulas. In the precipitation reaction of lead(II) nitrate with potassium iodide mentioned in Section 5.3, for example, only the parenthetical *aq* indicated that the reaction actually takes place in aqueous solution, and nowhere was it explicitly indicated that ions are involved:

$$Pb(NO_3)_2(aq) + 2\,KI(aq) \longrightarrow 2\,KNO_3(aq) + PbI_2(s)$$

Ionic equation An equation in which ions are explicitly shown.

In fact, lead (II) nitrate, potassium iodide, and potassium nitrate dissolve in water to yield solutions of ions. Thus, it is more accurate to write the reaction as an **ionic equation,** in which all the ions are explicitly shown:

$$\textit{An ionic equation:} \quad Pb^{2+}(aq) + 2\,NO_3^-(aq) + 2\,K^+(aq) + 2\,I^-(aq) \longrightarrow 2\,K^+(aq) + 2\,NO_3^-(aq) + PbI_2(s)$$

Spectator ion An ion that appears unchanged on both sides of a reaction arrow.

A look at this ionic equation shows that the NO_3^- and K^+ ions undergo no change during the reaction. They appear on both sides of the reaction arrow and act merely as **spectator ions,** that is, they are present but play no role. The actual reaction, when stripped to its essentials, can be described more simply by writing a **net ionic equation,** which includes only the ions that undergo change and ignores all spectator ions:

Net ionic equation An equation that does not include spectator ions.

$$\textit{Ionic equation:} \quad Pb^{2+}(aq) + 2\,NO_3^-(aq) + 2\,K^+(aq) + 2\,I^-(aq) \longrightarrow 2\,K^+(aq) + 2\,NO_3^-(aq) + PbI_2(s)$$

$$\textit{Net ionic equation:} \quad Pb^{2+}(aq) + 2\,I^-(aq) \longrightarrow PbI_2(s)$$

Note that a net ionic equation, like all chemical equations, must be balanced both for atoms and for charge, with all coefficients reduced to their lowest whole numbers. Note also that all compounds that do *not* give ions in solution—all insoluble compounds and all molecular compounds—are represented by their full formulas.

We can apply the concept of ionic equations to acid-base neutralization reactions and redox reactions as well. Consider the neutralization reaction between KOH and HNO_3:

$$KOH(aq) + HNO_3(aq) \longrightarrow H_2O(l) + KNO_3(aq)$$

Since acids and bases are identified based on the ions they form when dissolved in aqueous solutions, we can write an ionic equation for this reaction:

$$\textit{Ionic equation:} \quad K^+(aq) + OH^- + H^+(aq) + NO_3^-(aq) \longrightarrow H_2O(l) + K^+(aq) + NO_3^-(aq)$$

Eliminating the spectator ions (K^+ and NO_3^-), we obtain the net ionic equation for the neutralization reaction:

$$\textit{Net ionic equation:} \quad OH^-(aq) + H^+(aq) \longrightarrow H_2O(l)$$

The net ionic equation confirms the basis of the acid-base neutralization; the OH^- from the base and the H^+ from the acid neutralize each other to form water.

Similarly, many redox reactions can be viewed in terms of ionic equations. Consider the reaction between $Cu(s)$ and $AgNO_3$ from Section 5.6:

$$Cu(s) + 2\,AgNO_3(aq) \longrightarrow 2\,Ag^+(aq) + Cu(NO_3)_2(aq)$$

The aqueous products and reactants can be written as dissolved ions:

$$\textit{Ionic equation:} \quad Cu(s) + 2\,Ag^+(aq) + 2\,NO_3^-(aq) \longrightarrow 2\,Ag(s) + Cu^{2+}(aq) + 2\,NO_3^-(aq)$$

Again, eliminating the spectator ions (NO_3^-), we obtain the net ionic equation for this redox reaction:

$$\textit{Net ionic equation:} \quad Cu(s) + 2\,Ag^+(aq) \longrightarrow 2\,Ag(s) + Cu^{2+}(aq)$$

It is now clear that the $Cu(s)$ loses two electrons and is oxidized, whereas each Ag^+ ion gains an electron and is reduced.

Worked Example 5.12 Chemical Reactions: Net Ionic Reactions

Write balanced net ionic equations for the following reactions:

(a) $AgNO_3(aq) + ZnCl_2(aq) \longrightarrow$

(b) $HCl(aq) + Ca(OH)_2(aq) \longrightarrow$

(c) $6\,HCl(aq) + 2\,Al(s) \longrightarrow 2\,AlCl_3(aq) + 3\,H_2(g)$

SOLUTION

(a) The solubility guidelines discussed in Section 5.3 predict that a precipitate of insoluble AgCl forms when aqueous solutions of Ag^+ and Cl^- are mixed. Writing all the ions separately gives an ionic equation, and eliminating spectator ions Zn^{2+} and NO_3^- gives the net ionic equation.

Ionic equation: $2\,Ag^+(aq) + \cancel{2\,NO_3^-(aq)} + \cancel{Zn^{2+}(aq)} + 2\,Cl^-(aq) \longrightarrow 2\,AgCl(s) + \cancel{Zn^{2+}(aq)} + \cancel{2\,NO_3^-(aq)}$

Net ionic equation: $2\,Ag^+(aq) + 2\,Cl^-(aq) \longrightarrow 2\,AgCl(s)$

The coefficients can all be divided by 2 to give

Net ionic equation: $Ag^+(aq) + Cl^+(aq) \longrightarrow AgCl(s)$

A check shows that the equation is balanced for atoms and charge (zero on each side).

(b) Allowing the acid HCl to react with the base $Ca(OH)_2$ leads to a neutralization reaction. Writing the ions separately, and remembering to write a complete formula for water, gives an ionic equation. Then eliminating the spectator ions and dividing the coefficients by 2 gives the net ionic equation.

Ionic equation: $2\,H^+(aq) + \cancel{2\,Cl^-(aq)} + \cancel{Ca^{2+}(aq)} + 2\,OH^-(aq) \longrightarrow 2\,H_2O(l) + \cancel{Ca^{2+}(aq)} + \cancel{2\,Cl^-(aq)}$

Net ionic equation: $H^+(aq) + OH^-(aq) \longrightarrow H_2O(l)$

A check shows that atoms and charges are the same on both sides of the equation.

(c) The reaction of Al metal with acid (HCl) is a redox reaction. The Al is oxidized, since the oxidation number increases from $0 \longrightarrow +3$, whereas the H in HCl is reduced from $+1 \longrightarrow 0$. We write the ionic equation by showing the ions that are formed for each aqueous ionic species. Eliminating the spectator ions yields the net ionic equation.

Ionic equation: $6\,H^+(aq) + \cancel{6\,Cl^-(aq)} + 2\,Al(s) \longrightarrow 2\,Al^{3+}(aq) + \cancel{6\,Cl^-(aq)} + 3\,H_2(g)$

Net ionic equation: $6\,H^+(aq) + 2\,Al(s) \longrightarrow 2\,Al^{3+}(aq) + 3\,H_2(g)$

A check shows that atoms and charges are the same on both sides of the equation.

PROBLEM 5.13

Write net ionic equations for the following reactions:

(a) $Zn(s) + Pb(NO_3)_2(aq) \longrightarrow Zn(NO_3)_2(aq) + Pb(s)$

(b) $2\,KOH(aq) + H_2SO_4(aq) \longrightarrow K_2SO_4(aq) + 2\,H_2O(l)$

(c) $2\,FeCl_3(aq) + SnCl_2(aq) \longrightarrow 2\,FeCl_2(aq) + SnCl_4(aq)$

PROBLEM 5.14

Identify each of the reactions in Problem 5.13 as an acid-base neutralization, a precipitation, or a redox reaction.

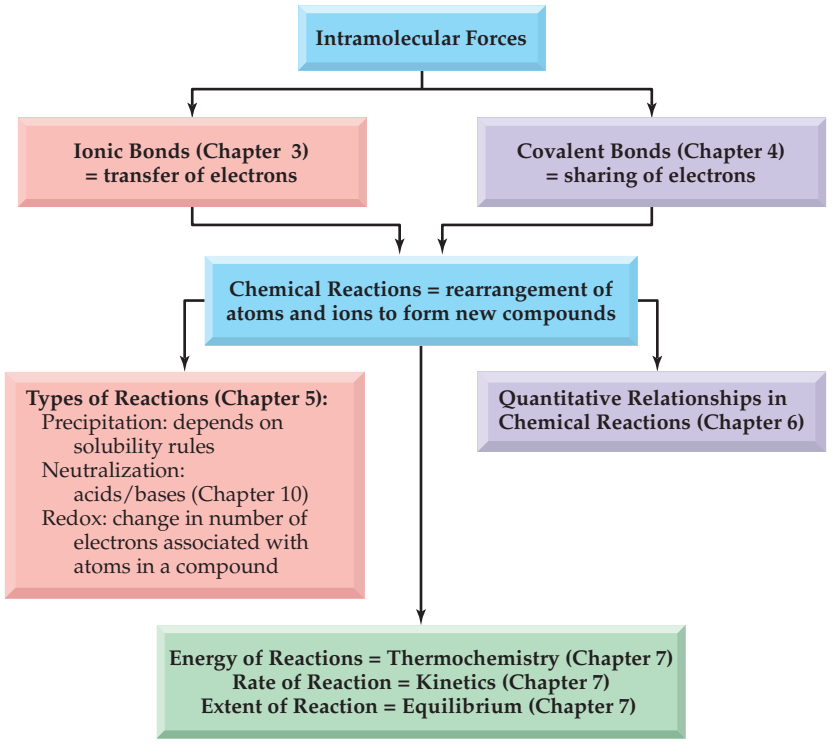
PROBLEM 5.15

For each reaction in Problem 5.13 that you identified as a redox reaction, determine the oxidation numbers for each of the products and reactants, and identify the substance that is oxidized and the substance that is reduced during the reaction.

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Understand the law of conservation of mass and how it applies to chemical equations.** Chemical equations must be *balanced;* in terms of the law of conservation of mass, that means the numbers and kinds of atoms must be the same in both the reactants and the products *(see Problems 16–19 and 22–24).*
- **Balance chemical equations.** To balance an equation, *coefficients* are placed before formulas but the formulas themselves cannot be changed. Starting with the unbalanced equation, you add coefficients to balance elements that appear in only one compound on the reactants and products side and then move on to other elements. Balance atoms that appear in their elemental state last. To verify that the equation is balanced, count the atoms of each type on both the left and ride side of the equation. Finally, divide or multiply the coefficients by an appropriate factor to obtain the lowest whole numbers *(see Problems 17–19, 24–33, 59, 60, 62, 63, 69–71, and 73).*
- **Apply solubility rules to predict if a precipitation reaction will occur, and write the appropriate balanced reaction.** *Precipitation reactions* are processes in which an insoluble solid called a *precipitate* is formed. Most precipitations take place when the anions and cations of two ionic compounds change partners. Solubility guidelines identify anions and cations that tend to form soluble or insoluble ionic compounds and are used to predict when precipitation will occur. If an insoluble anion is combined with an insoluble cation, a precipitation reaction will occur *(see Problems 20, 21, 34, 36–42, 45, 61, 62, and 66–68).*
- **Predict the products of an acid-base neutralization reaction.** *Acid-base neutralization reactions* are processes in which acids produce H^+ ions and bases produce OH^- ions when dissolved in water; a neutralization reaction removes H^+ and OH^- ions from solution and yields neutral H_2O. The products of *acid-base neutralization reactions* are water plus an ionic compound called a *salt.* The acid provides the anion for the salt (e.g., Cl^- from HCl), whereas the base provides the cation for the salt (e.g., Na^+ from NaOH) *(see Problems 34, 35, 37, 38, 62, 71, 74, and 75).*
- **Recognize redox reactions, and identify the species being oxidized and reduced.** *Oxidation-reduction (redox) reactions* are processes in which one or more electrons are transferred between reaction partners. An *oxidation* is defined as the loss of one or more electrons by an atom, and a *reduction* is the gain of one or more electrons. An *oxidizing agent* causes the oxidation of another reactant by accepting electrons, and a *reducing agent* causes the reduction of another reactant by donating electrons *(see Problems 34, 36–38, 47–50, 55–60, 62, 69, and 73).*
- **Determine the oxidation number of an atom in a compound.** *Oxidation numbers* are assigned to atoms in reactants and products to provide a measure of whether an atom is neutral, electron-rich, or electron-poor. By comparing the oxidation number of an atom before and after reaction, we can tell whether the atom has gained or lost shares in electrons and thus whether a redox reaction has occurred *(see Problems 47–58, 63–65, and 72).*
- **For ionic reactions, write the molecular, ionic, and net ionic reactions, and identify spectator ions.** The *net ionic equation* only includes those ions that are directly involved in the ionic reaction. These ions can be identified because they are found in different phases or compounds on the reactant and product sides of the chemical equation. The net ionic equation does not include *spectator ions,* which appear in the same state on both sides of the chemical equation *(see Problems 35, 36, 43, 44, and 66–68).*

CONCEPT MAP: ELECTROSTATIC FORCES



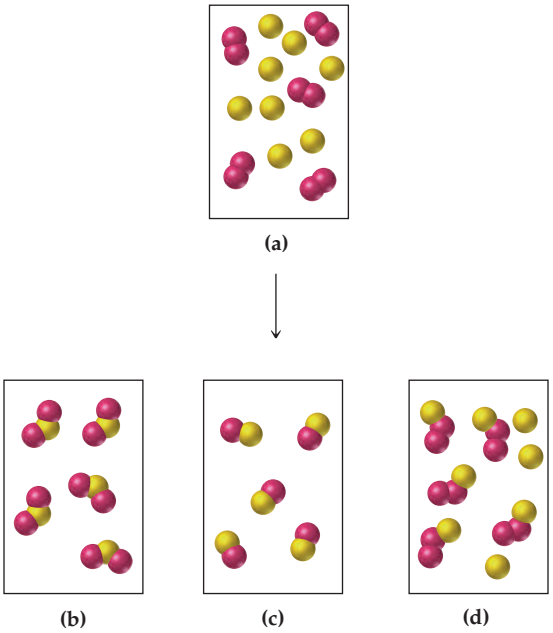
▲ **Figure 5.2 Concept Map.** By knowing the type of chemical reaction and the rules that govern the reaction, we can predict the products that will form and can balance the equation consistent with the law of conservation of mass.

KEY WORDS

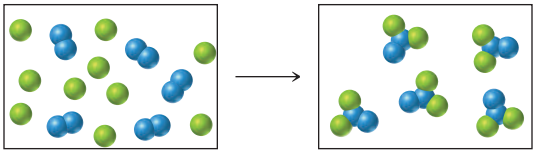
Balanced equation, *p. 172*
Chemical equation, *p. 171*
Coefficient, *p. 172*
Ionic equation, *p. 188*
Law of conservation of mass, *p. 171*
Net ionic equation, *p. 188*
Neutralization reaction, *p. 178*
Oxidation, *p. 179*
Oxidation number, *p. 185*
Oxidation-reduction (redox) reaction, *p. 179*
Oxidizing agent, *p. 180*
Precipitate, *p. 175*
Product, *p. 171*
Reactant, *p. 171*
Reducing agent, *p. 180*
Reduction, *p. 179*
Salt, *p. 177*
Solubility, *p. 175*
Spectator ion, *p. 188*

UNDERSTANDING KEY CONCEPTS

5.16 Assume that the mixture of substances in drawing (a) undergoes a reaction. Which of the drawings (b)–(d) represent a product mixture consistent with the law of conservation of mass?



5.17 Reaction of A (green spheres) with B (blue spheres) is shown in the following diagram:



Which equation best describes the reaction?

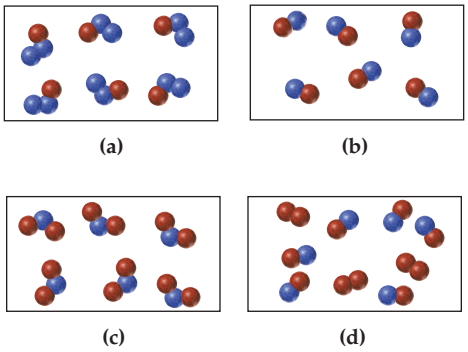
(a) $A_2 + 2\,B \longrightarrow A_2B_2$

(b) $10\,A + 5\,B_2 \longrightarrow 5\,A_2B_2$

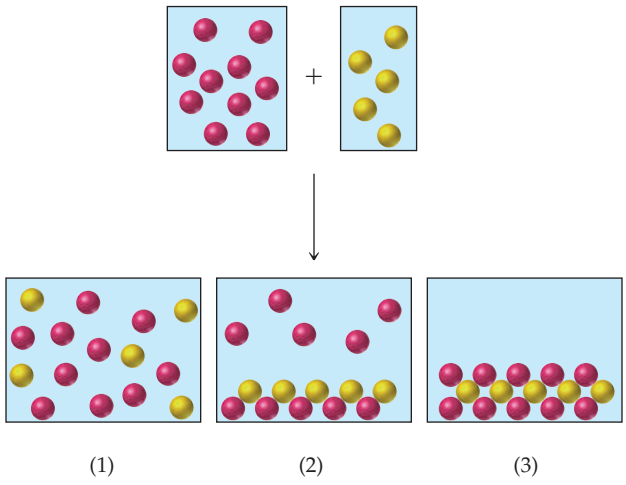
(c) $2\,A + B_2 \longrightarrow A_2B_2$

(d) $5\,A + 5\,B_2 \longrightarrow 5\,A_2B_2$

5.18 If blue spheres represent nitrogen atoms and red spheres represent oxygen atoms in the following diagrams, which box represents reactants and which represents products for the reaction $2\,NO(g) + O_2(g) \longrightarrow 2\,NO_2(g)$?



5.19 Assume that an aqueous solution of a cation (represented as red spheres in the diagram) is allowed to mix with a solution of an anion (represented as yellow spheres). Three possible outcomes are represented by boxes (1)–(3):



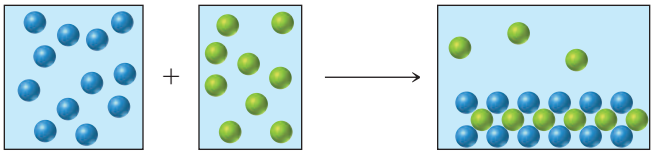
Which outcome corresponds to each of the following reactions?

(a) $2\,Na^+(aq) + CO_3^{2-}(aq) \longrightarrow$

(b) $Ba^{2+}(aq) + CrO_4^{2-}(aq) \longrightarrow$

(c) $2\,Ag^+(aq) + SO_3^{2-}(aq) \longrightarrow$

5.20 An aqueous solution of a cation (represented as blue spheres in the diagram) is allowed to mix with a solution of an anion (represented as green spheres) and the following result is obtained:

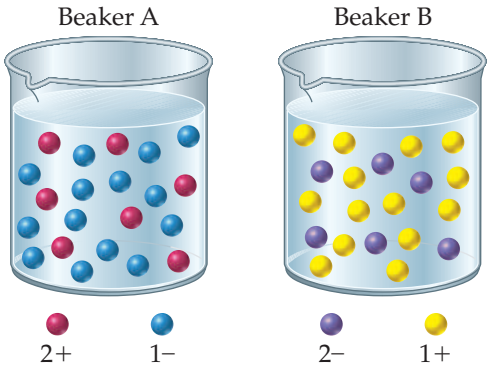


Which combinations of cation and anion, chosen from the following lists, are compatible with the observed results? Explain.

Cations: Na^+, Ca^{2+}, Ag^+, Ni^{2+}

Anions: Cl^-, CO_3^{2-}, CrO_4^{2-}, NO_3^-

5.21 A molecular view of two ionic solutions is presented right:



(a) Which compound is most likely dissolved in beaker A: KBr, $CaCl_2$, PbI_2, Na_2SO_4?

(b) Which compound is most likely dissolved in beaker B: Na_2CO_3, $BaSO_4$, $Cu(NO_3)_2$, $FeCl_3$?

(c) Identify the precipitate and spectator ions for any reaction that will result when beakers A and B are mixed.

ADDITIONAL PROBLEMS

BALANCING CHEMICAL EQUATIONS (SECTIONS 5.1 AND 5.2)

5.22 What is meant by the term "balanced equation"?

5.23 Why is it not possible to balance an equation by changing the subscript on a substance, say from H_2O to H_2O_2?

5.24 Write balanced equations for the following reactions:

(a) Hydrochloric acid reacts with calcium carbonate to form carbon dioxide and calcium chloride and water.

(b) Liquid bromine reacts with solid potassium metal to form solid potassium bromide.

(c) Gaseous propane (C_3H_8) burns in oxygen to form gaseous carbon dioxide and water vapor.

5.25 Balance the following equation for the synthesis of hydrazine, N_2H_4, a substance used as rocket fuel.

$$NH_3(g) + Cl_2(g) \longrightarrow N_2H_4(l) + NH_4Cl(s)$$

5.26 Which of the following equations are balanced? Balance those that need it.

(a) $2\,C_2H_6(g) + 5\,O_2(g) \longrightarrow 2\,CO_2(g) + 6\,H_2O(l)$

(b) $3\,Ca(OH)_2(aq) + 2\,H_3PO_4(aq) \longrightarrow Ca_3(PO_4)_2(aq) + 6\,H_2O(l)$

(c) $Mg(s) + O_2(g) \longrightarrow 2\,MgO(s)$

(d) $K(s) + H_2O(l) \longrightarrow KOH(aq) + H_2(g)$

5.27 Which of the following equations are balanced? Balance those that need it.

(a) $CaC_2 + 2\,H_2O \longrightarrow Ca(OH)_2 + C_2H_2$

(b) $C_2H_8N_2 + 2\,N_2O_4 \longrightarrow 2\,N_2 + 2\,CO_2 + 4\,H_2O$

(c) $3\,MgO + 2\,Fe \longrightarrow Fe_2O_3 + 3\,Mg$

(d) $N_2O \longrightarrow N_2 + O_2$

5.28 Balance the following equations:

(a) $Hg(NO_3)_2(aq) + LiI(aq) \longrightarrow LiNO_3(aq) + HgI_2(s)$

(b) $I_2(s) + Cl_2(g) \longrightarrow ICl_5(s)$

(c) $Al(s) + O_2(g) \longrightarrow Al_2O_3(s)$

(d) $CuSO_4(aq) + AgNO_3(aq) \longrightarrow Ag_2SO_4(s) + Cu(NO_3)_2(aq)$

(e) $Mn(NO_3)_3(aq) + Na_2S(aq) \longrightarrow Mn_2S_3(s) + NaNO_3(aq)$

5.29 Balance the following equations:

(a) $NO_2(g) + O_2(g) \longrightarrow N_2O_5(g)$

(b) $P_4O_{10}(s) + H_2O(l) \longrightarrow H_3PO_4(aq)$

(c) $B_2H_6(l) + O_2(g) \longrightarrow B_2O_3(s) + H_2O(l)$

(d) $Cr_2O_3(s) + CCl_4(l) \longrightarrow CrCl_3(s) + COCl_2(aq)$

(e) $Fe_3O_4(s) + O_2(g) \longrightarrow Fe_2O_3(s)$

5.30 When organic compounds are burned, they react with oxygen to form CO_2 and H_2O. Write balanced equations for the combustion reactions involving the following compounds. (Hint: When balancing combustion reactions, begin by balancing the C and H atoms first, and balance the O atoms last).

(a) C_4H_{10} (butane, used in lighters)

(b) C_2H_6O (ethanol, used in gasohol and as race car fuel)

(c) C_8H_{18} (octane, a component of gasoline)

5.31 When organic compounds are burned without enough oxygen, carbon monoxide is formed as a product instead of carbon dioxide. Write and balance the combustion reactions from Problem 5.30 using CO as a product instead of CO_2.

5.32 Hydrofluoric acid (HF) is used to etch glass (SiO_2). The products of the reaction are silicon tetrafluoride and water. Write the balanced chemical equation.

5.33 Write a balanced equation for the reaction of aqueous sodium carbonate (Na_2CO_3) with aqueous nitric acid (HNO_3) to yield CO_2, $NaNO_3$, and H_2O.

TYPES OF CHEMICAL REACTIONS (SECTIONS 5.3–5.5 AND 5.7)

5.34 Identify each of the following reactions as a precipitation, neutralization, or redox reaction:

(a) $Mg(s) + 2\,HCl(aq) \longrightarrow MgCl_2(aq) + H_2(g)$

(b) $KOH(aq) + HNO_3(aq) \longrightarrow KNO_3(aq) + H_2O(l)$

(c) $Pb(NO_3)_2(aq) + 2\,HBr(aq) \longrightarrow PbBr_2(s) + 2\,HNO_3(aq)$

(d) $Ca(OH)_2(aq) + 2\,HCl(aq) \longrightarrow 2\,H_2O(l) + CaCl_2(aq)$

5.35 Write balanced ionic equations and net ionic equations for the following reactions:

(a) Aqueous sulfuric acid is neutralized by aqueous potassium hydroxide.

(b) Aqueous magnesium hydroxide is neutralized by aqueous hydrochloric acid.

5.36 Write balanced ionic equations and net ionic equations for the following reactions:

(a) A precipitate of barium sulfate forms when aqueous solutions of barium nitrate and potassium sulfate are mixed.

(b) Zinc ion and hydrogen gas form when zinc metal reacts with aqueous sulfuric acid.

5.37 Identify each of the reactions in Problem 5.26 as a precipitation, neutralization, or redox reaction.

5.38 Identify each of the reactions in Problem 5.28 as a precipitation, neutralization, or redox reaction.

5.39 Which of the following substances are likely to be soluble in water?

(a) $ZnSO_4$ **(b)** $NiCO_3$

(c) $PbCl_2$ **(d)** $Ca_3(PO_4)_2$

5.40 Which of the following substances are likely to be soluble in water?

(a) Ag_2O **(b)** $Ba(NO_3)_2$

(c) $SnCO_3$ **(d)** Al_2S_3

5.41 Use the solubility guidelines in Section 5.3 to predict whether a precipitation reaction will occur when aqueous solutions of the following substances are mixed.

(a) $NaOH + HClO_4$

(b) $FeCl_2 + KOH$

(c) $(NH_4)_2SO_4 + NiCl_2$

5.42 Use the solubility guidelines in Section 5.3 to predict whether precipitation reactions will occur between the listed pairs of reactants. Write balanced equations for those reactions that should occur.

(a) NaBr and $Hg_2(NO_3)_2$

(b) $CuCl_2$ and K_2SO_4

(c) $LiNO_3$ and $Ca(CH_3CO_2)_2$

(d) $(NH_4)_2CO_3$ and $CaCl_2$

(e) KOH and $MnBr_2$

(f) Na_2S and $Al(NO_3)_3$

5.43 Write net ionic equations for the following reactions:

(a) $Mg(s) + CuCl_2(aq) \longrightarrow MgCl_2(aq) + Cu(s)$

(b) $2\,KCl(aq) + Pb(NO_3)_2(aq) \longrightarrow PbCl_2(s) + 2\,KNO_3(aq)$

(c) $2\,Cr(NO_3)_3(aq) + 3\,Na_2S(aq) \longrightarrow Cr_2S_3(s) + 6\,NaNO_3(aq)$

5.44 Write net ionic equations for the following reactions:

(a) $2\,AuCl_3(aq) + 3\,Sn(s) \longrightarrow 3\,SnCl_2(aq) + 2\,Au(s)$

(b) $2\,NaI(aq) + Br_2(l) \longrightarrow 2\,NaBr(aq) + I_2(s)$

(c) $2\,AgNO_3(aq) + Fe(s) \longrightarrow Fe(NO_3)_2(aq) + 2\,Ag(s)$

5.45 Complete the following precipitation reactions using balanced chemical equations:

(a) $FeSO_4(aq) + Sr(OH)_2(aq) \longrightarrow$

(b) $Na_2S(aq) + ZnSO_4(aq) \longrightarrow$

5.46 Write net ionic equations for each of the reactions in Problem 5.45.

REDOX REACTIONS AND OXIDATION NUMBERS (SECTIONS 5.5 AND 5.6)

5.47 Where in the periodic table are the best reducing agents found? The best oxidizing agents?

5.48 Where in the periodic table are the most easily reduced elements found? The most easily oxidized?

5.49 In each of the following, tell whether the substance gains electrons or loses electrons in a redox reaction:

(a) An oxidizing agent

(b) A reducing agent

(c) A substance undergoing oxidation

(d) A substance undergoing reduction

5.50 For the following substances, tell whether the oxidation number increases or decreases in a redox reaction:

(a) An oxidizing agent

(b) A reducing agent

(c) A substance undergoing oxidation

(d) A substance undergoing reduction

5.51 Assign an oxidation number to each element in the following compounds or ions:

(a) N_2O_5 **(b)** SO_3^{2-}

(c) CH_2O **(d)** $HClO_3$

5.52 Assign an oxidation number to the metal in the following compounds:

(a) $CoCl_3$ **(b)** $FeSO_4$ **(c)** UO_3

(d) CuF_2 **(e)** TiO_2 **(f)** SnS

5.53 Which element is oxidized and which is reduced in the following reactions?

(a) $Si(s) + 2\,Cl_2(g) \longrightarrow SiCl_4(l)$

(b) $Cl_2(g) + 2\,NaBr(aq) \longrightarrow Br_2(aq) + 2\,NaCl(aq)$

(c) $SbCl_3(s) + Cl_2(g) \longrightarrow SbCl_5(s)$

5.54 Which element is oxidized and which is reduced in the following reactions?

(a) $2\,SO_2(g) + O_2(g) \longrightarrow 2\,SO_3(g)$

(b) $2\,Na(s) + Cl_2(g) \longrightarrow 2\,NaCl(s)$

(c) $CuCl_2(aq) + Zn(s) \longrightarrow ZnCl_2(aq) + Cu(s)$

(d) $2\,NaCl(aq) + F_2(g) \longrightarrow 2\,NaF(aq) + Cl_2(g)$

5.55 Balance each of the following redox reactions:

(a) $Al(s) + H_2SO_4(aq) \longrightarrow Al_2(SO_4)_3(aq) + H_2(g)$

(b) $Fe(s) + Cl_2(g) \longrightarrow FeCl_3(s)$

(c) $CO(g) + I_2O_5(s) \longrightarrow I_2(s) + CO_2(g)$

5.56 Balance each of the following redox reactions:

(a) $N_2O_4(l) + N_2H_4(l) \longrightarrow N_2(g) + H_2O(g)$

(b) $CaH_2(s) + H_2O(l) \longrightarrow Ca(OH)_2(aq) + H_2(g)$

(c) $Al(s) + H_2O(l) \longrightarrow Al(OH)_3(s) + H_2(g)$

5.57 Identify the oxidizing agent and the reducing agent in Problem 5.55.

5.58 Identify the oxidizing agent and the reducing agent in Problem 5.56.

CONCEPTUAL PROBLEMS

5.59 Balance the following equations.

(a) The thermite reaction, used in welding:

$$Al(s) + Fe_2O_3(s) \longrightarrow Al_2O_3(l) + Fe(l)$$

(b) The explosion of ammonium nitrate:

$$NH_4NO_3(s) \longrightarrow N_2(g) + O_2(g) + H_2O(g)$$

5.60 Lithium oxide is used aboard the space shuttle to remove water from the atmosphere according to the equation:

$$Li_2O(s) + H_2O(g) \longrightarrow LiOH(s)$$

(a) Balance the chemical equation.

(b) Is this a redox reaction? Why or why not?

5.61 Look at the solubility guidelines in Section 5.3 and predict whether a precipitate forms when $CuCl_2(aq)$ and $Na_2CO_3(aq)$ are mixed. If so, write both the balanced equation and the net ionic equation for the process.

5.62 Balance the following equations and classify each as a precipitation, neutralization, or redox reaction:

(a) $Al(OH)_3(aq) + HNO_3(aq) \longrightarrow Al(NO_3)_3(aq) + H_2O(l)$

(b) $AgNO_3(aq) + FeCl_3(aq) \longrightarrow AgCl(s) + Fe(NO_3)_3(aq)$

(c) $(NH_4)_2Cr_2O_7(s) \longrightarrow Cr_2O_3(s) + H_2O(g) + N_2(g)$

(d) $Mn_2(CO_3)_3(s) \longrightarrow Mn_2O_3(s) + CO_2(g)$

5.63 White phosphorus (P_4) is a highly reactive form of elemental phosphorus that reacts with oxygen to form a variety of molecular compounds, including diphosphorus pentoxide.

(a) Write the balanced chemical equation for this reaction.

(b) Calculate the oxidation number for P and O on both sides of the reaction, and identify the oxidizing and reducing agents.

5.64 The transition metals form compounds with oxygen in which the metals have different oxidation states. Calculate the oxidation number for the transition metal in the following sets of compounds:

(a) Mn in MnO_2, Mn_2O_3, and $KMnO_4$

(b) Cr in CrO_2, CrO_3, and Cr_2O_3.

5.65 In the Breathalyzer test, blood alcohol is determined by reaction of the alcohol with potassium dichromate:

$$16\,H^+(aq) + 2\,Cr_2O_7^{2-}(aq) + C_2H_5OH(aq) \longrightarrow 4\,Cr^{3+}(aq) + 2\,CO_2(g) + 11\,H_2O(l)$$

(a) Calculate the oxidation number of Cr in $Cr_2O_7^{2-}$.

(b) Calculate the oxidation number of C in C_2H_5OH and in CO_2.

(c) Identify the oxidizing agent and the reducing agent in this reaction.

5.66 Iron in drinking water is removed by precipitation of the Fe^{3+} ion by reaction with NaOH to produce iron(III) hydroxide. Write the balanced chemical equation and the net ionic equation for this reaction.

5.67 Hard water contains magnesium and calcium ions (Mg^{2+}, Ca^{2+}), which can precipitate out in hot water pipes and water heaters as carbonates. Write the net ionic equation for this reaction.

5.68 Pepto-Bismol, an antacid and antidiarrheal, contains bismuth subsalicylate, $C_7H_5BiO_4$. Some users of this product can experience a condition known as "black tongue," which is caused by the reaction of bismuth(III) ions with trace amounts of S^{2-} in saliva to form a black precipitate. Write the balanced net ionic equation for this precipitation reaction.

5.69 Iron is produced from iron ore by reaction with carbon monoxide:

$$Fe_2O_3(s) + CO(g) \longrightarrow Fe(s) + CO_2(g)$$

(a) Balance the chemical equation.

(b) Classify the reaction as a precipitation, neutralization, or redox reaction.

5.70 Balance the reaction for the synthesis of urea, commonly used as a fertilizer:

$$CO_2(g) + NH_3(g) \longrightarrow NH_2CONH_2(s) + H_2O(l)$$

5.71 Geologists identify carbonate minerals by reaction with acids. Dolomite, for example, contains magnesium carbonate, which reacts with hydrochloric acid by the following reaction:

$$MgCO_3(s) + HCl(aq) \longrightarrow MgCl_2(aq) + CO_2(g) + H_2O(l)$$

(a) Balance the reaction and write the net ionic equation.

(b) Classify the reaction as a precipitation, neutralization, or redox reaction.

5.72 Iodine, used as an antiseptic agent, can be prepared in the laboratory by the following reaction:

$$2\,NaI(s) + 2\,H_2SO_4(aq) + MnO_2(s) \longrightarrow Na_2SO_4(aq) + MnSO_4(aq) + I_2(g) + 2\,H_2O(l)$$

(a) Determine the oxidation number for the Mn and I on both sides of the equation.

(b) Identify the oxidizing and reducing agents.

GROUP PROBLEMS

5.73 High temperature combustion processes, such as in combustion engines and coal-fired power plants, can result in the reaction of nitrogen and sulfur with oxygen to form nitrogen oxides (NO_x) and sulfur oxides (SO_x), where x can vary. These NO_x and SO_x compounds subsequently undergo further reaction in the atmosphere to create acidic compounds that contribute to acid rain.

(a) Do some research to determine the common products that are formed (i.e., what are the values of x) for the reactions of N and S with oxygen. Write balanced equations for these reactions.

(b) What additional reactions do these NO_x and SO_x compounds undergo in the atmosphere that lead to the formation of acidic compounds? Write balanced equations for these reactions.

(c) Classify each of the reactions you identified in parts (a) and (b) (precipitation, neutralization, or redox) and explain your reason for each classification.

5.74 Milk of magnesia is an over-the-counter product that is used to neutralize excess stomach acid.

(a) Look up the active ingredient in milk of magnesia.

(b) Stomach acid is predominantly hydrochloric acid. Write the balanced chemical equation for the neutralization reaction between HCl and the active ingredient from part (a).

5.75 Many pharmaceuticals are marketed with the designation "HCl" appended to the name of the drug. What does the "HCl" mean? What type of reaction would be involved in converting a drug to the HCl form? What are the advantages of this form of the drug?

6

Chemical Reactions: Mole and Mass Relationships

CONTENTS

CONCEPTS TO REVIEW

A. Problem Solving: Unit Conversions and Estimating Answers (Section 1.10)
B. Molecular Formulas and Formula Units (Sections 3.8 and 4.6)
C. Balancing Chemical Equations (Section 5.2)

▲ These foods represent good sources of iron, an essential nutrient. A lack of dietary iron can cause anemia.

Good health, in part, depends on a balanced diet containing adequate nutrients, vitamins, and minerals. For example, not enough iron can lead to anemia, not enough iodine can cause thyroid problems, and not enough vitamin C can cause diseases such as scurvy. The recommended daily allowances, or RDAs, of each vitamin and nutrient are set by regulatory groups such as the World Health Organization or the U.S. Department of Agriculture (USDA). The total allowances are based on the amounts needed to sustain the critical metabolic reactions in which these substances are involved. Foods such as red meats, beans, spinach, and dried fruits are rich in iron, a key component of hemoglobin, which is responsible for oxygen transport. Insufficient iron in the diet can cause fatigue and lethargy because of a lack of oxygen in the cells, which are symptoms of anemia, a condition that is explained in more detail in the Chemistry in Action feature on page 211 later in this chapter. But how do we know what amounts of iron and other nutrients are sufficient? To answer this question we need to be able to translate the molecular information—balanced chemical reactions and the relationships between reactants and products—into meaningful units that we can measure conveniently—mass!

Consider how these conversions are handled in the kitchen. When chefs prepare to cook a rice pudding, they do not count out individual grains of rice, or individual raisins, or individual sugar crystals. Rather, they measure out appropriate amounts of the necessary ingredients using more convenient units—such as cups or tablespoons. When chemists prepare chemical reactions, they use the same approach—they measure out grams of substances instead of individual molecules. From the mass of reactants, they can determine whether or not they have sufficient amounts of molecules to complete a reaction, and to calculate the mass

of products they should obtain. In this chapter, we introduce the concept of the mole and its relationship to mass, and how chemists use the mole–mass relationship when studying the quantitative relationships between reactants and products.

6.1 The Mole and Avogadro's Number

Learning Objective:

- Define the mole, and calculate the molar mass of a compound from the molecular formula.

In the previous chapter, we learned how to use the balanced chemical equation to indicate what is happening at the molecular level during a reaction. Now, let us imagine a laboratory experiment: the reaction of ethene (C_2H_4) with hydrogen chloride gas (HCl) to form chloroethane (C_2H_5Cl), a colorless, low-boiling liquid used by doctors and athletic trainers as a spray-on anesthetic. The reaction is represented as

$$C_2H_4(g) + HCl(g) \longrightarrow C_2H_5Cl(g)$$

In this reaction, one molecule of ethene reacts with one molecule of hydrogen chloride to produce one molecule of chloroethane. How, though, can you be sure you have a one-to-one ratio of reactant molecules in your reaction flask? Since it is impossible to hand-count the number of molecules correctly, you must weigh them instead.

We do this every day with all kinds of small objects: Nails, nuts, and grains of rice are all weighed in bulk rather than counted individually. Consider a common example: You wish to construct a storage rack and need nuts and bolts. Let's assume that each nut weighs 1 g and each bolt weighs 63 g. Not wishing to count out each nut + bolt combination separately, you can take advantage of the mass ratios—if you weigh out 10 g of nuts and 630 g of bolts, you will have 10 of each item for a 1:1 ratio. The same logic applies to the amounts of reactants needed for a balanced reaction.

But the weighing approach leads to another problem. How many *molecules* are there in 1 g of ethene, hydrogen chloride, or any other substance? The answer depends on the identity of the substance—just as nuts and bolts have different masses, different molecules have different masses.

To determine how many molecules of a given substance are in a certain mass, it is helpful to define a quantity called *molecular mass.* Just as the *atomic mass* of an element is the average mass of the element's *atoms,* the **molecular mass** of a molecule is the average mass of a substance's *molecules.* Numerically, a substance's molecular mass (or **formula mass** for an ionic compound) is equal to the sum of the atomic masses for all the atoms in the molecule or formula unit.

For example, the molecular mass of ethene (C_2H_4) is 28.0 amu, the molecular mass of HCl is 36.5 amu, and the molecular mass of chloroethane (C_2H_5Cl) is 64.5 amu. (The actual values are known more precisely but are rounded off here for convenience.)

***For ethene,* C_2H_4:**

Atomic mass of 2 C $= 2 \times 12.0$ amu	$= 24.0$ amu
Atomic mass of 4 H $= 4 \times 1.0$ amu	$= 4.0$ amu
Molecular mass of C_2H_4	$= 28.0$ amu

Molecular mass The sum of atomic masses of all atoms in a molecule.

Formula mass The sum of atomic masses of all atoms in one formula unit of any compound, whether molecular or ionic.

CONCEPTS TO REVIEW See Section 2.3 for a discussion of atomic mass.

▲ These samples of sulfur, copper, mercury, and helium each contain 1 mol. Do they all have the same mass?

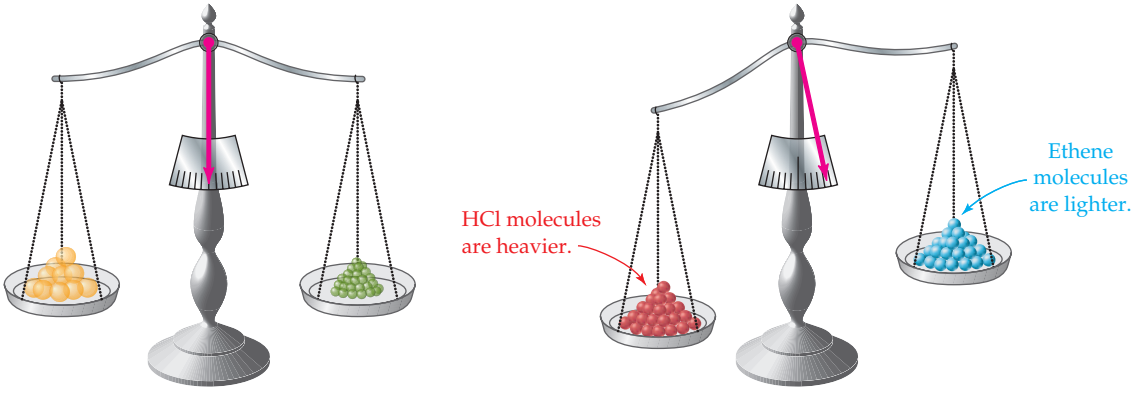
***For hydrogen chloride,* HCl:**

Atomic mass of H	= 1.0 amu
Atomic mass of Cl	= 35.5 amu
Molecular mass of HCl	= 36.5 amu

***For chloroethane,* C_2H_5Cl:**

Atomic mass of 2 C	= 2 × 12.0 amu	= 24.0 amu
Atomic mass of 5 H	= 5 × 1.0 amu	= 5.0 amu
Atomic mass of Cl		= 35.5 amu
Molecular mass of C_2H_5Cl		= 64.5 amu

How are molecular masses used? Since the mass ratio of one ethene molecule to one HCl molecule is 28.0 to 36.5, the mass ratio of *any* given number of ethene molecules to the same number of HCl molecules is also 28.0 to 36.5. In other words, a 28.0 to 36.5 *mass* ratio of ethene and HCl always guarantees a 1:1 *number* ratio. *Samples of different substances always contain the same number of molecules or formula units whenever their mass ratio is the same as their molecular or formula mass ratio* (Figure 6.1).



▲ **Figure 6.1**
(a) Because the yellow balls (left pan) are bigger than the green balls (right pan), you cannot get an equal number by taking equal masses. The same is true for atoms or molecules of different substances. (b) Equal numbers of ethene and HCl molecules always have a mass ratio equal to the ratio of their molecular masses, 28.0 to 36.5.

A particularly convenient way to use this mass/number relationship for molecules is to measure amounts in grams that are numerically equal to molecular masses. If, for instance, you were to carry out your experiment with 28.0 g of ethene and 36.5 g of HCl, you could be certain that you would have a 1:1 ratio of reactant molecules.

Mole The amount of a substance whose mass in grams is numerically equal to its molecular or formula mass.

Molar mass The mass in grams of 1 mole of a substance, numerically equal to molecular mass.

When referring to the vast numbers of molecules or formula units that take part in a visible chemical reaction, it is convenient to use a counting unit called a **mole,** abbreviated *mol.* One mole of any substance is the amount having a mass in grams—its **molar mass**—numerically equal to its molecular or formula mass in amu. One mole of ethene has a mass of 28.0 g, 1 mole of HCl has a mass of 36.5 g, and 1 mole of chloroethane has a mass of 64.5 g.

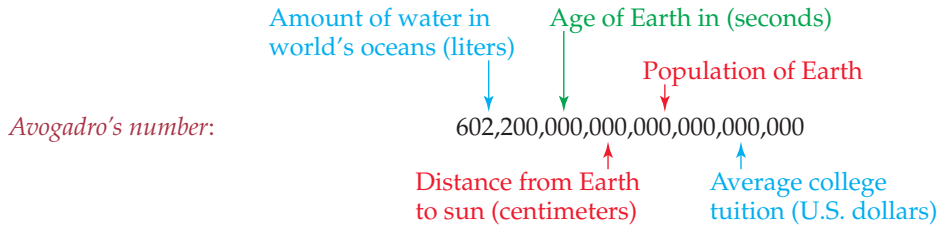
Just how many molecules are there in a mole? Think back to Chapter 2 where we learned to calculate the number of atoms in a sample of an element given its mass in grams, the atomic mass of the atom, and a gram/amu conversion factor. In Problems 2.37 and 2.38, you (hopefully!) found that a 15.99 g sample of oxygen (atomic mass 15.99 amu) and a 12 g sample of carbon (atomic mass 12.00 amu) each contain 6.022×10^{23} atoms. One mole of any substance, therefore, contains 6.022×10^{23} formula units, a value called **Avogadro's number (N_A)** after the Italian scientist who first recognized the importance of the mass/number relationship in molecules. Avogadro's number of formula units of any substance—that is, one mole—has a mass in grams numerically equal to the molecular mass of the substance. Just as we use specific units when dealing with large numbers of other substances—a dozen eggs, a

Avogadro's number (N_A) The number of formula units in 1 mol of anything; 6.022×10^{23}.

ream of paper, a ton of coal—we use the mole as a convenient unit to refer to a specific number of atoms or molecules.

$$1 \text{ mol HCl} = 6.022 \times 10^{23} \text{ HCl molecules} = 36.5 \text{g HCl}$$
$$1 \text{ mol } C_2H_4 = 6.022 \times 10^{23} C_2H_4 \text{ molecules} = 28.0 \text{ g } C_2H_4$$
$$1 \text{ mol } C_2H_5Cl = 6.022 \times 10^{23} C_2H_5Cl \text{ molecules} = 64.5 \text{ g } C_2H_5Cl$$

How big is Avogadro's number? Our minds cannot really conceive of the magnitude of a number like 6.022×10^{23}, but the following comparisons will give you a sense of the scale.



Worked Example 6.1 Molar Mass and Avogadro's Number: Number of Molecules

Pseudoephedrine hydrochloride ($C_{10}H_{16}ClNO$) is a nasal decongestant commonly found in cold medication. (a) What is the molar mass of pseudoephedrine hydrochloride? (b) How many molecules of pseudoephedrine hydrochloride are in a tablet that contains a dose of 30.0 mg of this decongestant?

ANALYSIS We are given a mass and need to convert to a number of molecules. This is most easily accomplished by using the molar mass of pseudoephedrine hydrochloride calculated in part (a) as the conversion factor from mass to moles and realizing that this mass (in grams) contains Avogadro's number of molecules (6.022×10^{23}).

BALLPARK ESTIMATE The formula for pseudoephedrine contains 10 carbon atoms (each one of atomic mass 12.0 amu), so the molecular mass is greater than 120 amu, probably near 200 amu. Thus, the molar mass should be near 200 g/mol. The mass of 30 mg of pseudoepinephrine HCl is less than the mass of 1 mol of this compound by a factor of roughly 10^4 (0.03 g versus 200 g), which means that the number of molecules should also be smaller by a factor of 10^4 (on the order of 10^{19} in the tablet versus 10^{23} in 1 mol).

SOLUTION

(a) The molecular mass of pseudoephedrine is found by summing the atomic masses of all atoms in the molecule as follows:

Atomic mass of 10 atoms of C:	10×12.011 amu	=	120.11 amu
16 atoms of H:	16×1.00794 amu	=	16.127 amu
1 atom of Cl:	1×35.4527 amu	=	35.4527 amu
1 atom of N:	1×14.0067 amu	=	14.0067 amu
1 atom of O:	1×15.9994 amu	=	15.9994 amu
Molecular mass of $C_{10}H_{16}ClNO$		=	201.6958 amu $\longrightarrow$ 201.70 g/mol

Remember that molecular mass in amu converts directly to molar mass in g/mol. Also, following the rules for significant figures from Sections 1.8 and 1.9, our final answer is rounded to the second decimal place.

(b) Since this problem involves unit conversions, we can use the step-wise solution introduced in Chapter 1.

STEP 1: Identify known information. We are given the mass of pseudoephedrine hydrochloride (in mg).	30.0 mg pseudoephedrine hydrochloride
STEP 2: Identify answer and units. We are looking for the number of molecules of pseudoephedrine hydrochloride in a 30 mg tablet.	?? = molecules

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STEP 3: Identify conversion factors. Since the molecular mass of pseudoephedrine hydrochloride is 201.70 amu, 201.70 g contains 6.022×10^{23} molecules. We can use this ratio as a conversion factor to convert from mass to molecules. We will also need to convert 30 mg to grams.

$$\frac{6.022 \times 10^{23} \text{ molecules}}{201.70 \text{ g}}$$

$$\frac{.001 \text{ g}}{1 \text{ mg}}$$

STEP 4: Solve. Set up an equation so that unwanted units cancel.

$$(30.0 \text{ mg pseudoephedrine hydrochloride}) \times \left(\frac{.001 \text{ g}}{1 \text{ mg}}\right) \times \left(\frac{6.022 \times 10^{23} \text{ molecules}}{201.70 \text{ g}}\right)$$

$$= 8.96 \times 10^{19} \text{ molecules of pseudoephedrine hydrochloride}$$

BALLPARK CHECK Our estimate for the number of molecules was on the order of 10^{19}, which is consistent with the calculated answer.

Worked Example 6.2 Avogadro's Number: Atom to Mass Conversions

A tiny pencil mark just visible to the naked eye contains about 3×10^{17} atoms of carbon. What is the mass of this pencil mark in grams?

ANALYSIS We are given a number of atoms and need to convert to mass. The conversion factor can be obtained by realizing that the atomic mass of carbon in grams contains Avogadro's number of atoms (6.022×10^{23}).

BALLPARK ESTIMATE Since we are given a number of atoms that is six orders of magnitude less than Avogadro's number, we should get a corresponding mass that is six orders of magnitude less than the molar mass of carbon, which means a mass for the pencil mark of about 10^{-6} g.

SOLUTION

STEP 1: Identify known information. We know the number of carbon atoms in the pencil mark.

3×10^{17} atoms of carbon

STEP 2: Identify answer and units.

Mass of carbon = ?? g

STEP 3: Identify conversion factors. The atomic mass of carbon is 12.01 amu, so 12.01 g of carbon contains 6.022×10^{23} atoms.

$$\frac{12.01 \text{ g carbon}}{6.022 \times 10^{23} \text{ atoms}}$$

STEP 4: Solve. Set up an equation using the conversion factors so that unwanted units cancel.

$$(3 \times 10^{17} \text{ atoms}) \left(\frac{12.01 \text{ g carbon}}{6.022 \times 10^{23} \text{ atoms}}\right) = 6 \times 10^{-6} \text{ g carbon}$$

BALLPARK CHECK The answer is of the same magnitude as our estimate and makes physical sense.

PROBLEM 6.1

Calculate the molecular mass of the following substances:

(a) Ibuprofen, $C_{13}H_{18}O_2$ (a drug used as for pain relief)

(b) Phenobarbital, $C_{12}H_{12}N_2O_3$ (a drug used as a sedative, hypnotic, and antiseizure medication)

PROBLEM 6.2

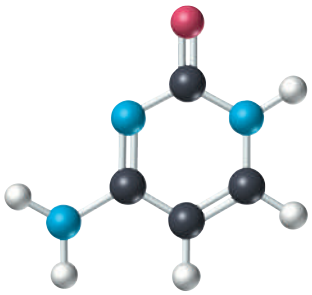
How many molecules of ascorbic acid (vitamin C, $C_6H_8O_6$) are in a 500 mg tablet? (Hint: First calculate molar mass, then use it as a conversion factor to convert mass to moles).

PROBLEM 6.3

What is the mass in grams of 5.0×10^{20} molecules of aspirin ($C_9H_8O_4$)? (Hint: Using Avogadro's number, convert the number of molecules to moles.)

KEY CONCEPT PROBLEM 6.4

What is the molecular mass of cytosine, a component of DNA (deoxyribonucleic acid)? (black = C, blue = N, red = O, white = H.)



Cytosine

6.2 Gram–Mole Conversions

Learning Objective:

- Convert between mass and moles using the molar mass of a substance.

To ensure that we have the correct molecule to molecule (or mole to mole) relationship between reactants as specified by the balanced chemical equation, we can take advantage of the constant mass ratio between reactants. The mass in grams of 1 mol of any substance (i.e., Avogadro's number of molecules or formula units) is called the molar mass of the substance.

$$\begin{aligned}\text{Molar mass} &= \text{Mass of 1 mol of substance}\\ &= \text{Mass of } 6.022 \times 10^{23} \text{ molecules (formula units) of substance}\\ &= \text{Molecular (formula) mass of substance in grams}\end{aligned}$$

In effect, molar mass serves as a conversion factor between numbers of moles and mass. If you know how many moles you have, you can calculate their mass; if you know the mass of a sample, you can calculate the number of moles. Suppose, for example, we need to know how much 0.25 mol of water weighs. The molecular mass of H_2O is $(2 \times 1.0 \text{ amu}) + 16.0 \text{ amu} = 18.0 \text{ amu}$, so the molar mass of water is 18.0 g/mol. Thus, the conversion factor between moles of water and mass of water is 18.0 g/mol.

Molar mass used as conversion factor

$$0.25 \text{ mol } H_2O \times \frac{18.0 \text{ g } H_2O}{1 \text{ mol } H_2O} = 4.5 \text{ g } H_2O$$

Alternatively, suppose we need to know how many moles of water are in 27 g of water. The conversion factor is 1 mol/18.0 g.

Molar mass used as conversion factor

$$27 \text{ g } H_2O \times \frac{1 \text{ mol } H_2O}{18.0 \text{ g } H_2O} = 1.5 \text{ mol } H_2O$$

Note that the 1 mol in the numerator is an exact number, so the number of significant figures in the final answer is based on the 27 g H_2O (2 significant figures). Worked Examples 6.3 and 6.4 give more practice in gram–mole conversions.

Worked Example 6.3 Molar Mass: Mole to Gram Conversion

The nonprescription pain relievers Advil and Nuprin contain ibuprofen ($C_{13}H_{18}O_2$), whose molecular mass is 206.3 amu (Problem 6.1a). If all the tablets in a bottle of pain reliever together contain 0.082 mol of ibuprofen, what is the number of grams of ibuprofen in the bottle?

ANALYSIS We are given a number of moles and asked to find the mass. Molar mass is the conversion factor between the two.

BALLPARK ESTIMATE Since 1 mol of ibuprofen has a mass of about 200 g, 0.08 mol has a mass of about $0.08 \times 200\ \text{g} = 16\ \text{g}$.

SOLUTION

STEP 1: Identify known information.

0.082 mol ibuprofen in bottle

STEP 2: Identify answer and units.

mass ibuprofen in bottle = ?? g

STEP 3: Identify conversion factor. We use the molecular mass of ibuprofen to convert from moles to grams.

1 mol ibuprofen = 206.3 g

$$\frac{206.3\ \text{g ibuprofen}}{1\ \text{mol ibuprofen}}$$

STEP 4: Solve. Set up an equation using the known information and conversion factor so that unwanted units cancel.

$$0.082\ \text{mol } C_{13}H_{18}O_2 \times \frac{206.3\ \text{g ibuprofen}}{1\ \text{mol ibuprofen}} = 17\ \text{g } C_{13}H_{18}O_2$$

BALLPARK CHECK The calculated answer is consistent with our estimate of 16 g.

Worked Example 6.4 Molar Mass: Gram to Mole Conversion

The maximum dose of sodium hydrogen phosphate (Na_2HPO_4, molecular mass = 142.0 amu) that should be taken in one day for use as a laxative is 3.8 g. How many moles of sodium hydrogen phosphate, how many moles of Na^+ ions, and how many total moles of ions are in this dose?

ANALYSIS Molar mass is the conversion factor between mass and number of moles. The chemical formula Na_2HPO_4 shows that each formula unit contains 2 Na^+ ions and 1 HPO_4^{2-} ion.

BALLPARK ESTIMATE The maximum dose is about two orders of magnitude smaller than the molecular mass (approximately 4 g compared to 142 g). Thus, the number of moles of sodium hydrogen phosphate in 3.8 g should be about two orders of magnitude less than 1 mole. The number of moles of Na_2HPO_4 and total moles of ions, then, should be on the order of 10^{-2}.

SOLUTION

STEP 1: Identify known information. We are given the mass and molecular mass of Na_2HPO_4.

3.8 g Na_2HPO_4; molecular mass = 142.0 amu

STEP 2: Identify answer and units. We need to find the number of moles of Na_2HPO_4 and the total number of moles of ions.

Moles of Na_2HPO = ?? mol
Moles of Na^+ ions = ?? mol
Total moles of ions = ?? mol

STEP 3: Identify conversion factor. We can use the molecular mass of Na_2HPO_4 to convert from grams to moles.

$$\frac{1\ \text{mol } Na_2HPO_4}{142.0\ \text{g } Na_2HPO_4}$$

STEP 4: Solve. We use the known information and conversion factor to obtain moles of Na_2HPO_4; since 1 mol of Na_2HPO_4 contains 2 mol of Na^+ ions and 1 mol of HPO_4^{2-} ions, we multiply these values by the number of moles in the sample.

$$3.8\ \text{g}\ \cancel{Na_2HPO_4} \times \frac{1\ \text{mol}\ Na_2HPO_4}{142.0\ \text{g}\ \cancel{Na_2HPO_4}} = 0.027\ \text{mol}\ Na_2HPO_4$$

$$\frac{2\ \text{mol}\ Na^+}{1\ \cancel{\text{mol}\ Na_2HPO_4}} \times 0.027\ \cancel{\text{mol}\ Na_2HPO_4} = 0.054\ \text{mol}\ Na^+$$

$$\frac{3\ \text{mol ions}}{1\ \cancel{\text{mol}\ Na_2HPO_4}} \times 0.027\ \cancel{\text{mol}\ Na_2HPO_4} = 0.081\ \text{mol ions}$$

BALLPARK CHECK The calculated answers (0.027 mol Na_2HPO_4, 0.081 mol ions) are on the order of 10^{-2}, consistent with our estimate.

PROBLEM 6.5

How many moles of ethanol, C_2H_6O, are in a 10.0 g sample? How many grams are in a 0.10 mol sample of ethanol?

PROBLEM 6.6

Which weighs more, 5.00 g or 0.0225 mol of acetaminophen ($C_8H_9NO_2$)?

PROBLEM 6.7

A small kidney stone (Chemistry in Action on p. 176) might contain 0.50 g of uric acid ($C_5H_4N_4O_3$). How many micromoles of uric acid are contained in this stone?

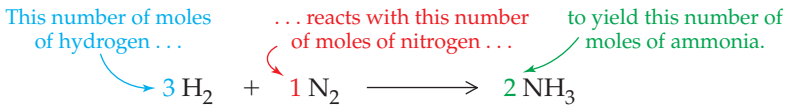
6.3 Mole Relationships and Chemical Equations

Learning Objective:

- Determine molar ratios of reactants and products using balanced chemical equations.

In a typical recipe, the amounts of ingredients needed are specified using a variety of units: The amount of flour, for example, is usually specified in cups, whereas the amount of salt or vanilla flavoring might be indicated in teaspoons. In chemical reactions, the appropriate unit to specify the relationship between reactants and products is the mole.

The coefficients in a balanced chemical equation tell how many *molecules,* and thus how many *moles,* of each reactant are needed and how many molecules, and thus, moles, of each product are formed. You can then use molar mass to calculate reactant and product masses. If, for example, you saw the following balanced equation for the industrial synthesis of ammonia, you would know that 3 mol of H_2 ($3\ \text{mol} \times 2.0\ \text{g/mol} = 6.0\ \text{g}$) are required for reaction with 1 mol of N_2 (28.0 g) to yield 2 mol of NH_3 ($2\ \text{mol} \times 17.0\ \text{g/mol} = 34.0\ \text{g}$).



The coefficients can be put in the form of *mole ratios,* which act as conversion factors when setting up factor-label calculations. In the ammonia synthesis, for example, the mole ratio of H_2 to N_2 is 3:1, the mole ratio of H_2 to NH_3 is 3:2, and the mole ratio of N_2 to NH_3 is 1:2.

$$\frac{3\ \text{mol}\ H_2}{1\ \text{mol}\ N_2} \quad \frac{3\ \text{mol}\ H_2}{2\ \text{mol}\ NH_3} \quad \frac{1\ \text{mol}\ N_2}{2\ \text{mol}\ NH_3}$$

Worked Example 6.5 shows how to set up and use mole ratios.

Worked Example 6.5 Balanced Chemical Equations: Mole Ratios

Rusting involves the reaction of iron with oxygen to form iron(III) oxide, Fe_2O_3:

$$4\,Fe(s) + 3\,O_2(g) \longrightarrow 2\,Fe_2O_3(s)$$

(a) What are the mole ratios of the product to each reactant and of the reactants to each other?
(b) How many moles of iron(III) oxide are formed by the complete oxidation of 6.2 mol of iron?

ANALYSIS AND SOLUTION

(a) The coefficients of a balanced equation represent the mole ratios.

$$\frac{2\text{ mol } Fe_2O_3}{4\text{ mol Fe}} \quad \frac{2\text{ mol } Fe_2O_3}{3\text{ mol } O_2} \quad \frac{4\text{ mol Fe}}{3\text{ mol } O_2}$$

(b) To find how many moles of Fe_2O_3 are formed, write down the known information—6.2 mol of iron—and select the mole ratio that allows the quantities to cancel, leaving the desired quantity.

$$6.2\ \cancel{\text{mol Fe}} \times \frac{2\text{ mol } Fe_2O_3}{4\ \cancel{\text{mol Fe}}} = 3.1\text{ mol } Fe_2O_3$$

Note that mole ratios are exact numbers and therefore do not limit the number of significant figures in the result of a calculation.

PROBLEM 6.8

(a) Balance the following equation, and tell how many moles of nickel will react with 9.81 mol of hydrochloric acid.

$$Ni(s) + HCl(aq) \longrightarrow NiCl_2(aq) + H_2(g)$$

(b) How many moles of $NiCl_2$ can be formed in the reaction of 6.00 mol of Ni and 12.0 mol of HCl?

PROBLEM 6.9

Plants convert carbon dioxide and water to glucose $(C_6H_{12}O_6)$ and oxygen in the process of photosynthesis. Write a balanced equation for this reaction, and determine how many moles of CO_2 are required to produce 15.0 mol of glucose.

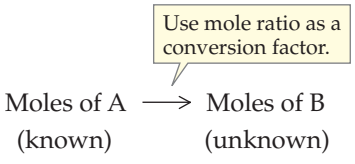
6.4 Mass Relationships and Chemical Equations

Learning Objective:

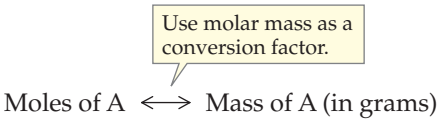
- Using mole ratios, calculate the mass of product that can be formed from a given mass of reactant.

It is important to remember that the coefficients in a balanced chemical equation represent molecule to molecule (or mole to mole) relationships between reactants and products. Mole ratios make it possible to calculate the molar amounts of reactants and products, but actual amounts of substances used in the laboratory are weighed out in grams. Regardless of what units we use to specify the amount of reactants and/or products (mass, volume, number of molecules, and so on), the reaction always takes place on a mole to mole basis. Thus, we need to be able to carry out three kinds of conversions when doing chemical arithmetic.

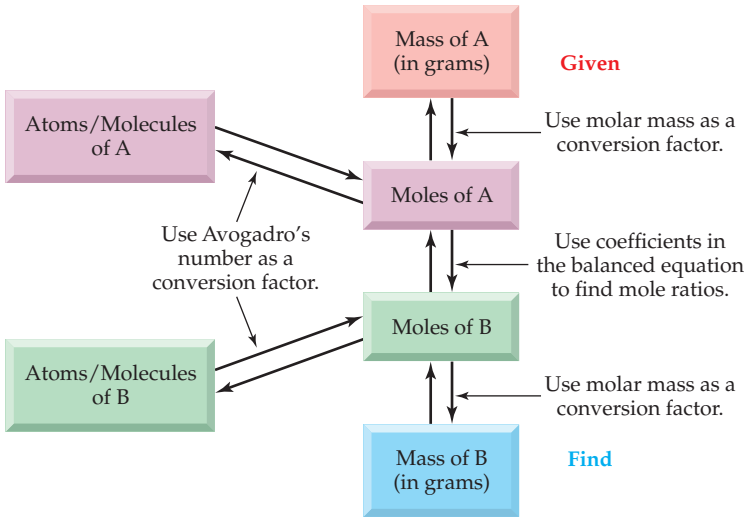
- **Mole to mole conversions** are carried out using *mole ratios* as conversion factors. Worked Example 6.5 at the end of the preceding section is an example of this kind of calculation.



- **Mole to mass and mass to mole conversions** are carried out using *molar mass* as a conversion factor. Worked Examples 6.3 and 6.4 at the end of Section 6.2 are examples of this kind of calculation.



- **Mass to mass conversions** are frequently needed but cannot be carried out directly. If you know the mass of substance A and need to find the mass of substance B, you must first convert the mass of A into moles of A, then carry out a mole to mole conversion to find moles of B, and then convert moles of B into the mass of B (Figure 6.2).



◂ Figure 6.2
A summary of conversions between moles, grams, and number of atoms or molecules for substances in a chemical reaction.
The numbers of moles tell how many molecules of each substance are needed, as given by the coefficients in the balanced equation; the numbers of grams tell what mass of each substance is needed.

Overall, there are four steps for determining mass relationships among reactants and products.

STEP 1: Write the balanced chemical equation.

STEP 2: Choose molar masses and mole ratios to convert the known information into the needed information.

STEP 3: Set up the factor-label expressions.

STEP 4: Calculate the answer and check the answer against the ballpark estimate you made before you began your calculations.

Worked Example 6.6 Mole Ratios: Mole to Mass Conversions

In the atmosphere, nitrogen dioxide reacts with water to produce NO and nitric acid, which contributes to pollution by acid rain.

$$3\,NO_2(g) + H_2O(l) \longrightarrow 2\,HNO_3(aq) + NO(g)$$

How many grams of HNO_3 are produced for every 1.0 mol of NO_2 that reacts? The molecular mass of HNO_3 is 63.0 amu.

ANALYSIS We are given the number of moles of a reactant and are asked to find the mass of a product. Problems of this sort always require working in moles and then converting to mass, as outlined in Figure 6.2.

BALLPARK ESTIMATE The molar mass of nitric acid is approximately 60 g/mol, and the coefficients in the balanced equation say that 2 mol of HNO_3 are formed for each 3 mol of NO_2 that undergo reaction. Thus, 1 mol of NO_2 should give about 2/3 mol HNO_3, or 2/3 mol $\times$ 60 g/mol $=$ 40 g.

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SOLUTION

STEP 1: Write balanced equation.

$$3\,NO_2(g) + H_2O(l) \longrightarrow 2\,HNO_3(aq) + NO(g)$$

STEP 2: Identify conversion factors. We need a mole to mole conversion to find the number of moles of product, and then a mole to mass conversion to find the mass of product. For the first conversion, we use the mole ratio of HNO_3 to NO_2 as a conversion factor, and for the mole to mass calculation, we use the molar mass of HNO_3 (63.0 g/mol) as a conversion factor.

$$\frac{2\text{ mol }HNO_3}{3\text{ mol }NO_2}$$

$$\frac{63.0\text{ g }HNO_3}{1\text{ mol }HNO_3}$$

STEP 3: Set up factor labels. Identify appropriate mole ratio factor labels to convert moles NO_2 to moles HNO_3 and moles HNO_3 to grams.

$$1.0\text{ mol }NO_2 \times \frac{2\text{ mol }HNO_3}{3\text{ mol }NO_2} \times \frac{63.0\text{ g }HNO_3}{1\text{ mol }HNO_3}$$

STEP 4: Solve.

$$= 42\text{ g }HNO_3$$

BALLPARK CHECK Our estimate was 40 g!

Worked Example 6.7 Mole Ratios: Mass to Mole/Mole to Mass Conversions

The following reaction produced 0.022 g of calcium oxalate (CaC_2O_4). What mass of calcium chloride was used as reactant? (The molar mass of CaC_2O_4 is 128.1 g/mol, and the molar mass of $CaCl_2$ is 111.0 g/mol.)

$$CaCl_2(aq) + Na_2C_2O_4(aq) \longrightarrow CaC_2O_4(s) + 2\,NaCl(aq)$$

ANALYSIS Both the known information and that to be found are masses, so this is a mass to mass conversion problem. The mass of CaC_2O_4 is first converted into moles, a mole ratio is used to find moles of $CaCl_2$, and the number of moles of $CaCl_2$ is converted into mass.

BALLPARK ESTIMATE The balanced equation says that 1 mol of CaC_2O_4 is formed for each mole of $CaCl_2$ that reacts. Because the formula masses of the two substances are similar, it should take about 0.02 g of $CaCl_2$ to form 0.02 g of CaC_2O_4.

SOLUTION

STEP 1: Write the balanced equation.

$$CaCl_2(aq) + Na_2C_2O_4(aq) \longrightarrow CaC_2O_4(s) + 2\,NaCl(aq)$$

STEP 2: Identify conversion factors. Convert the mass of CaC_2O_4 into moles, use a mole ratio to find moles of $CaCl_2$, and convert the number of moles of $CaCl_2$ to mass. We will need three conversion factors.

$$\text{mass } CaC_2O_4 \text{ to moles: } \frac{1\text{ mol }CaC_2O_4}{128.1\text{ g}}$$

$$\text{moles } CaC_2O_4 \text{ to moles } CaCl_2\text{: } \frac{1\text{ mol }CaCl_2}{1\text{ mol }CaC_2O_4}$$

$$\text{moles } CaCl_2 \text{ to mass: } \frac{111.0\text{ g }CaCl_2}{1\text{ mol }CaCl_2}$$

STEP 3: Set up factor-labels. We will need to perform gram to mole and mole to mole conversions to get from grams CaC_2O_4 to grams $CaCl_2$.

$$0.022\text{ g }CaC_2O_4 \times \frac{1\text{ mol }CaC_2O_4}{128.1\text{ g }CaC_2O_4} \times \frac{1\text{ mol }CaCl_2}{1\text{ mol }CaCl_2O_4} \times \frac{111.0\text{ g }CaCl_2}{1\text{ mol }CaCl_2}$$

STEP 4: Solve.

$$= 0.019\text{ g }CaCl_2$$

BALLPARK CHECK The calculated answer (0.019 g) is consistent with our estimate (0.02 g).

PROBLEM 6.10

Hydrogen fluoride is one of the few substances that react with glass (which is made of silicon dioxide, SiO_2).

$$4\,HF(g) + SiO_2(s) \longrightarrow SiF_4(g) + 2\,H_2O(l)$$

(a) How many moles of HF will react completely with 9.90 mol of SiO_2?
(b) What mass of water (in grams) is produced by the reaction of 23.0 g of SiO_2?

PROBLEM 6.11

The tungsten metal used for filaments in light bulbs is made by reaction of tungsten(VI) oxide with hydrogen:

$$WO_3(s) + 3\,H_2(g) \longrightarrow W(s) + 3\,H_2O(g)$$

The above reaction was performed and produced 5.00 g of tungsten.
(a) How many moles of tungsten were formed?
(b) How many moles of tungsten(VI) oxide and hydrogen were required to produce the 5.00 g of tungsten?
(c) How many grams of tungsten(VI) oxide, and how many grams of hydrogen must you start with to prepare 5.00 g of tungsten? (For WO_3, molecular mass = 231.8 amu.)

6.5 Limiting Reagent and Percent Yield

Learning Objective:

- Using mole ratios and the mass of reactants, calculate the theoretical yield and percent yield for a reaction.

All the calculations we have done in the past several sections have assumed that 100% of the reactants are converted to products. Only rarely is this the case in practice, though. Let us return to the recipe for s'mores presented in the previous chapter:

$$2\ \text{Graham crackers} + 1\ \text{Roasted marshmallow} + \tfrac{1}{4}\ \text{Chocolate bar} \longrightarrow 1\ \text{S'more}$$

When you check your supplies, you find that you have 20 graham crackers, 8 marshmallows, and 3 chocolate bars. How many s'mores can you make? (Answer = 8!) You have enough graham crackers and chocolate bars to make more, but you will run out of marshmallows after you have made eight s'mores. In a similar way, when running a chemical reaction we do not always have the exact amounts of reagents to allow all of them to react completely. As a real example, consider a typical combustion reaction—such as a burning candle made of paraffin wax:

$$C_{31}H_{64}(s) + 47\,O_2(g) \longrightarrow 31\,CO_2(g) + 32\,H_2O(g) + \text{heat}$$

As long as there is a ready supply of oxygen and wax, the reaction will continue (i.e., the candle will continue to burn). However, if we cover the candle with a jar to limit the amount of oxygen, the candle will burn until all the available O_2 is consumed, and then the reaction would stop and the candle would go out. The reactant that is exhausted first in such a reaction (oxygen, in the case of the candle) is called the **limiting reagent.** The amount of product you obtain if the limiting reagent is completely consumed is called the **theoretical yield** of the reaction.

Limiting reagent The reactant that runs out first in any given reaction.

Theoretical yield The amount of product formed, assuming complete reaction of the limiting reagent.

One way to identify the limiting reagent is to compare the mole ratio of reactants in the balanced chemical equation with the actual amounts of reactants available. Consider again the reaction of nitrogen with hydrogen to form ammonia.

$$N_2(g) + 3\,H_2(g) \longrightarrow 2\,NH_3(g)$$

Based on the balanced chemical equation, we know that the mole ratio of H_2 to N_2 is 3:1, or

$$\frac{3\ \text{moles}\ H_2}{1\ \text{mole}\ N_2} = 3.0$$

Now, suppose you have 14.3 moles of H_2 and 4.5 moles of N_2; this ratio is $(14.3/4.5 = 3.18)$. The mole ratio is greater than the 3.0 from the balanced chemical equation, which implies that you have more H_2 than you need, or not enough N_2. So, nitrogen is the limiting reagent. Alternatively, you could use mole ratios to determine how much product (ammonia) could be formed by complete reaction of each reactant.

$$14.3 \text{ moles } H_2 \times \frac{2 \text{ moles } NH_3}{3 \text{ moles } H_2} = 9.53 \text{ moles } NH_3$$

$$4.5 \text{ moles } N_2 \times \frac{2 \text{ moles } NH_3}{1 \text{ mole } N_2} = 9.0 \text{ moles } NH_3*$$

Once all the available N_2 has reacted, only 9.0 mol of NH_3 has been produced and the reaction stops. Nitrogen is identified as the limiting reagent (*) because it "limits" the amount of product that can be formed.

Suppose that, while you are making s'mores, one of your eight marshmallows gets burned to a crisp. If this happens, the actual number of s'mores produced will be less than what you predicted based on the amount of starting materials. Similarly, chemical reactions do not always yield the exact amount of product predicted by the initial amount of reactants. More frequently, a majority of the reactant molecules behave as written, but other processes, called *side reactions,* also occur. For example, limiting the amount of O_2 in a combustion reaction may result in side reactions to produce carbon monoxide (CO) instead of carbon dioxide (CO_2). In addition, some of the product may be lost in handling. As a result, the amount of product actually obtained—the reaction's **actual yield**—is somewhat less than the theoretical yield. The amount of product actually obtained in a reaction is usually expressed as a **percent yield.**

Actual yield The amount of product actually formed in a reaction.

Percent yield The percentage of the theoretical yield actually obtained from a chemical reaction.

$$\text{Percent yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100$$

A reaction's actual yield is found by weighing the amount of product obtained. The theoretical yield is found by using the amount of limiting reagent in a mass to mass calculation like those illustrated in the preceding section (see Worked Example 6.7). Worked Examples 6.8–6.10 involve limiting reagent, percent yield, actual yield, and theoretical yield calculations.

Worked Example 6.8 Percent Yield

The combustion of ethyne gas (C_2H_2) produces carbon dioxide and water, as indicated in the following reaction:

$$2\,C_2H_2(g) + 5\,O_2(g) \longrightarrow 4\,CO_2(g) + 2\,H_2O(g)$$

When 26.0 g of ethyne is burned in sufficient oxygen for complete reaction, the theoretical yield of CO_2 is 88.0 g. Calculate the percent yield for this reaction if the actual yield is only 72.4 g CO_2.

ANALYSIS The percent yield is calculated by dividing the actual yield by the theoretical yield and multiplying by 100.

BALLPARK ESTIMATE The theoretical yield (88.0 g) is close to 100 g. The actual yield (72.4 g) is about 15 g less than the theoretical yield. The actual yield is thus about 15% less than the theoretical yield, so the percent yield is about 85%.

SOLUTION

$$\text{Percent yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100 = \frac{72.4 \text{ g } CO_2}{88.0 \text{ g } CO_2} \times 100 = 82.3$$

BALLPARK CHECK The calculated percent yield agrees very well with our estimate of 85%.

Worked Example 6.9 Mass to Mole Conversions: Limiting Reagent and Theoretical Yield

The element boron is produced commercially by the reaction of boric oxide with magnesium at high temperature.

$$B_2O_3(l) + 3\,Mg(s) \longrightarrow 2\,B(s) + 3\,MgO(s)$$

What is the theoretical yield of boron when 2350 g of boric oxide is reacted with 3580 g of magnesium? The molar masses of boric oxide and magnesium are 69.6 g/mol and 24.3 g/mol, respectively.

ANALYSIS To calculate theoretical yield, we first have to identify the limiting reagent. The theoretical yield in grams is then calculated from the amount of limiting reagent used in the reaction. The calculation involves the mass to mole and mole to mass conversions discussed in the preceding section.

SOLUTION

STEP 1: Identify known information. We have the masses and molar masses of the reagents.

2350 g B_2O_3, molar mass 69.6 g/mol
3580 g Mg, molar mass 24.3 g/mol

STEP 2: Identify answer and units. We are solving for the theoretical yield of boron.

Theoretical mass of B = ?? g

STEP 3: Identify conversion factors. We can use the molar masses to convert from masses to moles of reactants (B_2O_3, Mg). From moles of reactants, we can use mole ratios from the balanced chemical equation to find the number of moles of B produced, assuming complete conversion of a given reactant. B_2O_3 is the limiting reagent, since complete conversion of this reagent yields less product (67.6 mol B formed) than does complete conversion of Mg (98.0 mol B formed).

$$(2350\ \text{g}\ \cancel{B_2O_3}) \times \frac{1\ \text{mol}\ B_2O_3}{69.6\ \text{g}\ \cancel{B_2O_3}} = 33.8\ \text{mol}\ B_2O_3$$

$$(3580\ \text{g}\ \cancel{Mg}) \times \frac{1\ \text{mol Mg}}{24.3\ \text{g}\ \cancel{Mg}} = 147\ \text{mol Mg}$$

$$33.8\ \cancel{\text{mol}\ B_2O_3} \times \frac{2\ \text{mol B}}{1\ \cancel{\text{mol}\ B_2O_3}} = 67.6\ \text{mol B}^*$$

$$147\ \cancel{\text{mol Mg}} \times \frac{2\ \text{mol B}}{3\ \cancel{\text{mol Mg}}} = 98.0\ \text{mol B}$$

(*B_2O_3 is the limiting reagent because it yields fewer moles of B!)

STEP 4: Solve. Once the limiting reagent has been identified (B_2O_3), the theoretical amount of B that should be formed can be calculated using a mole to mass conversion.

$$67.6\ \cancel{\text{mol B}} \times \frac{10.8\ \text{g B}}{1\ \cancel{\text{mol B}}} = 730\ \text{g B}$$

Worked Example 6.10 Mass to Mole Conversion: Percent Yield

The reaction of ethene with water to give ethanol (CH_3CH_2OH) occurs with 78.5% actual yield. How many grams of ethanol are formed by reaction of 25.0 g of ethene? (For ethene, molecular mass = 28.0 amu; for ethanol, molecular mass = 46.0 amu.)

$$H_2C{=}CH_2 + H_2O \longrightarrow CH_3CH_2OH$$

ANALYSIS Treat this as a typical mass relationship problem to find the amount of ethanol that can theoretically be formed from 25.0 g of ethene, and then multiply the answer by 0.785 (the fraction of the theoretical yield actually obtained) to find the amount actually formed.

BALLPARK ESTIMATE The 25.0 g of ethene is a bit less than 1 mol; since the percent yield is about 78%, a bit less than 0.78 mol of ethanol will form—perhaps about 3/4 mol, or 3/4 × 46 g = 34 g.

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SOLUTION

The theoretical yield of ethanol is as follows:

$$25.0 \text{ g ethene} \times \frac{1 \text{ mol ethene}}{28.0 \text{ g ethene}} \times \frac{1 \text{ mol ethanol}}{1 \text{ mol ethene}} \times \frac{46.0 \text{ g ethanol}}{1 \text{ mol ethanol}}$$

$$= 41.1 \text{ g ethanol}$$

and so the actual yield is as follows:

$$41.1 \text{ g ethanol} \times 0.785 = 32.3 \text{ g ethanol}$$

BALLPARK CHECK The calculated result (32.3 g) is close to our estimate (34 g).

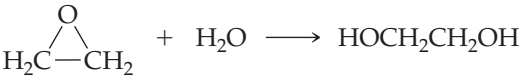
PROBLEM 6.12

What is the theoretical yield of chloroethane in the reaction of 19.4 g of ethene with 50 g of hydrogen chloride? What is the percent yield if 25.5 g of chloroethane is actually formed? (For ethene, molecular mass = 28.0 amu; for hydrogen chloride, molecular mass = 36.5 amu; for chloroethane, molecular mass = 64.5 amu.)

$$H_2C{=}CH_2 + HCl \longrightarrow CH_3CH_2Cl$$

PROBLEM 6.13

The reaction of epoxyethane with water to give ethane-1,2-diol (automobile antifreeze) occurs in 96.0% actual yield. How many grams of ethane-1,2-diol are formed by reaction of 35.0 g of epoxyethane? (For epoxyethane, molecular mass = 44.0 amu; for ethane-1,2-diol, molecular mass = 62.0 amu.)

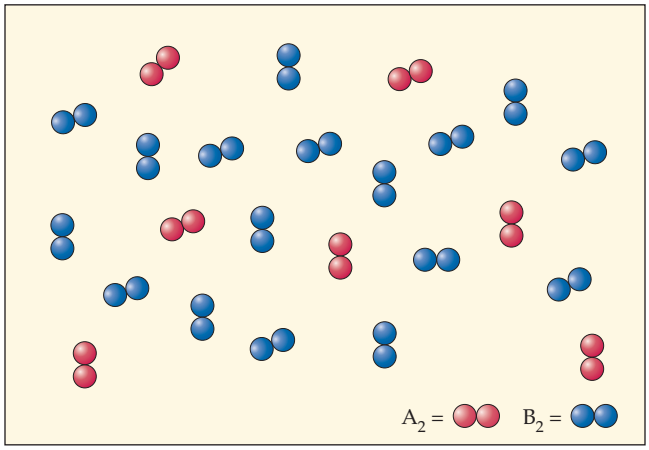


Epoxyethane Ethane-1,2-diol

KEY CONCEPT PROBLEM 6.14

Identify the limiting reagent in the reaction mixture shown next. The balanced reaction is as follows:

$$A_2 + 2\,B_2 \longrightarrow 2\,AB_2$$



HANDS-ON CHEMISTRY 6.1

This activity illustrates the concepts of mole ratios and limiting reagents, and the product is a tasty snack. Assemble the following items: a packet of crackers, a jar of peanut butter, and a banana (or a chocolate bar that can be divided into sections). If the packet of crackers is small (less than 10), you can use the entire package; if you are using a box of crackers, remove a handful (but don't count them!) and place them in a pile. Then, peel the banana and cut it into slices and place them in a bowl; if you use a chocolate bar, divide it into sections. Finally, get a spoon, a plate, and the jar of peanut butter.

a. Assemble all the ingredients, and count how many crackers and banana slices (or chocolate sections) you have—we will assume that the jar of peanut butter represents a sufficient amount for complete reaction. Now, make your "product" based on the following recipe (reaction):

2 Crackers + 1 Scoop of peanut butter + 1 Slice of banana (or section of chocolate) ⟶ 1 Treat!

Scoop a small spoonful of peanut butter onto one of the crackers, add a banana slice or a piece of chocolate, and place the second cracker on top. Put the finished product on the plate. Continue making product until one of the ingredients/reagents runs out. Which ran out first? How many treats did you make?

b. Now, from the number of each ingredient and the "mole ratios" from the recipe, calculate the theoretical yield you would expect from complete reaction of each ingredient (crackers/banana slices/chocolate sections). How do your calculated yields compare to your actual yield?

CHEMISTRY IN ACTION

Anemia—A Limiting Reagent Problem?

Anemia, which we first introduced in the opening of this chapter, is the most commonly diagnosed blood disorder, with symptoms typically including lethargy, fatigue, poor concentration, and sensitivity to cold. Although anemia has many causes, including genetic factors, the most common cause is insufficient dietary intake or absorption of iron.

Hemoglobin (abbreviated Hb), the iron-containing protein found in red blood cells, is responsible for oxygen transport throughout the body. Low iron levels in the body result in decreased production and incorporation of Hb into red blood cells. In addition, blood loss due to injury or to menstruation in women increases the body's demand for iron in order to replace lost Hb. In the United States, nearly 20% of women of child-bearing age suffer from iron-deficiency anemia compared to only 2% of adult men.

The recommended minimum daily iron intake is 8 mg for adult men and 18 mg for premenopausal women. One way to ensure sufficient iron intake is a well-balanced diet that includes iron-fortified grains and cereals, red meat, egg yolks, leafy green vegetables, tomatoes, and raisins. Vegetarians should pay extra attention to their diet, because the iron in fruits and vegetables is not as readily absorbed by the body as the iron in meat, poultry, and fish. Vitamin supplements containing folic acid and either ferrous sulfate or ferrous gluconate can decrease iron deficiencies, and vitamin C increases the absorption of iron by the body.

However, the simplest way to increase dietary iron may be to use cast iron cookware. Studies have demonstrated that the iron content of many foods increases when cooked in an iron pot. Other studies involving Ethiopian children showed that those who ate food cooked in iron cookware were less likely to suffer from iron-deficiency anemia than their playmates who ate similar foods prepared in aluminum cookware.

▲ Can cooking in cast iron pans decrease anemia?

CIA Problem 6.1 Dietary iron forms a 1:1 complex with hemoglobin (Hb), which is responsible for O_2 transport in the body based on the following equation:

$$Hb + 4\,O_2 \longrightarrow Hb(O_2)_4$$

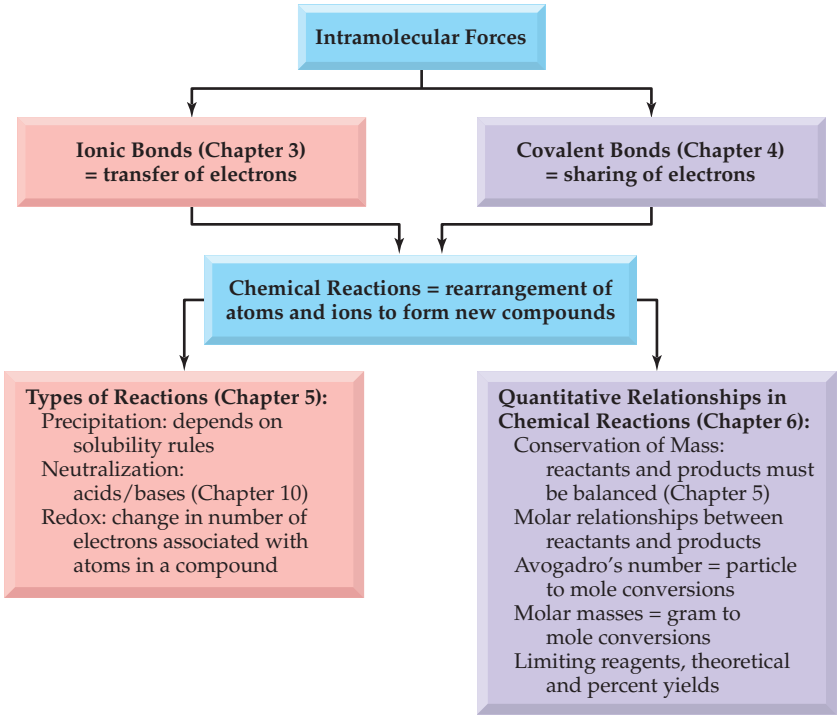
How many moles of oxygen could be transported by the hemoglobin complex formed from 8 mg of dietary iron?

CIA Problem 6.2 Ferrous sulfate is one dietary supplement used to treat iron-deficiency anemia. What are the molecular formula and molecular mass of this compound? How many milligrams of iron are in 250 mg of ferrous sulfate?

CIA Problem 6.3 The recommended daily intake of iron is 8 mg for adult men and 18 mg for premenopausal women. Convert these masses of iron into moles.

LOOKING AHEAD We'll explore the role of hemoglobin in oxygen transport in greater detail in Chapter 9.

CONCEPT MAP: CHEMICAL REACTIONS (CHAPTERS 5 AND 6)



▲ **Figure 6.3 Concept Map.** As shown in this concept map, chemical reactions represent a rearrangement of the bonding forces within compounds as bonds in the reactants are broken and new bonds are formed to generate products. The quantitative relationships between reactants and products can be represented in terms of molar quantities or as masses, and these relationships can be used to determine limiting reagents and theoretical yields.

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

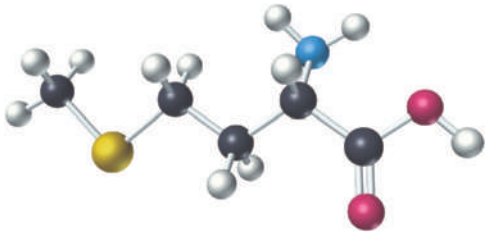
- **Define the mole, and calculate molar mass of a compound from the molecular formula.** A *mole* refers to *Avogadro's number* (6.022×10^{23}) of formula units of a substance. One mole of any substance has a mass (*molar mass*) equal to the molecular or formula mass of the substance in grams *(see Problems 15, 20–34, 26–28, 31, 32, 35,55, and 71–74).*
- **Convert between mass and moles using the molar mass of a substance.** Because equal numbers of moles contain equal numbers of formula units, molar masses act as conversion factors between numbers of moles and masses in grams *(see Problems 19, 24, 25, 29, 30, 33–35, 44, 46–48, 56–60, 62, and 68–74).*
- **Determine molar ratios of reactants and products using balanced chemical equations.** The coefficients in a balanced chemical equation represent the numbers of moles of reactants and products in a reaction. Thus, the ratios of coefficients act as *mole ratios* that relate amounts of reactants and/or products *(see Problems 16, 36–41, 43, 45–54, 56, 58–62, 66, 68–70, and 73).*
- **Using mole ratios, calculate the mass of product that can be formed from a given mass of reactant.** By using molar masses and mole ratios in factor-label calculations, unknown masses or molar amounts can be found from known masses or molar amounts *(see Problems 37–39, 41–54, 56, 57, 60, 61, 63–66, and 68).*
- **Using mole ratios and the mass of reactants, calculate the theoretical yield and percent yield for a reaction.** The *limiting reagent* is the reactant that runs out first. The *theoretical yield* is the calculated amount of product that would be formed based on the amount of the limiting reagent. The *actual yield* of a reaction is the amount of product obtained experimentally. The *percent yield* is the amount of product obtained divided by the amount theoretically possible and multiplied by 100% *(see Problems 17, 18, 49–54, and 64–67).*

KEY WORDS

Actual yield, *p. 208*
Avogadro's number (N_A), *p. 198*
Formula mass, *p. 197*
Limiting reagent, *p. 207*
Molar mass, *p. 198*
Mole, *p. 198*
Molecular mass, *p. 197*
Percent yield, *p. 208*
Theoretical yield, *p. 207*

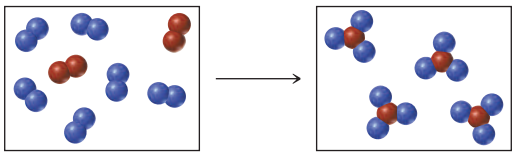
UNDERSTANDING KEY CONCEPTS

6.15 Methionine, an amino acid used by organisms to make proteins, can be represented by the following ball-and-stick molecular model. Write the formula for methionine, and give its molecular mass (red = O, black = C, blue = N, yellow = S, white = H).



Methionine

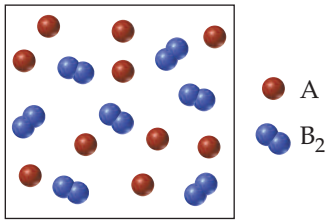
6.16 The following diagram represents the reaction of A_2 (red spheres) with B_2 (blue spheres):



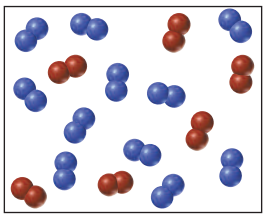
(a) Write a balanced equation for the reaction.

(b) How many moles of product can be made from 1.0 mol of A_2? From 1.0 mol of B_2?

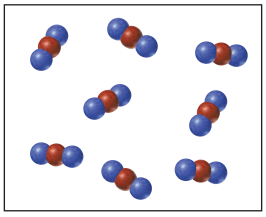
6.17 Consider the balanced chemical equation: $2A + B_2 \longrightarrow 2AB$. Given the following reaction vessel, determine the theoretical yield of product.



6.18 Consider the balanced chemical equation: $A_2 + 2\,B_2 \longrightarrow 2\,AB_2$. A reaction is performed with the initial amounts of A_2 and B_2 shown in part (a). The amount of product obtained is shown in part (b). Calculate the percent yield.

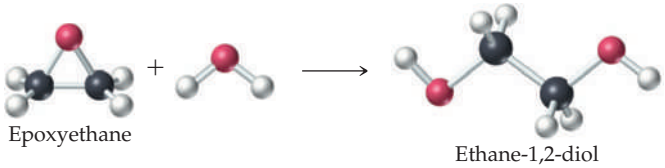


(a)



(b)

6.19 The following drawing represents the reaction of epoxyethane with water to give ethane-1,2-diol, a compound used as automobile antifreeze. What mass in grams of epoxyethane is needed to react with 9.0 g of water, and what mass in grams of ethane-1,2-diol is formed?



Epoxyethane Ethane-1,2-diol

ADDITIONAL PROBLEMS

MOLAR MASSES AND MOLES (SECTIONS 6.1 AND 6.2)

6.20 What is a mole of a substance? How many molecules are in 1 mol of a molecular compound?

6.21 What is the difference between molecular mass and formula mass? Between molecular mass and molar mass?

6.22 How many Na^+ ions are in a mole of Na_2SO_4? How many SO_4^{2-} ions?

6.23 How many moles of ions are in 1.75 mol of K_2SO_4?

6.24 How many calcium atoms are in 16.2 g of calcium?

6.25 What is the mass in grams of 2.68×10^{22} atoms of uranium?

6.26 Calculate the molar mass of each of the following compounds:

(a) Calcium carbonate, $CaCO_3$

(b) Urea, $CO(NH_2)_2$

(c) Ethane-1,2-diol, $C_2H_6O_2$

6.27 How many moles of carbon atoms are there in 1 mol of each compound in Problem 6.26?

6.28 How many atoms of carbon and how many grams of carbon are there in 1 mol of each compound in Problem 6.26?

6.29 Caffeine has the formula $C_8H_{10}N_4O_2$. If an average cup of coffee contains approximately 125 mg of caffeine, how many moles of caffeine are in one cup?

6.30 How many moles of aspirin, $C_9H_8O_4$, are in a 500 mg tablet?

6.31 What is the molar mass of diazepam (Valium), $C_{16}H_{13}ClN_2O$?

6.32 Calculate the molar masses of the following substances:

(a) Aluminum sulfate, $Al_2(SO_4)_3$

(b) Sodium hydrogen carbonate, $NaHCO_3$

(c) Diethyl ether, $(C_2H_5)_2O$

(d) Penicillin V, $C_{16}H_{18}N_2O_5S$

6.33 How many moles are present in a 4.50 g sample of each compound listed in Problem 6.32?

6.34 How many grams are present in a 0.075 mol sample of each compound listed in Problem 6.32?

6.35 The principal component of many kidney stones is calcium oxalate, CaC_2O_4. A kidney stone recovered from a typical patient contains 8.5×10^{20} formula units of calcium oxalate. How many moles of CaC_2O_4 are present in this kidney stone? What is the mass of the kidney stone in grams?

MOLE AND MASS RELATIONSHIPS FROM CHEMICAL EQUATIONS (SECTIONS 6.2–6.4)

6.36 At elevated temperatures in an automobile engine, N_2 and O_2 can react to yield NO, an important cause of air pollution.

(a) Write a balanced equation for the reaction.

(b) How many moles of N_2 are needed to react with 7.50 mol of O_2?

(c) How many moles of NO can be formed when 3.81 mol of N_2 reacts?

(d) How many moles of O_2 must react to produce 0.250 mol of NO?

6.37 Ethyl acetate reacts with H_2 in the presence of a catalyst to yield ethanol.

$$C_4H_8O_2(l) + H_2(g) \longrightarrow C_2H_6O(l)$$

(a) Write a balanced equation for the reaction.

(b) How many moles of ethanol are produced by reaction of 1.5 mol of ethyl acetate?

(c) How many grams of ethanol are produced by reaction of 1.5 mol of ethyl acetate with H_2?

(d) How many grams of ethanol are produced by reaction of 12.0 g of ethyl acetate with H_2?

(e) How many grams of H_2 are needed to react with 12.0 g of ethyl acetate?

6.38 The active ingredient in milk of magnesia (an antacid) is magnesium hydroxide, $Mg(OH)_2$. A typical dose (one tablespoon) contains 1.2 g of $Mg(OH)_2$. Calculate (a) the molar mass of magnesium hydroxide and (b) the amount of magnesium hydroxide (in moles) in one tablespoon.

6.39 Ammonia, NH_3, is prepared for use as a fertilizer by reacting N_2 with H_2.

(a) Write a balanced equation for the reaction.

(b) How many moles of N_2 are needed for reaction to make 16.0 g of NH_3?

(c) How many grams of H_2 are needed to react with 75.0 g of N_2?

6.40 Hydrazine, N_2H_4, a substance used as rocket fuel, reacts with oxygen as follows:

$$N_2H_4(l) + O_2(g) \longrightarrow NO_2(g) + H_2O(g)$$

(a) Balance the equation.

(b) How many moles of oxygen are needed to react with 165 g of hydrazine?

(c) How many grams of oxygen are needed to react with 165 g of hydrazine?

6.41 One method for preparing pure iron from Fe_2O_3 is by reaction with carbon monoxide.

$$Fe_2O_3(s) + CO(g) \longrightarrow Fe(s) + CO_2(g)$$

(a) Balance the equation.

(b) How many grams of CO are needed to react with 3.02 g of Fe_2O_3?

(c) How many grams of CO are needed to react with 1.68 mol of Fe_2O_3?

6.42 Magnesium metal burns in oxygen to form magnesium oxide, MgO.

(a) Write a balanced equation for the reaction.

(b) How many grams of oxygen are needed to react with 25.0 g of Mg? How many grams of MgO will result?

(c) How many grams of Mg are needed to react with 25.0 g of O_2? How many grams of MgO will result?

6.43 Titanium metal is obtained from the mineral rutile, which is primarily composed of TiO_2. The process requires multiple steps, as shown in the following reactions:

$$TiO_2(s) + 2\,Cl_2(g) + 2\,C(s) \longrightarrow TiCl_4(s) + 2\,CO(g)$$

$$TiCl_4(s) + 2\,Mg(s) \longrightarrow Ti(s) + 2\,MgCl_2(s)$$

(a) Write mole ratios to show the relationship between the reactants and products for each reaction.

(b) How many moles of TiO_2 are needed to form one mole of titanium?

(c) How many kilograms of rutile are needed to produce 95 kg of Ti?

6.44 In the preparation of iron from hematite (Problem 6.43), how many moles of carbon monoxide are needed to react completely with 105 kg of Fe_2O_3?

6.45 The eruption of Mount St. Helens volcano in 1980 injected 4×10^8 kg of SO_2 into the atmosphere. If all this SO_2 was converted to sulfuric acid, how many moles of H_2SO_4 would be produced? How many kilograms?

6.46 The thermite reaction was used to produce molten iron for welding applications before arc welding was available. The thermite reaction is as follows:

$$Fe_2O_3(s) + 2\,Al(s) \longrightarrow Al_2O_3(s) + 2\,Fe(l)$$

How many moles of molten iron can be produced from 1.5 kg of iron(III) oxide? NaOH?

6.47 In closed environments, such as submarines, elevated levels of carbon dioxide can be toxic. Excess CO_2 is removed by scrubbers that take advantage of the reaction of CO_2 with soda lime, a mixture of sodium hydroxide and calcium hydroxide.

$$CO_2 + NaOH \longrightarrow NaHCO_3$$
$$2CO_2 + Ca(OH)_2 \longrightarrow Ca(HCO_3)_2$$

How many moles of CO_2 could be removed from the air by 1.0 kg of NaOH? By 1.0 kg of $Ca(OH)_2$?

6.48 Diborane (B_2H_6) is a gas at room temperature that forms explosive mixtures with air. It reacts with oxygen according to the following equation:

$$B_2H_6(g) + 3\,O_2(g) \longrightarrow B_2O_3(s) + 3\,H_2O(l)$$

How many grams of diborane will react with 7.5 mol of O_2?

LIMITING REAGENT AND PERCENT YIELD (SECTION 6.5)

6.49 Once made by heating wood in the absence of air, methanol (CH_3OH) is now made by reacting carbon monoxide and hydrogen at high pressure.

$$CO(g) + 2\,H_2(g) \longrightarrow CH_3OH(l)$$

(a) If 25.0 g of CO is reacted with 6.00 g of H_2, which is the limiting reagent?

(b) How many grams of CH_3OH can be made from 10.0 g of CO if it all reacts?

(c) If 9.55 g of CH_3OH is recovered when the amounts in part (b) are used, what is the percent yield?

6.50 In Problem 6.40, hydrazine reacted with oxygen according to the following (unbalanced) equation:

$$N_2H_4(l) + O_2(g) \longrightarrow NO_2(g) + H_2O(g)$$

(a) If 75.0 kg of hydrazine are reacted with 75.0 kg of oxygen, which is the limiting reagent?

(b) How many kilograms of NO_2 are produced from the reaction of 75.0 kg of the limiting reagent?

(c) If 59.3 kg of NO_2 are obtained from the reaction in part (a), what is the percent yield?

6.51 Dichloromethane, CH_2Cl_2, the solvent used to decaffeinate coffee beans, is prepared by reaction of CH_4 with Cl_2.

(a) Write the balanced equation. (HCl is also formed.)

(b) How many grams of Cl_2 are needed to react with 50.0 g of CH_4?

(c) How many grams of dichloromethane are formed from 50.0 g of CH_4 if the percent yield for the reaction is 76%?

6.52 Cisplatin [$Pt(NH_3)_2Cl_2$], a compound used in cancer treatment, is prepared by reaction of ammonia with potassium tetrachloroplatinate:

$$K_2PtCl_4 + 2\,NH_3 \longrightarrow 2\,KCl + Pt(NH_3)_2Cl_2$$

(a) How many grams of NH_3 are needed to react with 55.8 g of K_2PtCl_4?

(b) How many grams of cisplatin are formed from 55.8 g of K_2PtCl_4 if the percent yield for the reaction is 95%?

6.53 Nitrobenzene ($C_6H_5NO_2$) is used in small quantities as a flavoring agent or in perfumes but can be toxic in large amounts. It is produced by reaction of benzene (C_6H_6) with nitric acid:

$$C_6H_6(l) + HNO_3(aq) \longrightarrow C_6H_5NO_2(l) + H_2O(l).$$

(a) Identify the limiting reagent in the reaction of 27.5 g of nitric acid with 75 g of benzene.

(b) Calculate the theoretical yield for this reaction.

6.54 Calculate the percent yield if 48.2 g of nitrobenzene is obtained from the reaction described in Problem 6.53.

CONCEPTUAL PROBLEMS

6.55 Batrachotoxin, $C_{31}H_{42}N_2O_6$, an active component of South American arrow poison, is so toxic that 0.05 μg can kill a person. How many molecules is this?

6.56 Zinc metal reacts with hydrochloric acid (HCl) according to the following equation:

$$Zn(s) + 2\,HCl(aq) \longrightarrow ZnCl_2(aq) + H_2(g)$$

(a) How many grams of hydrogen are produced if 15.0 g of zinc reacts?

(b) Is this a redox reaction? If so, tell what is reduced, what is oxidized, and identify the reducing and oxidizing agents.

6.57 When table sugar (sucrose, $C_{12}H_{22}O_{11}$) is heated, it decomposes to form C and H_2O.

(a) Write a balanced equation for the process.

(b) How many grams of carbon are formed by the breakdown of 60.0 g of sucrose?

(c) How many grams of water are formed when 6.50 g of carbon are formed?

6.58 Although Cu is not sufficiently active to react with acids, it can be dissolved by concentrated nitric acid, which functions as an oxidizing agent according to the following equation:

$$Cu(s) + 4\,HNO_3(aq) \longrightarrow Cu(NO_3)_2(aq) + 2\,NO_2(g) + 2\,H_2O(l)$$

(a) Write the net ionic equation for this process.

(b) Is 35.0 g of HNO_3 sufficient to dissolve 5.00 g of copper?

6.59 The net ionic equation for the Breathalyzer test used to indicate alcohol concentration in the body is as follows:

$$16\,H^+(aq) + 2\,Cr_2O_7^{2-}(aq) + 3\,C_2H_6O(aq) \longrightarrow 3\,C_2H_4O_2(aq) + 4\,Cr^{3+}(aq) + 11\,H_2O(l)$$

(a) How many grams of $K_2Cr_2O_7$ must be used to consume 1.50 g of C_2H_6O?

(b) How many grams of $C_2H_4O_2$ can be produced from 80.0 g of C_2H_6O?

6.60 Ethanol is formed by enzyme action on sugars and starches during fermentation.

$$C_6H_{12}O_6 \longrightarrow 2\,CO_2 + 2\,C_2H_6O$$

If the density of ethanol is 0.789 g/mL, how many cm^3 can be produced by the fermentation of 45.4 kg of sugar?

6.61 Gaseous ammonia reacts with oxygen in the presence of a platinum catalyst to produce nitrogen monoxide and water vapor.

(a) Write a balanced chemical equation for this reaction.

(b) What mass of nitrogen monoxide would be produced by complete reaction of 17.0 g of ammonia?

6.62 Sodium hypochlorite, the primary component in commercial bleach, is prepared by bubbling chlorine gas through solutions of sodium hydroxide.

$$NaOH(aq) + Cl_2(g) \longrightarrow NaOCl(aq) + H_2O(l)$$

How many moles of sodium hypochlorite can be prepared from 32.5 g of NaOH?

6.63 Barium sulfate is an insoluble ionic compound swallowed by patients before having an X ray of their gastrointestinal tract.

(a) Write the balanced chemical equation for the precipitation reaction between barium chloride and sodium sulfate.

(b) What mass of barium sulfate can be produced by complete reaction of 27.4 g of Na_2SO_4?

6.64 The last step in the production of nitric acid is the reaction of nitrogen dioxide with water.

$$NO_2(g) + H_2O(l) \longrightarrow HNO_3(aq) + NO(g)$$

(a) Balance the chemical equation.

(b) If 65.0 g of nitrogen dioxide is reacted with excess water, calculate the theoretical yield.

(c) If only 43.8 g of nitric acid is obtained, calculate the percent yield.

6.65 Acetylsalicylic acid, the active ingredient in aspirin, is prepared from salicylic acid by reaction with acetic anhydride.

$$\underset{\text{(salicylic acid)}}{C_7H_6O_3} + \underset{\text{(acetic anhydride)}}{C_4H_6O_3} \longrightarrow \underset{\text{(acetylsalicylic acid)}}{C_9H_8O_4} + \underset{\text{(acetic acid)}}{C_2H_4O_2}$$

(a) Calculate the theoretical yield if 47 g of salicylic acid is reacted with 25 g of acetic anhydride.

(b) What is the percent yield if only 35 g is obtained?

6.66 Jewelry and tableware can be silver-plated by reduction of silver ions from a solution of silver nitrate. The net ionic equation is $Ag^+(aq) + e^- \longrightarrow Ag(s)$. How many grams of silver nitrate would be needed to plate 15.2 g of silver on a piece of jewelry?

6.67 Elemental phosphorus exists as molecules of P_4. It reacts with $Cl_2(g)$ to produce phosphorus pentachloride.

(a) Write the balanced chemical equation for this reaction.

(b) What mass of phosphorus pentachloride would be produced by the complete reaction of 15.2 g of P_4?

6.68 Lithium oxide is used aboard the International Space Station to remove water from the atmosphere according to the equation

$$Li_2O(s) + H_2O(g) \longrightarrow 2\,LiOH(s)$$

How many grams of lithium oxide must be carried on board to remove 80.0 kg of water?

6.69 One of the reactions used to provide thrust for the International Space Station involves the reaction of ammonium perchlorate with aluminum to produce $Al_2O_3(s)$, $AlCl_3(s)$, $H_2O(g)$, and $N_2(g)$.

(a) Write the balanced chemical equation for this reaction.

(b) How many moles of gas are produced by the reaction of 14.5 kg of ammonium perchlorate?

GROUP PROBLEMS

6.70 Calcium citrate, $Ca_3(C_6H_5O_7)_2$ (Molecular mass = 498.5 amu), is a common dietary supplement to provide calcium needed for strong teeth and bones.

(a) Look up the recommended daily dietary intake of calcium for adult men and premenopausal women.

(b) What mass of calcium citrate would be needed to provide the recommended daily intake of calcium?

6.71 Obtain a bottle of aspirin and identify the amount of active ingredient (acetylsalicylic acid, $C_9H_8O_4$) per tablet.

(a) How many moles of aspirin are in one tablet?

(b) How many aspirin molecules are there in one tablet?

6.72 Lovastatin is a drug used to lower serum cholesterol.

(a) Look up the molecular formula for Lovastatin and calculate the molar mass.

(b) How many moles of Lovastatin are present in a typical dose of one 10 mg tablet?

6.73 Pyrite, also known as fool's gold, is used commercially to produce SO_2 used in the production of paper products.

(a) What is the formula of pyrite, and what is its molar mass?

(b) How many moles of SO_2 can be produced from 1.0 kg of pyrite?

6.74 Look up the recommended daily intake of vitamin C (ascorbic acid, $C_6H_8O_6$).

(a) Obtain a bottle of a daily vitamin supplement. How many milligrams of vitamin C are contained per tablet?

(b) What percentage of the recommended daily dosage does this represent?

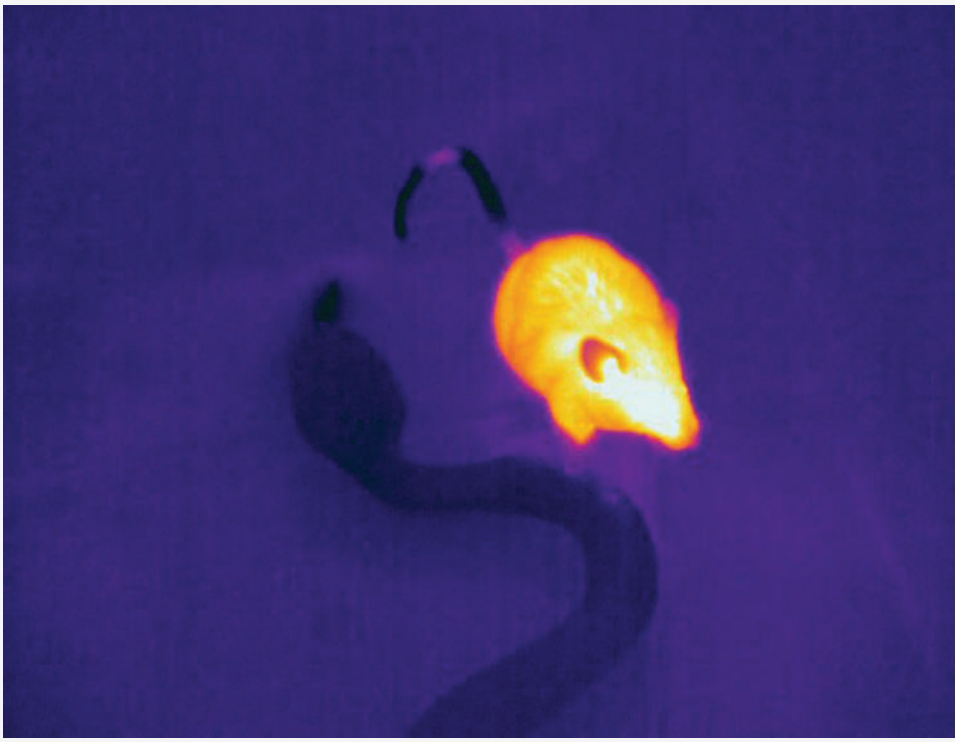
7

Chemical Reactions: Energy, Rates, and Equilibrium

CONTENTS

CONCEPTS TO REVIEW

A. Energy and Heat (Section 1.11)
B. Ionic Bonds (Section 3.7)
C. Covalent Bonds (Section 4.1)
D. Chemical Equations (Section 5.1)
E. Stoichiometry of Reactions (Sections 6.3 and 6.4)



▲ This thermal image photo dramatically illustrates the differences between warm-blooded and cold-blooded animals. Warm-blooded animals use the heat generated by metabolic chemical reactions to maintain a constant body temperature.

Have you ever come across a snake or lizard warming itself on a rock in the sun? Lizards and other so-called cold-blooded animals are very active in warm weather but very sluggish in cool weather. Warm-blooded animals, including mammals, can remain very active in spite of environmental conditions. To maintain a fairly constant body temperature, they must consume substantial amounts of food and have developed complex mechanisms to generate heat when it is too cold or to cool down when it is too hot, which we will learn more about in the Chemistry in Action feature on p. 242. Still, other animals, such as bears, can lower their body temperature when food is scarce and go into hibernation. These substantial differences in animal behavior are all related to a complex system of biochemical reactions that are collectively known as metabolism. But in order to fully appreciate metabolic processes, we must examine chemical reactions, and the factors that control a reaction, in more detail.

In the two previous chapters, we began our study of reactions—reaction types, how to balance reactions, and the stoichiometric relationships between reactants and products—but we have yet to answer many questions about reactions. Why, for instance, do some reactions occur while others do not, or occur to a limited extent? Just because a balanced equation can be written does not mean it will take place. We can write a balanced equation for the reaction of gold with water, for example, but the reaction does not occur in practice—so your gold jewelry is safe in the shower.

Balanced but does not occur

$$2\,Au(s) + 3\,H_2O(l) \longrightarrow Au_2O_3(s) + 3\,H_2(g)$$

Other reactions may proceed only partially, generating some products but leaving most of the original reactants unreacted. The amount of products that are formed can also be affected by other factors, including temperature. To understand chemical reactions more completely, several fundamental questions are commonly asked: Is energy released or absorbed when a reaction occurs? Is a given reaction fast or slow? Does a reaction continue until all reactants are converted to products, or is there a point beyond which no additional product forms? In this chapter, we will examine how reactions occur and identify the factors that affect both the rate and the extent of a reaction.

7.1 Energy and Chemical Bonds

Learning Objective:

- Distinguish between potential and kinetic energy.

There are two fundamental kinds of energy: *potential* and *kinetic*. **Potential energy** is stored energy. The water in a reservoir behind a dam, an automobile poised to coast downhill, and a coiled spring have potential energy waiting to be released. **Kinetic energy,** by contrast, is the energy of motion. When the water falls over the dam and turns a turbine, when the car rolls downhill, or when the spring uncoils and makes the hands on a clock move, the potential energy in each is converted to kinetic energy. Of course, once all the potential energy is converted, nothing further occurs. The water at the bottom of the dam, the car at the bottom of the hill, and the uncoiled spring no longer have potential energy and, thus, undergo no further change.

Potential energy Stored energy.

Kinetic energy The energy of motion of an object in motion.

In chemical compounds, the attractive forces between ions or atoms are a form of potential energy, similar to the attractive forces between the poles of a magnet. When these attractive forces result in the formation of ionic or covalent bonds between ions or atoms, the potential energy is often converted into **heat**—a measure of the kinetic energy of the particles that make up the molecule. Breaking these bonds requires an input of energy.

Heat A measure of the transfer of thermal energy.

In chemical reactions, some of the chemical bonds in the reactants must break (energy in) so that new bonds can form in the products (energy out). If the reaction products have less potential energy than the reactants, we say that the products are *more stable* than the reactants. The term "stable" is used in chemistry to describe a substance that has little remaining potential energy and consequently little tendency to undergo further change. Whether a reaction occurs, and how much energy or heat is associated with the reaction, depends on the difference in the amount of potential energy contained in the reactants and products.

PROBLEM 7.1

Classify each of the following as having potential or kinetic energy. For those identified as having potential energy, discuss how the potential energy would be realized by conversion to another form of energy.

(a) gunpowder
(b) a bullet in flight
(c) a cell phone (lithium ion) battery
(d) wind
(e) a candy bar
(f) spinning wind mill blades

7.2 Heat Changes during Chemical Reactions

Learning Objective:

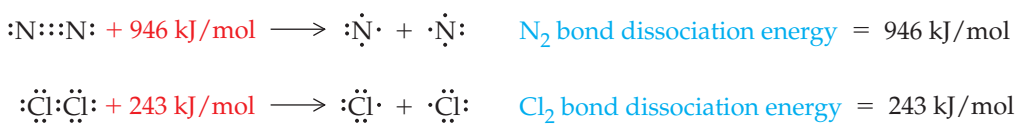
- Identify chemical reactions as endothermic or exothermic and explain how the heats of reaction relate to the law of conservation of energy.

Why does chlorine react so easily with many elements and compounds but nitrogen does not? What dissimilarity between Cl_2 molecules and N_2 molecules accounts for their different reactivities? The answer is that the nitrogen–nitrogen triple bond is much *stronger* than the chlorine–chlorine single bond and cannot be broken as easily in chemical reactions.

The strength of a covalent bond is measured by its **bond dissociation energy,** defined as the amount of energy that must be absorbed to break the bond and separate the atoms in an isolated gaseous molecule. The greater the bond dissociation energy, the more stable the chemical bond between the atoms or ions. The triple bond in N_2, for example, has a

Bond dissociation energy The amount of energy that must be supplied to break a bond and separate the atoms in an isolated gaseous molecule.

bond dissociation energy of 946 kJ/mol, whereas the single bond in chlorine has a bond dissociation energy of only 243 kJ/mol:



The greater stability of the triple bond in N_2 explains why nitrogen molecules are less reactive than Cl_2 molecules. Some typical bond dissociation energies are given in Table 7.1.

Table 7.1 Average Bond Dissociation Energies

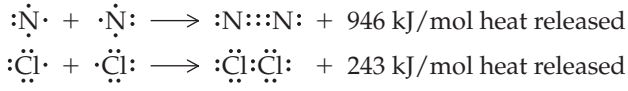
Bond	Bond Dissociation Energy KJ/mol	Bond	Bond Dissociation Energy KJ/mol	Bond	Bond Dissociation Energy KJ/mol
C—H	413	N—H	391	C=C	614
C—C	347	N—N	160	C≡C	839
C—N	305	N—Cl	200	C=O*	745
C—O	358	N—O	201	O=O	498
C—Cl	339	H—H	432	N=O	607
Cl—Cl	243	O—H	467	O≡N	891
H—Cl	427	O—Cl	203	N≡N	946

*The C=O bond dissociation energies in CO_2 are 799 kJ/mol.

Endothermic A process or reaction that absorbs heat.

A chemical change that absorbs heat, like the breaking of bonds, is **endothermic,** from the Greek words *endon* (within) and *therme* (heat), meaning that *heat* is required as a condition for reaction and would appear on the left side of the equation. The reverse of bond breaking is bond formation, a process that *releases* heat and is **exothermic,** from the Greek *exo* (outside), meaning that heat goes *out* and appears on the right side of the equation as a product. The amount of energy released in forming a bond is numerically the same as that absorbed in breaking it. When nitrogen atoms combine to give N_2, 946 kJ/mol of heat is released. Similarly, when chlorine atoms combine to give Cl_2, 243 kJ/mol of heat is released.

Exothermic A process or reaction that releases heat.



For bond breakage and bond formation, the numerical value of the heat associated with the process is the same, but the direction of energy flow depends on the reaction. We indicate the direction of energy flow based on whether the energy is absorbed (gained) or released (lost) during the process. For endothermic processes, heat is absorbed (gained) and is indicated by a positive sign. For exothermic processes, heat is released (lost) and is indicated with a negative sign.

The same energy relationships that govern bond breaking and bond formation apply to every physical or chemical change. That is, the amount of heat transferred during a change in one direction is numerically equal to the amount of heat transferred during the change in the opposite direction. Only the *direction* of the heat transfer is different. This relationship reflects a fundamental law of nature called the *law of conservation of energy:*

Law of conservation of energy Energy can be neither created nor destroyed in any physical or chemical change.

If more energy could be released by an exothermic reaction than was consumed in its reverse, the law would be violated, and we could "manufacture" energy out of nowhere by cycling back and forth between forward and reverse reactions—a clear impossibility.

In every chemical reaction, some bonds in the reactants are broken, and new bonds are formed in the products. The difference between the heat energy absorbed in breaking bonds and the heat energy released in forming bonds is called the **heat of reaction** and is a quantity that we can measure. Heats of reaction that are measured when a reaction is held at constant pressure are represented by the abbreviation ΔH, where Δ (the Greek capital letter delta) is a general symbol used to indicate "a change in," and H is a quantity called **enthalpy.** Thus, the value of ΔH represents the **enthalpy change** that occurs during a reaction. The terms *enthalpy change* and *heat of reaction* are often used interchangeably, but we will generally use the latter term in this book.

Heat of reaction or Enthalpy change (ΔH) The difference between the energy of bonds broken in reactants and the energy of bonds formed in products.

Enthalpy (H) A measure of the amount of energy associated with substances involved in a reaction.

PROBLEM 7.2

Based on bond energies, which atmospheric gas in each pair do you think is more stable? Explain.

(a) O_2 or N_2 **(b)** CO or CO_2

7.3 Exothermic and Endothermic Reactions

Learning Objective:

- Use bond energies and stoichiometric relationships to calculate the enthalpy of a reaction and the total amount of heat consumed or produced.

When the total strength of the bonds formed in the products is *greater* than the total strength of the bonds broken in the reactants, the net result is that energy is released and the reaction is exothermic. All combustion reactions are exothermic; for example, burning 1 mol of methane releases 891 kJ of energy in the form of heat. The heat released in an exothermic reaction can be thought of as a reaction product, and the heat of reaction ΔH is assigned a *negative* value, because overall, heat is *lost* during the reaction.

An exothermic reaction—negative ΔH

Heat is a product.

$$CH_4(g) + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(l) + 891\text{ kJ}$$

or

$$CH_4(g) + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(l) \qquad \Delta H = -891\text{ kJ/mol}$$

The heat of reaction can be calculated as the difference between the bond dissociation energies in the products and the bond dissociation energies of the reactants:

$$\Delta H = \Sigma(\text{Bond dissociation energies})_{\text{reactants}} - \Sigma(\text{Bond dissociation energies})_{\text{products}}$$

Look again at the reaction involving the combustion of methane. By determining the types of bonds and then counting the number of bonds of each type on each side of the chemical equation, we can use the average bond dissociation energies from Table 7.1 to estimate ΔH for the reaction.

Reactants	Bond Dissociation Energies (kJ/mol)	Products	Bond Dissociation Energies (kJ/mol)
(C—H) × 4	413 × 4 = 1652 kJ	(C═O) × 2	800 × 2 = 1600 kJ
(O═O) × 2	498 × 2 = 996 kJ	(H—O) × 4	467 × 4 = 1868 kJ
Total:	= 2648 kJ		= 3468 kJ

$$\Delta H = (2648\text{ kJ})_{\text{reactants}} - (3468\text{ kJ})_{\text{products}} = -820\text{ kJ}$$

▲ The reaction between aluminum metal and iron(III) oxide, called the *thermite reaction,* is so strongly exothermic that it melts iron.

In this reaction, the input of energy needed to break the bonds in the reactants is less than the amount of energy released when forming bonds in the products. The excess energy is released as heat, and the reaction is exothermic (ΔH = negative).

Note that the bond energies in Table 7.1 are average values, and that actual bond energies may vary depending on the chemical environment in which the bond is found. The average C═O bond energy, for example, is 745 kJ/mol, but the actual value for the C═O bonds in the CO_2 molecule is 800 kJ/mol. The average C—H bond energy is 413 kJ/mol, but in CH_3CH_3 the C—H bond dissociation energy is actually 423 kJ/mol. Thus, the calculated ΔH for a reaction using average bond energies may differ slightly from the value obtained by experiment. For the combustion of methane, for example, the ΔH estimated from bond energies is −820 kJ/mol, while the value measured experimentally is −891 kJ/mol, a difference of about 9%.

Note that ΔH is in units of kilojoules per mole, where "per mole" means the reaction of *molar amounts of products and reactants as represented by the coefficients of the balanced equation*. Thus, the experimental value $\Delta H = -891$ kJ/mol refers to the amount of heat released when 1 mol (16.0 g) of methane reacts with 2 mol of O_2 to give 1 mol of CO_2 gas and 2 mol of liquid H_2O. If we were to double the amount of methane from 1 mol to 2 mol, the amount of heat released would also double.

The quantities of heat released in the combustion of several fuels, including natural gas (which is primarily methane), are compared in Table 7.2. The values are in kilojoules per gram to make comparisons easier. Based on the greater energy value (amount of energy per gram), you can see from the table why there is interest in the potential of hydrogen as a fuel.

Table 7.2 Energy Values of Some Common Fuels

Fuel	Energy Value kJ/g
Wood (pine)	18.0
Ethanol	29.7
Coal (anthracite)	31.0
Crude oil (Texas)	43.9
Gasoline	48.1
Natural gas	49.0
Hydrogen	142

When the total energy released upon bond formation in the products is *less* than the total energy added to break the bonds in the reactants, the net result is that energy is absorbed and the reaction is endothermic. The combination of nitrogen and oxygen to give nitrogen oxide (also known as nitric oxide), a gas present in automobile exhaust, is such a reaction. The heat added in an endothermic reaction is like a reactant, and ΔH is assigned a *positive* value because heat is *added*.

An endothermic reaction—positive ΔH

Heat is a reactant.

$$N_2(g) + O_2(g) + 180\text{ kJ} \longrightarrow 2\,NO(g)$$

or

$$N_2(g) + O_2(g) \longrightarrow 2\,NO(g) \qquad \Delta H = +180\text{ kJ/mol}$$

Important Points about Heat Transfers and Chemical Reactions

- An exothermic reaction releases heat to the surroundings; ΔH is negative.
- An endothermic reaction absorbs heat from the surroundings; ΔH is positive.
- The reverse of an exothermic reaction is endothermic.
- The reverse of an endothermic reaction is exothermic.
- The amount of heat absorbed or released in the reverse of a reaction is equal to that released or absorbed in the forward reaction, but ΔH has the opposite sign.

Worked Examples 7.1–7.4 show how to calculate the amount of heat absorbed or released for reaction of a given amount of reactant. All that is needed is the balanced equation and its accompanying ΔH or the bond dissociation energies to permit calculation of ΔH. Mole ratios and molar masses are used to convert between masses and moles of reactants or products, as discussed in Sections 6.3 and 6.4.

Worked Example 7.1 Heat of Reaction from Bond Energies

Estimate the ΔH (in kJ/mol) for the reaction of hydrogen and oxygen to form water:

$$2\,H_2 + O_2 \longrightarrow 2\,H_2O \quad \Delta H = ?$$

ANALYSIS Use the individual bond energies from Table 7.1 to calculate the total bond energies of reactants and products. ΔH can then be calculated as

$$\Delta H = \Sigma(\text{Bond dissociation energies})_{\text{reactants}} - \Sigma(\text{Bond dissociation energies})_{\text{products}}$$

BALLPARK ESTIMATE The average H—H bond energy is ~430 kJ/mol, and the O=O bond energy is ~500 kJ/mol. Thus, the total energy needed to break reactant bonds is ~(860 + 500) = 1360 kJ/mol. The O—H bonds are ~470 kJ/mol, so the total energy released when product bonds are formed is ~1880 kJ/mol. Based on these estimates, ΔH ~500 kJ/mol.

SOLUTION

$$\begin{aligned}\Delta H &= \Sigma(\text{Bond dissociation energies})_{\text{reactants}} - \Sigma(\text{Bond dissociation energies})_{\text{products}}\\ &= (2(\text{H—H}) + (\text{O=O})) - (4(\text{O—H}))\\ &= (2(432\ \text{kJ/mol}) + (498\ \text{kJ/mol})) - (4(467\ \text{kJ/mol})) = -506\ \text{kJ/mol}\end{aligned}$$

BALLPARK CHECK Our estimate was −500 kJ/mol, within 3% of the calculated answer.

Worked Example 7.2 Heat of Reaction: Moles

Methane undergoes combustion with O_2 according to the following equation:

$$CH_4(g) + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(l) \quad \Delta H = -891\ \frac{\text{kJ}}{\text{mol}\ CH_4}$$

How much heat (in kJ) is released during the combustion of 0.35 mol of methane?

ANALYSIS Since the value of ΔH for the reaction (891 kJ/mol) is negative, it indicates the amount of heat released when 1 mol of methane reacts with O_2. We need to find the amount of heat released when an amount other than 1 mol reacts, using appropriate factor-label calculations to convert from our known or given units to kilojoules.

BALLPARK ESTIMATE Since 891 kJ is released for each mole of methane that reacts, 0.35 mol of methane should release about one-third of 891 kJ, or about 300 kJ.

SOLUTION

To find the amount of heat released (in kilojoules) by combustion of 0.35 mol of methane, we multiply the value of −891 kJ with 0.35 mol:

$$0.35\ \cancel{\text{mol}\ CH_4} \times \frac{-891\ \text{kJ}}{1\ \cancel{\text{mol}\ CH_4}} = -312\ \text{kJ}$$

The negative sign indicates that the 312 kJ of heat is released.

BALLPARK CHECK The calculated answer is consistent with our estimate 300 kJ.

Worked Example 7.3 Heat of Reaction: Mass to Mole Conversion

How much heat is released during the combustion of 7.50 g of methane (molar mass = 16.0 g/mol)?

$$CH_4(g) + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(l) \quad \Delta H = -891\ \frac{\text{kJ}}{\text{mol } CH_4}$$

ANALYSIS We can find the moles of methane involved in the reaction by using the molecular mass in a mass to mole conversion, and then use ΔH to find the heat released.

BALLPARK ESTIMATE Since 1 mol of methane (molar mass = 16.0 g/mol) has a mass of 16.0 g, 7.50 g of methane is a little less than 0.5 mol. Thus, less than half of 891 kJ, or about 418 kJ, is released from combustion of 7.50 g.

SOLUTION
Going from a given mass of methane to the amount of heat released in a reaction requires that we first find the number of moles of methane by including molar mass (in mol/g) in the calculation and then converting moles to kilojoules:

$$7.50\ \text{g}\ \cancel{CH_4} \times \frac{1\ \cancel{\text{mol } CH_4}}{16.0\ \cancel{\text{g } CH_4}} \times \frac{-891\ \text{kJ}}{1\ \cancel{\text{mol } CH_4}} = -418\ \text{kJ}$$

The negative sign indicates that the 418 kJ of heat is released.

BALLPARK CHECK Our estimate was −418 kJ!

Worked Example 7.4 Heat of Reaction: Mole Ratio Calculations

How much heat is released in kJ when 2.50 mol of O_2 reacts completely with methane?

$$CH_4(g) + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(l) \quad \Delta H = -891\ \frac{\text{kJ}}{\text{mol } CH_4}$$

ANALYSIS Since the ΔH for the reaction is based on the combustion of 1 mol of methane, we will need to perform a mole ratio calculation.

BALLPARK ESTIMATE The balanced equation shows that 891 kJ is released for each 2 mol of oxygen that reacts. Thus, 2.50 mol of oxygen should release a bit more than 891 kJ, perhaps about 1050 kJ.

SOLUTION
To find the amount of heat released by combustion of 2.50 mol of oxygen, we include in our calculation a mole ratio based on the balanced chemical equation:

$$2.50\ \cancel{\text{mol } O_2} \times \frac{1\ \cancel{\text{mol } CH_4}}{2\ \cancel{\text{mol } O_2}} \times \frac{-891\ \text{kJ}}{1\ \cancel{\text{mol } CH_4}} = -1110\ \text{kJ}$$

The negative sign indicates that the 1110 kJ of heat is released.

BALLPARK CHECK The calculated answer is close to our estimate −1050 kJ.

CHEMISTRY IN ACTION

Energy from Food

Any serious effort to lose weight usually leads to studying the caloric values of foods. Have you ever wondered how the numbers quoted on food labels are obtained?

All living organisms require fuel to produce the energy needed for daily activity. When the food consumed provides more energy than what is required, the "extra" energy is converted to potential energy in the form of body mass, usually fat. Conversely, when the energy expended during physical activity exceeds the amount provided from food intake, then the body taps into the potential energy stored as fat to meet the current demand. Food is "burned" in the body to yield H_2O, CO_2, and energy, just as natural gas is burned in furnaces to yield the same products. In fact, the "caloric value" of a food is just the heat of reaction for complete combustion of the food (minus a small correction factor). The value is the same whether the food is burned in the body or in the laboratory. One gram of protein releases 17 kJ, 1 g of table sugar (a carbohydrate) releases 17 kJ, and 1 g of fat releases 38 kJ (see table).

Caloric Values of Some Foods

Substance, Sample Size	Caloric Value kJ
Protein, 1 g	17
Carbohydrate, 1 g	17
Fat, 1 g	38
Alcohol, 1 g	29.7
Cola drink, 369 g	670
Apple, one medium (138 g)	330
Iceberg lettuce, 1 cup shredded (55 g)	21
White bread, 1 slice (25 g)	270
Hamburger patty, 85 g	1030
Pizza, 1 slice (120 g)	1200
Vanilla ice cream, 1 cup (133 g)	1130

The caloric value of a food is usually given in "Calories" (note the capital C), where 1 Cal = 1000 cal = 1 kcal = 4.184 kJ. To determine these values experimentally, a carefully dried and weighed food sample is placed together with oxygen in an instrument called a *calorimeter,* the food is ignited, the temperature change is measured, and the amount of heat given off is calculated from the temperature change. In the calorimeter, the heat from the food is released very quickly and the temperature rises dramatically. Clearly, though, something a bit different goes on when food is burned in the body, otherwise we would burst into flames after a meal!

▲ These products are specially formulated to provide the energy needed for sustained physical activity.

It is a fundamental principle of chemistry that the total heat released or absorbed in going from reactants to products is the same, no matter how many reactions are involved. The body applies this principle by withdrawing energy from food a bit at a time in a long series of interconnected reactions rather than all at once in a single reaction. These and other reactions that are continually taking place in the body—called the body's *metabolism*—will be examined in later chapters.

CIA Problem 7.1 Which provides more energy, 1 g of carbohydrate or 1 g of fat?

CIA Problem 7.2 How many kilojoules are in a 45.0 g serving of potato chips if we assume that they are essentially 50% carbohydrate and 50% fats?

PROBLEM 7.3

In photosynthesis, green plants convert carbon dioxide and water into glucose ($C_6H_{12}O_6$) according to the following equation:

$$6\,CO_2(g) + 6\,H_2O(l) \longrightarrow C_6H_{12}O_6(aq) + 6\,O_2(g)$$

(a) Estimate ΔH for the reaction using bond dissociation energies from Table 7.1. Give your answer in kJ/mol. ($C_6H_{12}O_6$ has five C—C bonds, seven C—H bonds, seven C—O bonds, and five O—H bonds).

(b) Is the reaction endothermic or exothermic?

PROBLEM 7.4

The following equation shows the conversion of aluminum oxide (from the ore bauxite) to aluminum:

$$2\,Al_2O_3(s) \longrightarrow 4\,Al(s) + 3\,O_2(g) \quad \Delta H = +3350\ kJ/mol$$

(a) Is the reaction exothermic or endothermic?

(b) How many kilojoules are required to produce 1.00 mol of aluminum?

(c) How many kilojoules are required to produce 10.0 g of aluminum?

PROBLEM 7.5

How much heat is absorbed (in kilojoules) during production of 127 g of NO by the combination of nitrogen and oxygen?

$$N_2(g) + O_2(g) \longrightarrow 2\,NO(g) \quad \Delta H = +180\ kJ/mol$$

PROBLEM 7.6

Once consumed, the body metabolizes alcohol (ethanol, CH_3CH_2OH; molar mass = 46 g/mol) to carbon dioxide and water. The balanced reaction is: $CH_3CH_2OH + 3\,O_2 \longrightarrow 2\,CO_2 + 3\,H_2O$. Using the bond energies in Table 7.1, estimate the ΔH for this reaction in kJ/mol. How does it compare to the energy value of alcohol (in J/g) given in the Chemistry in Action feature "Energy from Food" on p. 225?

HANDS-ON CHEMISTRY 7.1

Obtain an energy bar and look at the nutritional information included on the wrapper or label. How many grams of fat are included in each bar? How many grams of protein? How many grams of carbohydrate?

a. Using this information and the caloric values in the Chemistry in Action feature on p. 225, estimate the total caloric value of the energy bar and compare your answer to the nutritional information on the wrapper.

b. Now obtain a typical candy bar and perform the same evaluation. How do the two bars compare in terms of total calories? In terms of composition?

▲ Events that lead to lower energy tend to occur spontaneously. Thus, water always flows *down* a waterfall, not up.

7.4 Why Do Chemical Reactions Occur? Free Energy

Learning Objective:

- Use enthalpy, entropy, and free energy to determine the spontaneity of a chemical reaction or process.

Events that lead to lower energy states tend to occur spontaneously. Water falls downhill, for instance, releasing its stored (potential) energy and reaching a lower-energy, more stable position. Similarly, a wound-up spring uncoils when set free. Applying this lesson to chemistry, the obvious conclusion is that exothermic processes—those that release heat energy—should be spontaneous. A log burning in a fireplace is just one example of a spontaneous reaction that releases heat. At the same time, endothermic processes, which absorb heat energy, should not be spontaneous. Often, these conclusions are correct, but not always. Many, but not all, exothermic processes take place spontaneously, and many, but not all, endothermic processes are nonspontaneous.

Before exploring the situation further, it is important to understand what the word "spontaneous" means in chemistry, which is not quite the same as in everyday language. A **spontaneous process** is one that, once started, proceeds on its own without any external influence. The change does not necessarily happen quickly, like a spring suddenly uncoiling or a car coasting downhill. It can also happen slowly, like the

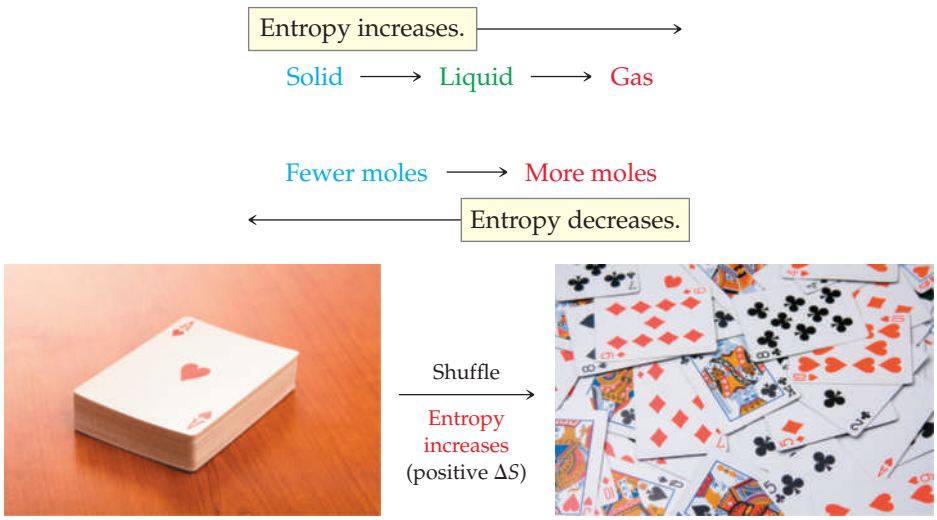
Spontaneous process A process or reaction that, once started, proceeds on its own without any external influence.

gradual rusting away of an abandoned bicycle. A *nonspontaneous process,* by contrast, takes place only in the presence of a continuous external influence. Energy must be continually expended to rewind a spring or push a car uphill. The reverse of a spontaneous process is always nonspontaneous.

As an example of a process that takes place spontaneously yet absorbs heat, think about what happens when you take an ice cube out of the freezer. The ice spontaneously melts to give liquid water above 273 K, even though it *absorbs* heat energy from the surroundings. What this and other spontaneous endothermic processes have in common is *an increase in molecular disorder,* or *randomness.* When the solid ice melts, the H_2O molecules are no longer locked in position but are now free to move around randomly in the liquid water.

The amount of disorder in a system is called the system's **entropy,** symbolized by S and expressed in units of Joules per mole-kelvin $[J/(mol \cdot K)]$. The greater the disorder, or randomness, of the particles in a substance or mixture, the larger the value of S (Figure 7.1). Gases have more disorder and therefore higher entropy than liquids because particles in the gas move around more freely than particles in the liquid. Similarly, liquids have higher entropy than solids. In chemical reactions, entropy increases when, for example, a gas is produced from a solid or when 2 mol of reactants split into 4 mol of products.

Entropy *(S)* A measure of the amount of molecular disorder in a system.



◂ Figure 7.1
Entropy and values of *S*.
A new deck of cards, neatly stacked, has more order and lower entropy than the randomly shuffled and strewn cards on the right. The value of the entropy change, ΔS, for converting the system on the left to that on the right is positive because entropy increases.

The **entropy change (ΔS)** for a process has a *positive* value if disorder increases because the process adds disorder to the system. The melting of ice to give water is an example. Conversely, ΔS has a *negative* value if the disorder of a system decreases. The freezing of water to give ice is an example.

Entropy change (ΔS) A measure of the increase in disorder ($\Delta S = +$) or decrease in disorder ($\Delta S = -$) as a chemical reaction or physical change occurs.

It thus appears that two factors determine the spontaneity of a chemical or physical change: the release or absorption of heat, ΔH, and the increase or decrease in entropy, ΔS. *To decide whether a process is spontaneous, both the enthalpy change and the entropy change must be taken into account.* We have already seen that a negative ΔH favors spontaneity, but what about ΔS? The answer is that an increase in molecular disorder (ΔS positive) favors spontaneity. A good analogy is the bedroom or office that seems to spontaneously become more messy over time (an increase in disorder, ΔS positive); to clean it up (a decrease in disorder, ΔS negative) requires an input of energy, a nonspontaneous process. Using our chemical example, the combustion of a log spontaneously converts large, complex molecules like lignin and cellulose (high molecular order, low entropy) into CO_2 and H_2O (a large number of small molecules with higher entropy). For this process, the level of disorder increases, and so ΔS is positive. The reverse process—turning CO_2 and H_2O back into cellulose—does occur in photosynthesis, but it requires a significant input of energy in the form of sunlight. Another useful example is complex living organisms; as highly ordered systems, they would have a large *negative* ΔS and would not be expected to occur spontaneously. However, remember that most living organisms consume large complex molecules as

food and convert them to smaller molecules (CO_2, H_2O, etc.), a process that has a large *positive* ΔS and would favor spontaneity.

When enthalpy and entropy are both favorable (ΔH negative, ΔS positive), a process is spontaneous; when both are unfavorable, a process is nonspontaneous. Clearly, however, the two factors do not have to operate in the same direction. It is possible for a process to be *unfavored* by enthalpy (the process absorbs heat, and so, has a positive ΔH) and yet be *favored* by entropy (there is an increase in disorder, and so, ΔS is positive). The melting of an ice cube above 273 K, for which $\Delta H + 6.02\ \text{kJ/mol}$ and $\Delta S = +22.0\ \text{J/(mol·K)}$, is such a process. To take both heat of reaction (ΔH) and change in disorder (ΔS) into account when determining the spontaneity of a process, a quantity called the **free-energy change (ΔG),** is needed:

Free-energy change (ΔG) A measure of the change in free energy as a chemical reaction or physical change occurs.

Free-energy change

Heat of reaction | Temperature (in kelvins) | Entropy change

$$\Delta G = \Delta H - T\Delta S$$

The value of the free-energy change, ΔG, determines spontaneity. A negative value for ΔG means that free energy is released and the reaction or process is spontaneous. Such events are said to be **exergonic.** A positive value for ΔG means that free energy must be added and the process is nonspontaneous. Such events are said to be **endergonic.**

Exergonic A spontaneous reaction or process that releases free energy and has a negative ΔG.

Endergonic A nonspontaneous reaction or process that absorbs free energy and has a positive ΔG.

LOOKING AHEAD In later chapters, we will see that a knowledge of free-energy changes is especially important for understanding how metabolic reactions work. Living organisms cannot raise their temperatures to convert nonspontaneous reactions into spontaneous reactions, so they must resort to other strategies, which we will explore in Chapter 21.

Important Points about Spontaneity and Free Energy

- A spontaneous process, once begun, proceeds without any external assistance and is exergonic; that is, free energy is released and it has a negative value of ΔG.
- A nonspontaneous process requires continuous external influence and is endergonic; that is, free energy is added and it has a positive value of ΔG.
- The value of ΔG for the reverse of a reaction is numerically equal to the value of ΔG for the forward reaction but has the opposite sign.
- Some nonspontaneous processes become spontaneous with a change in temperature.

Worked Example 7.5 Entropy Change of Processes

Does entropy increase or decrease in the following processes?

(a) Smoke from a cigarette disperses throughout a room rather than remaining in a cloud over the smoker's head.

(b) Water boils, changing from liquid to vapor.

(c) A chemical reaction occurs: $3\ H_2(g) + N_2(g) \longrightarrow 2\ NH_3(g)$

ANALYSIS Entropy is a measure of molecular disorder. Entropy increases when the products are more disordered than the reactants; entropy decreases when the products are less disordered than the reactants.

SOLUTION

(a) Entropy increases because smoke particles are more disordered when they are randomly distributed in the larger volume.

(b) Entropy increases because H_2O molecules have more freedom and disorder in the gas phase than in the liquid phase.

(c) Entropy decreases because 4 mol of reactant gas particles becomes 2 mol of product gas particles, with a consequent decrease in freedom and disorder.

PROBLEM 7.7

Does entropy increase or decrease in the following processes?

(a) Polymeric complex carbohydrates are metabolized by the body, converted into smaller simple sugars.

(b) Steam condenses on a glass surface.

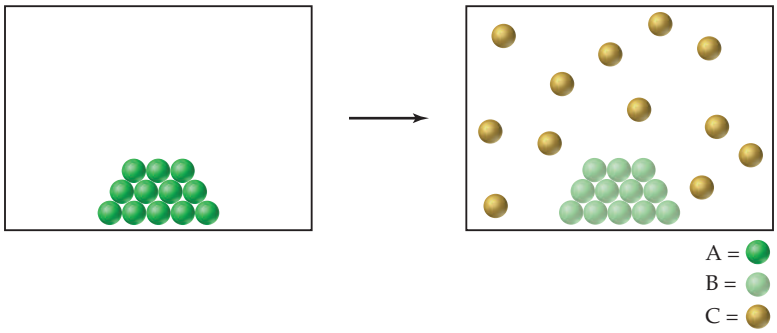
(c) $2\ SO_2(g) + O_2(g) \longrightarrow 2\ SO_3(g)$

KEY CONCEPT PROBLEM 7.8

The following diagram portrays a reaction of the type $A(s) \longrightarrow B(s) + C(g)$, where the different-colored spheres represent different molecular structures. Assume that the reaction has ΔH = negative.

(a) What is the sign of ΔS for the reaction?

(b) Is the reaction likely to be spontaneous at all temperatures, nonspontaneous at all temperatures, or spontaneous at some but nonspontaneous at others?



7.5 How Do Chemical Reactions Occur? Reaction Rates

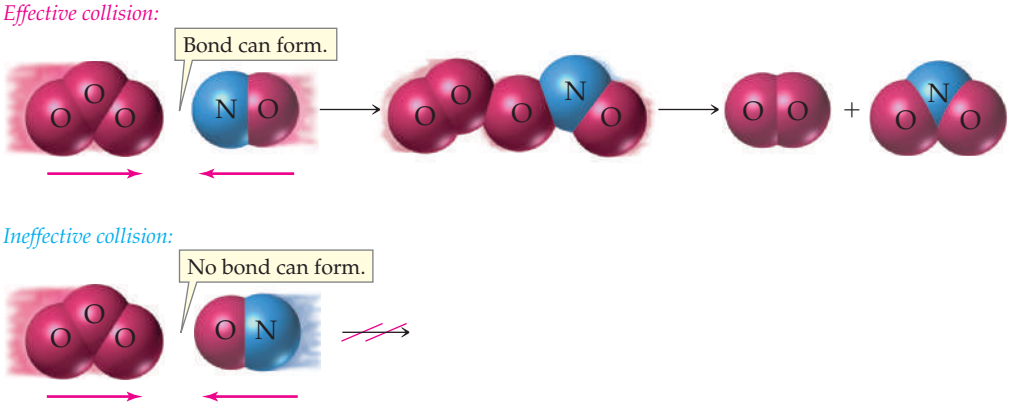
Learning Objective:

- Use collision theory and reaction diagrams to explain the activation energy and free-energy change of a chemical reaction.

Just because a chemical reaction has a favorable free-energy change does not mean that it occurs rapidly. The value of ΔG tells us only whether a reaction *can* occur; it says nothing about how *fast* the reaction will occur or about the details of the molecular changes that take place during the reaction.

For a chemical reaction to occur, reactant particles must collide, some chemical bonds have to break, and new bonds have to form. Not all collisions lead to products, however. One requirement for a productive collision is that the colliding molecules must approach each other with the correct orientation so that the atoms about to form new bonds can connect. In the reaction of ozone (O_3) with nitric oxide (NO) to give oxygen (O_2) and nitrogen dioxide (NO_2), for example, the two reactants must collide so that the nitrogen atom of NO strikes a terminal oxygen atom of O_3 (Figure 7.2).

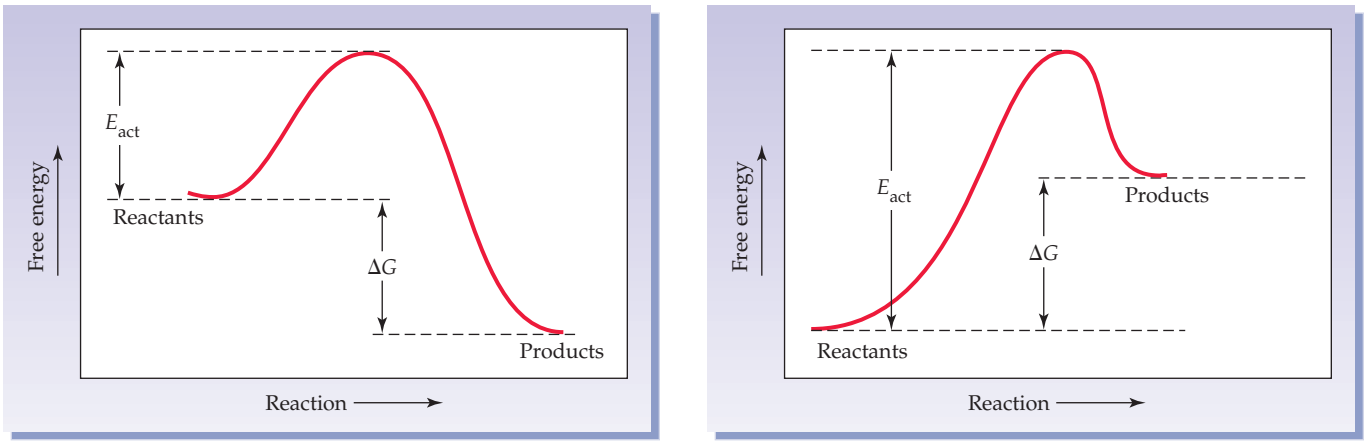
Another requirement for a reaction to occur is that the collision must take place with enough energy to break the appropriate bonds in the reactant. If the reactant particles are moving slowly, collisions might be too gentle to overcome the repulsion between electrons in the different reactants, and the particles will simply bounce apart. A reaction will only occur if the collisions between reactant molecules are sufficiently energetic.



◂ **Figure 7.2**
How do chemical reactions occur? For a collision between NO and O_3 molecules to give O_2 and NO_2, the molecules must collide so that the correct atoms come into contact. No bond forms if the molecules collide with the wrong orientation.

For this reason, many reactions with a favorable free-energy change do not occur at room temperature. To get such a reaction started, energy (heat) must be added. The heat causes the reactant particles to move faster, thereby increasing both the frequency and the force of the collisions. We all know that matches burn, for instance, but we also know that they do not burst into flame until struck. The heat of friction provides enough energy for a few molecules to react. Once started, the reaction sustains itself as the energy released by reacting molecules gives other molecules enough energy to react.

The energy change that occurs during the course of a chemical reaction can be visualized in an energy diagram like that in Figure 7.3. At the beginning of the reaction (left side of the diagram), the reactants are at the energy level indicated. At the end of the reaction (right side of the diagram), the products are at a lower energy level than the reactants if the reaction is exergonic (Figure 7.3a) but higher than the reactants if the reaction is endergonic (Figure 7.3b).



(a) An exergonic reaction

(b) An endergonic reaction

▲ **Figure 7.3**

Reaction energy diagrams show energy changes during a chemical reaction.

A reaction begins on the left and proceeds to the right. (a) In an exergonic reaction, the product energy level is lower than that of reactants. (b) In an endergonic reaction, the situation is reversed. The height of the barrier between reactant and product energy levels is the activation energy, E_{act}. The difference between reactant and product energy levels is the free-energy change, ΔG.

Activation energy (E_{act}) The amount of energy necessary for a reaction to occur; it determines the reaction rate.

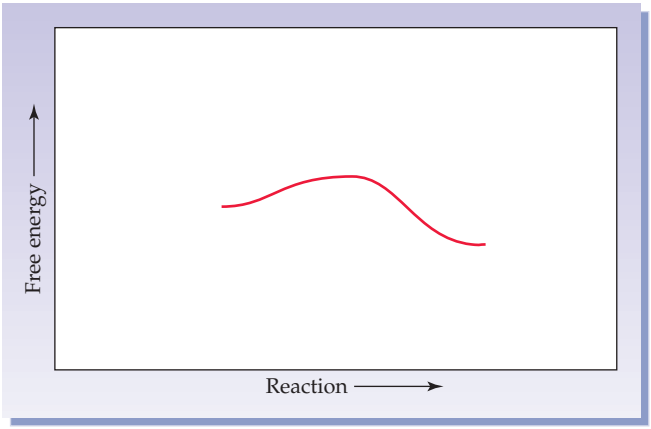
Reaction rate A measure of how rapidly a reaction occurs; determined by E_{act}.

Lying between the reactants and the products is an energy "barrier" that must be surmounted. The height of this barrier represents the amount of energy the colliding particles must have for productive collisions to occur, an amount called the **activation energy (E_{act})** of the reaction. The size of the activation energy determines the **reaction rate,** or how fast the reaction occurs. Consider an example of rolling a handful of marbles over a bump in the rug—if the bump is small, a greater number of marbles will make it over the bump (i.e., progress to form products) than if the bump is large. Similarly for a chemical reaction, the lower the activation energy, the greater the number of productive collisions in a given amount of time, and the faster the reaction. Conversely, the higher the activation energy, the lower the number of productive collisions, and the slower the reaction.

Note that the size of the activation energy and the size of the free-energy change are unrelated. A reaction with a large E_{act} takes place very slowly even if it has a large negative ΔG. Every reaction is different; each has its own characteristic activation energy and free-energy change.

Worked Example 7.6 Energy of Reactions: Energy Diagrams

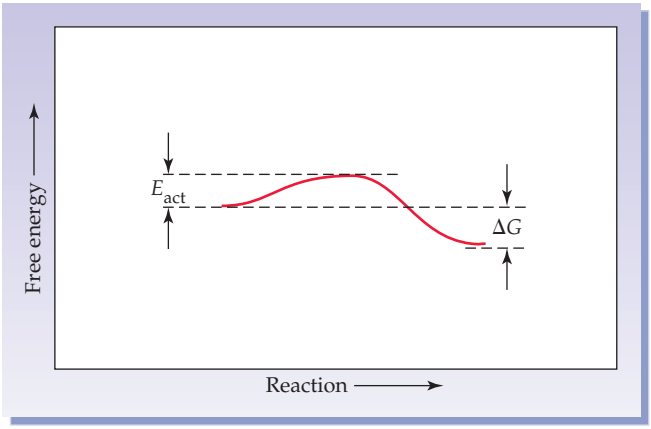
Consider the following energy diagram for a reaction. Is the reaction fast or slow? Is the reaction endergonic or exergonic? Would the reaction be spontaneous?



ANALYSIS The rate of the reaction is determined by the activation energy, E_{act}, while the free energy change (endergonic or exergonic) depends on the difference in free energy of the products compared to the reactants.

SOLUTION

The E_{act} for the reaction is small, as indicated in the following energy diagram, so we would expect the reaction to proceed rapidly. The free energy decreases slightly as the reaction proceeds from reactants to products, so ΔG is negative and the reaction is exergonic and spontaneous.



PROBLEM 7.9

The reaction between iron and oxygen to form rust occurs spontaneously. Based on your experience, does this reaction occur rapidly? What does this imply about the relative magnitudes of the activation energy and ΔG for the reaction? Explain.

7.6 Effects of Temperature, Concentration, and Catalysts on Reaction Rates

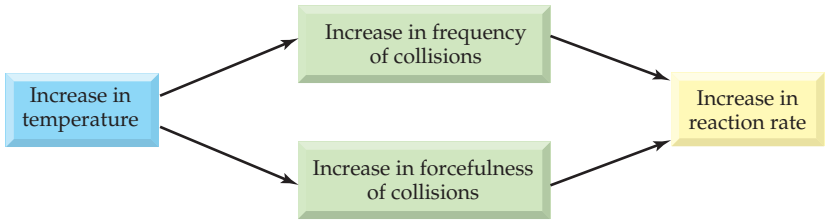
Learning Objective:

- Explain how temperature, concentration of reactants, and presence of a catalyst affect the rate of a reaction.

Several things can be done to help reactants over an activation energy barrier and thereby speed up a reaction. Let us look at some possibilities.

Temperature

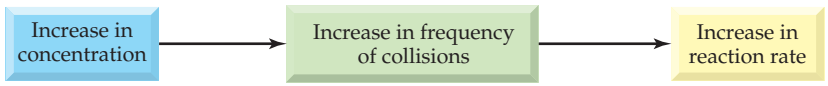
One way to increase reaction rate is to add energy to the reactants by raising the temperature. With more energy in the system, the reactants move faster, so the frequency of collisions increases. Furthermore, the force with which collisions occur increases, making them more likely to overcome the activation barrier. As a rule of thumb, a 283 K rise in temperature causes a reaction rate to double.



Concentration

Concentration A measure of the amount of a given substance in a mixture.

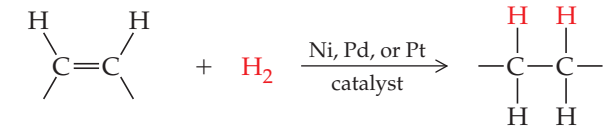
A second way to speed up a reaction is to increase the **concentrations** of the reactants. As the concentration increases, reactants are crowded together, and collisions between reactant molecules become more frequent. As the frequency of collisions increases, reactions between molecules become more likely. Flammable materials burn more rapidly in pure oxygen than in air, for instance, because the concentration of O_2 molecules is higher (air is approximately 21% oxygen). Hospitals must therefore take extraordinary precautions to ensure that no flames are used near patients receiving oxygen. Although different reactions respond differently to concentration changes, doubling or tripling a reactant concentration often doubles or triples the reaction rate.



Catalysts

Catalyst A substance that speeds up the rate of a chemical reaction but is itself unchanged.

A third way to speed up a reaction is to add a **catalyst**—a substance that accelerates a chemical reaction but is itself unchanged in the process. For example, metals such as nickel, palladium, and platinum catalyze the addition of hydrogen to the carbon–carbon double bonds in vegetable oils to yield semisolid margarine. Without the metal catalyst, the reaction does not occur.

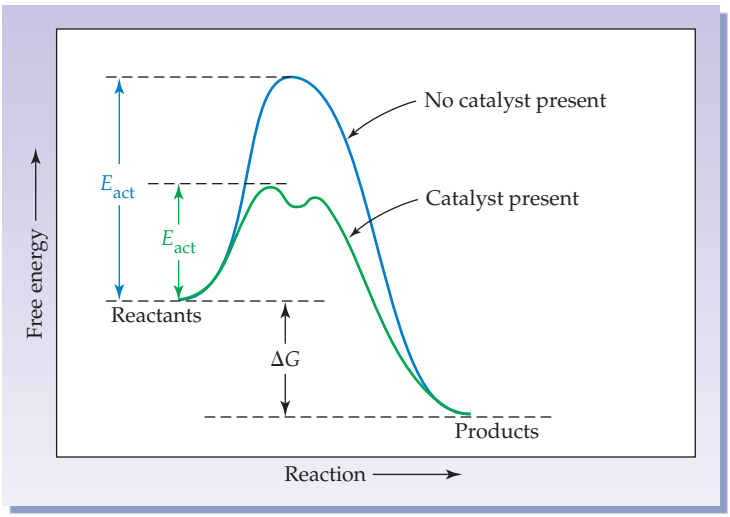


A double bond in vegetable oil

A single bond in margarine

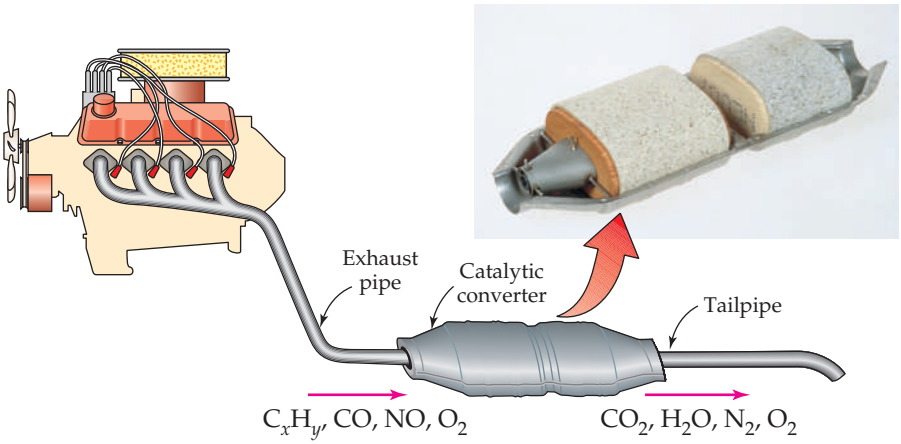
A catalyst does not affect the energy level of either reactants or products. Rather, it increases reaction rate either by letting a reaction take place by an alternative set of reaction steps with a lower activation energy or by orienting the reacting molecules appropriately. In a reaction energy diagram, the catalyzed reaction has a lower activation energy (Figure 7.4). A catalyzed reaction releases (or absorbs) the same amount of energy as an uncatalyzed reaction; it simply occurs more rapidly.

In addition to their widespread use in industry, we also rely on catalysts to reduce the air pollution created by exhaust from automobile engines. The catalytic converters in most automobiles are tubes packed with catalysts of two types (Figure 7.5). One catalyst accelerates the complete combustion of hydrocarbons and CO in the exhaust to give CO_2 and H_2O and the other decomposes NO to N_2 and O_2.



◀ **Figure 7.4**
A reaction energy diagram for a reaction in the presence (green curve) and absence (blue curve) of a catalyst.
The catalyzed reaction has a lower (E_{act}) because it uses an alternative pathway (represented by the multiple bumps in the green line) with a lower energy barrier.

The thousands of biochemical reactions continually taking place in our bodies are catalyzed by large protein molecules called *enzymes,* which promote reactions by controlling the orientation of the reacting molecules. Since almost every reaction is catalyzed by its own specific enzyme, the study of enzyme structure, activity, and control is a central part of biochemistry. We will look more closely at enzymes and how they work in Chapter 19.



▲ **Figure 7.5**
A catalytic converter.
The exhaust gases from an automobile pass through a two-stage catalytic converter. In one stage, carbon monoxide and unburned hydrocarbons are converted to CO_2 and H_2O. In the second stage, NO is converted to N_2 and O_2.

Table 7.3 summarizes the effects of changing conditions on reaction rates.

Table 7.3 Effects of Changes in Reaction Conditions on Reaction Rates

Change	Effect
Concentration	Increase in reactant concentration increases rate. Decrease in reactant concentration decreases rate.
Temperature	Increase in temperature increases rate. Decrease in temperature decreases rate.
Catalyst added	Increases reaction rate.

PROBLEM 7.10

Ammonia is synthesized industrially by reaction of nitrogen and hydrogen according to the equation $3\,H_2(g) + N_2(g) \longrightarrow 2\,NH_3(g)$. The free-energy change for this reaction is $\Delta G = -16\,kJ/mol$, yet this reaction does not readily occur at room temperature. List three ways to increase the rate of this reaction.

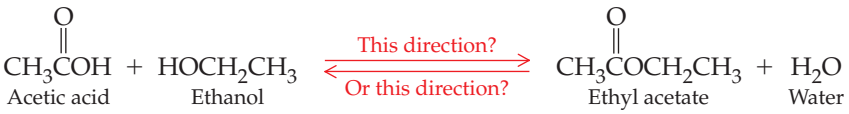
7.7 Reversible Reactions and Chemical Equilibrium

Learning Objective:

- Define chemical equilibrium for reversible reactions.

Many chemical reactions result in the complete conversion of reactants into products. When sodium metal reacts with chlorine gas, for example, both are entirely consumed. The sodium chloride product is so much more stable than the reactants that, once started, the reaction keeps going until it is complete.

What happens, though, when the reactants and products are of approximately equal stability? This is the case, for example, in the reaction of acetic acid (the main organic constituent of vinegar) with ethanol to yield ethyl acetate, a solvent used in nail-polish remover and glue.



Imagine the situation if you mix acetic acid and ethanol. The two begin to form ethyl acetate and water. But as soon as ethyl acetate and water form, they begin to go back to acetic acid and ethanol. Such a reaction, which easily goes in either direction, is a **reversible reaction** and is indicated by a double arrow ($\rightleftharpoons$) in equations. The reaction read from left to right as written is referred to as the *forward reaction,* and the reaction from right to left is the *reverse reaction.*

Reversible reaction A reaction that can go in either direction, from products to reactants or reactants to products.

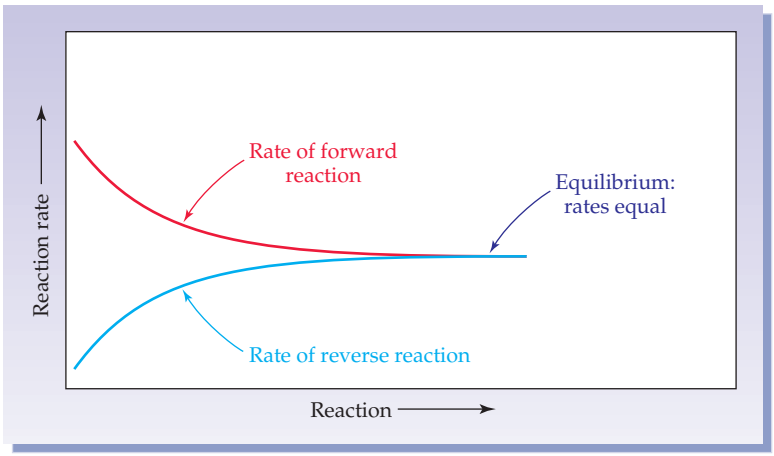
Now, suppose you mix some ethyl acetate and water. The same thing occurs: as soon as small quantities of acetic acid and ethanol form, the reaction in the other direction begins to take place. No matter which pair of reactants is mixed together, both reactions occur until ultimately the concentrations of reactants and products reach constant values and undergo no further change. At this point, the reaction vessel contains all four substances—acetic acid, ethyl acetate, ethanol, and water—and the reaction is in a state of **chemical equilibrium.**

Chemical equilibrium A state in which the rates of forward and reverse reactions are the same.

Since the reactant and product concentrations undergo no further change once equilibrium is reached, you might conclude that the forward and reverse reactions have stopped. That is not the case, however. The forward reaction takes place rapidly at the beginning of the reaction but then slows down as reactant concentrations decrease. At the same time, the reverse reaction takes place slowly at the beginning but then speeds up as product concentrations increase (Figure 7.6). Ultimately, the forward and reverse rates become equal and change no further.

Chemical equilibrium is an active, dynamic condition. All substances present are continuously being made and unmade at the same rate, so their concentrations are constant at equilibrium. As an analogy, think of two floors of a building connected by up and down escalators. If the number of people moving up is the same as the number of people moving down, the numbers of people on each floor remain constant. *Individual people* are continuously changing from one floor to the other, but the *total populations* of the two floors are in equilibrium. In complex biological systems, many reactions may be linked together to establish an equilibrium, called *homeostasis,* in which certain conditions such as body temperature or pH of blood are maintained at optimal levels.

Note that it is not necessary for the concentrations of reactants and products at equilibrium to be equal (just as it is not necessary for the numbers of people on two floors connected by escalators to be equal). Equilibrium can be reached at any point between pure products and pure reactants. The extent to which the forward or reverse reaction is favored over the other is a characteristic property of a given reaction under given conditions.



▲ **Figure 7.6**
Reaction rates in an equilibrium reaction.
The forward rate is large initially but decreases as the concentrations of reactants drop. The reverse rate is small initially but increases as the concentrations of products increase. At equilibrium, the forward and reverse reaction rates are equal.

7.8 Equilibrium Equations and Equilibrium Constants

Learning Objective:

- Define the equilibrium constant *(K)*, and use the value of *K* to predict the extent of reaction.

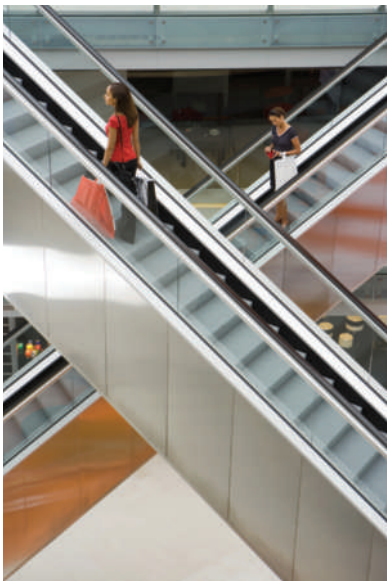
Remember that the rate of a reaction depends on the number of collisions between molecules (Section 7.5), and that the number of collisions in turn depends on concentration, that is, the number of molecules in a given volume (Section 7.6). For a reversible reaction, then, the rates of both the forward *and* the reverse reactions must depend on the concentration of reactants and products, respectively. When a reaction reaches equilibrium, the rates of the forward and reverse reactions are equal, and the concentrations of reactants and products remain constant. We can use this fact to obtain useful information about a reaction.

Let us look at the details of a specific equilibrium reaction. Suppose that you allow various mixtures of sulfur dioxide and oxygen to come to equilibrium with sulfur trioxide at a temperature of 1000 K and then measure the concentrations of all three gases in the mixtures.

$$2\,SO_2(g) + O_2(g) \rightleftharpoons 2\,SO_3(g)$$

In one experiment, we start with only 1.00 mol of SO_2 and 1.00 mol of O_2 in a 1.00 L container. In other words, the initial concentrations of reactants are 1.00 mol/L. When the reaction reaches equilibrium, we have 0.0620 mol/L of SO_2, 0.538 mol/L of O_2, and 0.938 mol/L of SO_3. In another experiment, we start with 1.00 mol/L of SO_3. When this reaction reaches equilibrium, we have 0.150 mol/L of SO_2, 0.0751 mol/L of O_2, and 0.850 mol/L of SO_3. In both cases, we see that there is substantially more product (SO_3) than reactants when the reaction reaches equilibrium, regardless of the starting conditions. Is it possible to predict what the equilibrium conditions will be for any given reaction?

As it turns out, the answer is YES! No matter what the original concentrations were, and no matter what concentrations remain at equilibrium, we find that a constant



▲ When the number of people moving up is the same as the number of people moving down, the number of people on each floor remains constant, and the two populations are in equilibrium.

numerical value is obtained if the equilibrium concentrations are substituted into the expression

$$\frac{[SO_3]^2}{[SO_2]^2[O_2]} = \text{constant at a given temperature}$$

The square brackets in this expression indicate the concentration of each substance expressed as moles per liter. Using the equilibrium concentrations for each of the experiments previously described, we can calculate the value and verify that it is constant:

$$\text{Experiment 1.} \quad \frac{[SO_3]^2}{[SO_2]^2[O_2]} = \frac{(0.938\ \text{mol/L})^2}{(0.0620\ \text{mol/L})^2(0.538\ \text{mol/L})} = 425$$

$$\text{Experiment 2.} \quad \frac{[SO_3]^2}{[SO_2]^2[O_2]} = \frac{(0.850\ \text{mol/L})^2}{(0.150\ \text{mol/L})^2(0.0751\ \text{mol/L})} = 428$$

At a temperature of 1000 K, the actual value of the constant is 429. Within experimental error, the ratios of product and reactant concentrations for the two experiments at equilibrium yield the same result. Numerous experiments like those just described have led to a general equation that is valid for any reaction. Consider a general reversible reaction:

$$a\text{A} + b\text{B} + \ldots \rightleftharpoons m\text{M} + n\text{N} + \ldots$$

where A, B, . . . are reactants; M, N, . . . are products; and *a, b,* . . . , *m, n,* . . . are coefficients in the balanced equation. At equilibrium, the composition of the reaction mixture obeys the following *equilibrium equation,* where *K* is the **equilibrium constant.**

Equilibrium constant *(K)* Value obtained at a given temperature from the ratio of the concentrations of products and reactants, each raised to a power equal to its coefficient in the balanced equation.

Equilibrium equation $K = \dfrac{[M]^m[N]^n \cdots}{[A]^a[B]^b \cdots}$ (Product concentrations; Reactant concentrations; *Equilibrium constant*)

The equilibrium constant *K* is the number obtained by multiplying the equilibrium concentrations of the products and dividing by the equilibrium concentrations of the reactants, with the concentration of each substance raised to a power equal to its coefficient in the balanced equation. If we take another look at the reaction between sulfur dioxide and oxygen, we can now see how the equilibrium constant was obtained:

$$2\,SO_2(g) + O_2(g) \rightleftharpoons 2\,SO_3(g)$$

$$K = \frac{[SO_3]^2}{[SO_2]^2\,[O_2]}$$

Note that if there is no coefficient for a reactant or product in the reaction equation, it is assumed to be 1. The value of *K* varies with temperature, but a temperature of 298 K is assumed unless otherwise specified—and units are usually omitted.

For reactions that involve pure solids or liquids, these pure substances are omitted when writing the equilibrium constant expression. To explain why, consider the decomposition of limestone:

The practice of omitting pure substances in the equilibrium constant expression will be utilized in Chapter 10 when we discuss equilibria involving acids and bases.

$$CaCO_3(s) \longrightarrow CaO(s) + CO_2(g)$$

Writing the equilibrium constant expression for this reaction as the concentration of products over the concentration of reactions would yield

$$K = \frac{[CaO][CO_2]}{[CaCO_3]}$$

Consider the solids CaO and $CaCO_3$. Their concentrations (in mol/L) can be calculated from their molar masses and densities at a given temperature. For example, the concentration of CaO at 298 K can be calculated as

$$\frac{\left(3.25\ \frac{\text{g CaO}}{\text{cm}^3}\right)\cdot\left(\frac{1000\ \text{cm}^3}{\text{L}}\right)}{56.08\ \frac{\text{g CaO}}{\text{mol CaO}}} = 58.0\ \frac{\text{mol CaO}}{\text{L}}$$

The ratio of products over reactants would change if CO_2 was added to or removed from the reaction. The concentration of CaO, however, is the same whether we have 10 g or 500 g. Adding solid CaO will not change the ratio of products over reactants. Since the concentration of solids is independent of the amount of solid present, these concentrations are omitted and the expression for K becomes

$$K = \frac{[\text{CaO}][\text{CO}_2]}{[\text{CaCO}_3]} = [\text{CO}_2]$$

The value of the equilibrium constant indicates the position of a reaction at equilibrium. If the forward reaction is favored, the product term $[\text{M}]^m[\text{N}]^n$ (numerator) is larger than the reactant term $[\text{A}]^a[\text{B}]^b$ (denominator), and the value of K is larger than one. If instead the reverse reaction is favored, $[\text{M}]^m[\text{N}]^n$ is smaller than $[\text{A}]^a[\text{B}]^b$ at equilibrium, and the value of K is smaller than one.

For a reaction such as the combination of hydrogen and oxygen to form water vapor, the equilibrium constant is enormous (3.1×10^{81}), showing how greatly the formation of water is favored. Equilibrium is effectively nonexistent for such reactions, and the reaction is described as *going to completion*.

On the other hand, the equilibrium constant is very small for a reaction such as the combination of nitrogen and oxygen at 298 K to give NO (4.7×10^{-31}), showing what we know from observation—that N_2 and O_2 in the air do not combine noticeably at room temperature:

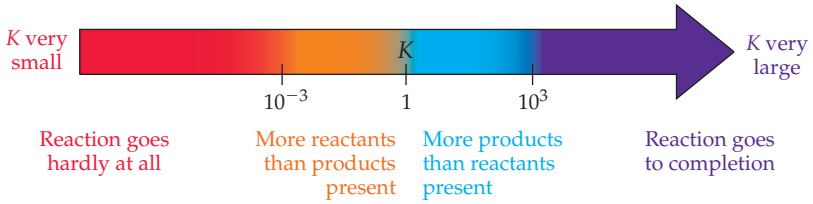
$$\text{N}_2(g) + \text{O}_2(g) \rightleftharpoons 2\,\text{NO}(g) \quad K = \frac{[\text{NO}]^2}{[\text{N}_2][\text{O}_2]} = 4.7 \times 10^{-31}$$

When K is close to 1, say between 10^3 and 10^{-3}, significant amounts of both reactants and products are present at equilibrium. An example is the reaction of acetic acid with ethanol to give ethyl acetate (Section 7.7). For this reaction, $K = 3.4$.

$$\text{CH}_3\text{CO}_2\text{H} + \text{CH}_3\text{CH}_2\text{OH} \rightleftharpoons \text{CH}_3\text{CO}_2\text{CH}_2\text{CH}_3 + \text{H}_2\text{O}$$

$$K = \frac{[\text{CH}_3\text{CO}_2\text{CH}_2\text{CH}_3][\text{H}_2\text{O}]}{[\text{CH}_3\text{CO}_2\text{H}][\text{CH}_3\text{CH}_2\text{OH}]} = 3.4$$

We can summarize the meaning of equilibrium constants in the following way:



K much smaller than 0.001	Only reactants are present at equilibrium; essentially no reaction occurs.
K between 0.001 and 1	More reactants than products are present at equilibrium.
K between 1 and 1000	More products than reactants are present at equilibrium.
K much larger than 1000	Only products are present at equilibrium; reaction goes essentially to completion.

Worked Example 7.7 Writing Equilibrium Equations

The first step in the industrial synthesis of hydrogen is the reaction of steam with methane to give carbon monoxide and hydrogen. Write the equilibrium equation for the reaction.

$$H_2O(g) + CH_4(g) \rightleftharpoons CO(g) + 3\,H_2(g)$$

ANALYSIS The equilibrium constant K is the number obtained by multiplying the equilibrium concentrations of the products (CO and H_2) and dividing by the equilibrium concentrations of the reactants (H_2O and CH_4), with the concentration of each substance raised to the power of its coefficient in the balanced equation.

SOLUTION

$$K = \frac{[CO][H_2]^3}{[H_2O][CH_4]}$$

Worked Example 7.8 Equilibrium Equations: Calculating *K*

In the reaction of Cl_2 with PCl_3, the concentrations of reactants and products were determined experimentally at equilibrium and found to be 7.2 mol/L for PCl_3, 7.2 mol/L for Cl_2, and 0.050 mol/L for PCl_5.

$$PCl_3(g) + Cl_2(g) \rightleftharpoons PCl_5(g)$$

Write the equilibrium equation, and calculate the equilibrium constant for the reaction. Which reaction is favored, the forward one or the reverse one?

ANALYSIS All the coefficients in the balanced equation are 1, so the equilibrium constant equals the concentration of the product, PCl_5, divided by the product of the concentrations of the two reactants, PCl_3 and Cl_2. Insert the values given for each concentration, and calculate the value of K.

BALLPARK ESTIMATE At equilibrium, the concentration of the reactants (7.2 mol/L for each reactant) is higher than the concentration of the product (0.05 mol/L), so we expect a value of K less than 1.

SOLUTION

$$K = \frac{[PCl_5]}{[PCl_3][Cl_2]} = \frac{0.050\ \text{mol/L}}{(7.2\ \text{mol/L})(7.2\ \text{mol/L})} = 9.6 \times 10^{-4}$$

The value of K is less than 1, so the reverse reaction is favored. Note that units for K are omitted.

BALLPARK CHECK Our calculated value of K is just as we predicted: $K < 1$.

PROBLEM 7.11

Write equilibrium equations for the following reactions:

(a) $N_2O_4(g) \rightleftharpoons 2\,NO_2(g)$

(b) $2\,H_2S(g) + O_2(g) \rightleftharpoons 2\,S(s) + 2\,H_2O(g)$

(c) $2\,BrF_5(g) \rightleftharpoons Br_2(g) + 5\,F_2(g)$

PROBLEM 7.12

Do the following reactions favor reactants or products at equilibrium? Give relative concentrations at equilibrium.

(a) $\text{Sucrose}(aq) + H_2O(l) \rightleftharpoons \text{Glucose}(aq) + \text{Fructose}(aq) \quad K = 1.4 \times 10^5$

(b) $NH_3(aq) + H_2O(l) \rightleftharpoons NH_4^+(aq) + OH^-(aq) \quad K = 1.6 \times 10^{-5}$

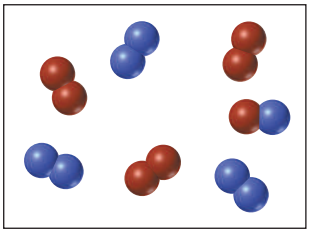
(c) $Fe_2O_3(s) + 3\,CO(g) \rightleftharpoons 2\,Fe(s) + 3\,CO_2(g) \quad K\,(\text{at } 1000\ \text{K}) = 24.2$

PROBLEM 7.13

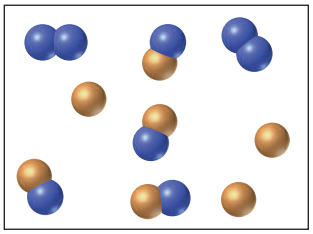
For the reaction $H_2(g) + I_2(g) \rightleftharpoons 2\,HI(g)$, equilibrium concentrations at 298 K are $[H_2] = 0.0510$ mol/L, $[I_2] = 0.174$ mol/L, and $[HI] = 0.507$ mol/L. What is the value of K at 298 K?

KEY CONCEPT PROBLEM 7.14

The following diagrams represent two similar reactions that have achieved equilibrium:



$A_2 + B_2 \longrightarrow 2\,AB$



$A_2 + 2B \longrightarrow 2\,AB$

(a) Write the expression for the equilibrium constant for each reaction.

(b) Calculate the value for the equilibrium constant for each reaction.

7.9 Le Châtelier's Principle: The Effect of Changing Conditions on Equilibria

Learning Objective:

- Use Le Châtelier's principle to predict the effect of changes in temperature, pressure, and concentrations on an equilibrium reaction.

The effect of a change in reaction conditions on chemical equilibrium is predicted by a general rule called *Le Châtelier's principle*.

Le Châtelier's principle When a stress is applied to a system at equilibrium, the equilibrium shifts to relieve the stress.

The word "stress" in this context means any change in concentration, pressure, volume, or temperature that disturbs the original equilibrium and causes the rates of the forward and reverse reactions to become temporarily unequal.

We saw in Section 7.6 that reaction rates are affected by changes in temperature and concentration and by addition of a catalyst. But what about equilibria? Are they similarly affected? The answer is that changes in concentration, temperature, and pressure *do* affect equilibria, but that addition of a catalyst does not (except to reduce the time it takes to reach equilibrium). The change caused by a catalyst affects forward and reverse reactions equally so that equilibrium concentrations are the same in both the presence and the absence of the catalyst.

Effect of Changes in Concentration

Let us look at the effect of a concentration change by considering the reaction of CO with H_2 to form CH_3OH (methanol). Once equilibrium is reached, the concentrations of the reactants and product are constant, and the forward and reverse reaction rates are equal.

$$CO(g) + 2\,H_2(g) \rightleftharpoons CH_3OH(g)$$

What happens if the concentration of CO is increased? To relieve the stress of added CO, according to Le Châtelier's principle, the extra CO must be used up. In other words, the rate of the forward reaction must increase to consume CO. Think of the CO added on the left as "pushing" the equilibrium to the right:

$$[CO \longrightarrow]$$
$$CO(g) + 2\,H_2(g) \rightleftharpoons CH_3OH(g)$$

Of course, as soon as more CH_3OH forms, the reverse reaction also speeds up, some CH_3OH converts back to CO and H_2. Ultimately, the forward and reverse reaction rates adjust until they are again equal, and equilibrium is reestablished. At this new

equilibrium state, the value of $[H_2]$ is lower because some of the H_2 reacted with the added CO and the value of $[CH_3OH]$ is higher because CH_3OH formed as the reaction was driven to the right by the addition of CO. The changes offset each other, however, so that the value of the equilibrium constant K remains constant.

$$CO(g) + 2\,H_2(g) \rightleftharpoons CH_3OH(g)$$

If this increases . . . . . then this decreases . . . . . and this increases . . .

. . . but this remains constant.

$$K = \frac{[CH_3OH]}{[CO]\,[H_2]^2}$$

What happens if CH_3OH is added to the reaction at equilibrium? Some of the methanol reacts to yield CO and H_2, making the values of $[CO]$, $[H_2]$, and $[CH_3OH]$ higher when equilibrium is reestablished. As before, the value of K does not change.

If this increases . . .

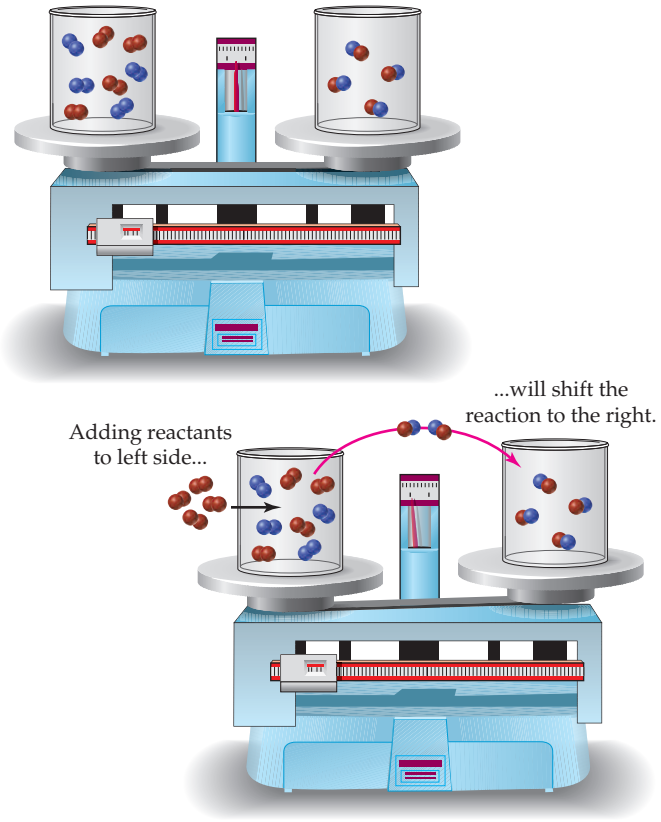
$$CO(g) + 2\,H_2(g) \rightleftharpoons CH_3OH(g)$$

. . . then this increases . . . . . and this increases . . .

. . . but this remains constant.

$$K = \frac{[CH_3OH]}{[CO]\,[H_2]^2}$$

Alternatively, we can view chemical equilibrium as a *balance* between the free energy of the reactants (on the left) and the free energy of the products (on the right). Adding more reactants tips the balance in favor of the reactants. In order to restore the balance, reactants must be converted to products, or the reaction must shift to the right. If, instead, we remove reactants, then the balance is too heavy on the product side and the reaction must shift left, generating more reactants to restore balance.



▶ Equilibrium represents a balance between the free energy of reactants and products. Adding reactants (or products) to one side upsets the balance, and the reaction will proceed in a direction to restore the balance.

Finally, what happens if a reactant is continuously supplied or a product is continuously removed? Because the concentrations are continuously changing, equilibrium can never be reached. As a result, it is sometimes possible to force a reaction to produce large quantities of a desirable product even when the equilibrium constant is unfavorable. Take the reaction of acetic acid with ethanol to yield ethyl acetate, for example. As discussed in the preceding section, the equilibrium constant K for this reaction is 3.4, meaning that substantial amounts of reactants and products are both present at equilibrium. If, however, the ethyl acetate is removed as soon as it is formed, the production of more and more product is forced to occur, in accord with Le Châtelier's principle.

Continuously removing this product from the reaction forces more of it to be produced.

$$\underset{\text{Acetic acid}}{CH_3COH} + \underset{\text{Ethanol}}{CH_3CH_2OH} \rightleftharpoons \underset{\text{Ethyl acetate}}{CH_3COCH_2CH_3} + H_2O$$

Metabolic reactions sometimes take advantage of this effect, with one reaction prevented from reaching equilibrium by the continuous consumption of its product in a further reaction.

Effect of Changes in Temperature and Pressure

We noted in Section 7.2 that the reverse of an exothermic reaction is always endothermic. Equilibrium reactions are therefore exothermic in one direction and endothermic in the other. Le Châtelier's principle predicts that an increase in temperature will cause an equilibrium to shift in favor of the endothermic reaction so the additional heat is absorbed. Conversely, a decrease in temperature will cause an equilibrium to shift in favor of the exothermic reaction so additional heat is released. In other words, you can think of heat as a reactant or product whose increase or decrease stresses an equilibrium just as a change in reactant or product concentration does.

Endothermic reaction (Heat is absorbed) — Favored by increase in temperature

Exothermic reaction (Heat is released) — Favored by decrease in temperature

In the exothermic reaction of N_2 with H_2 to form NH_3, for example, raising the temperature favors the reverse reaction, which absorbs the heat:

$$N_2(g) + 3\,H_2(g) \rightleftharpoons 2\,NH_3(g) + \text{Heat} \quad [\leftarrow \text{Heat}]$$

We can also use the balance analogy to predict the effect of temperature on an equilibrium mixture; again, we can think of heat as a reactant or product. Increasing the temperature of the reaction is the same as adding heat to the left side (for an endothermic reaction) or to the right side (for an exothermic reaction). The reaction then proceeds in the appropriate direction to restore "balance" to the system.

What about changing the pressure? Pressure influences an equilibrium only if one or more of the substances involved is a gas. As predicted by Le Châtelier's principle, increasing the pressure (by decreasing the volume) in such a reaction shifts the equilibrium in the direction that decreases the number of molecules in the gas phase and thus, decreases the pressure. For the ammonia synthesis, decreasing the volume *increases* the concentration of reactants and products but has a greater effect on the reactant side of the equilibrium since there are more moles of gas phase reactants. Increasing the pressure, therefore, favors the forward reaction because 4 mol of gas is converted to 2 mol of gas.

$$[\text{Pressure} \longrightarrow] \qquad \underbrace{N_2(g) + 3\,H_2(g)}_{\text{4 mol of gas}} \rightleftharpoons \underbrace{2\,NH_3(g)}_{\text{2 mol of gas}}$$

CHEMISTRY IN ACTION

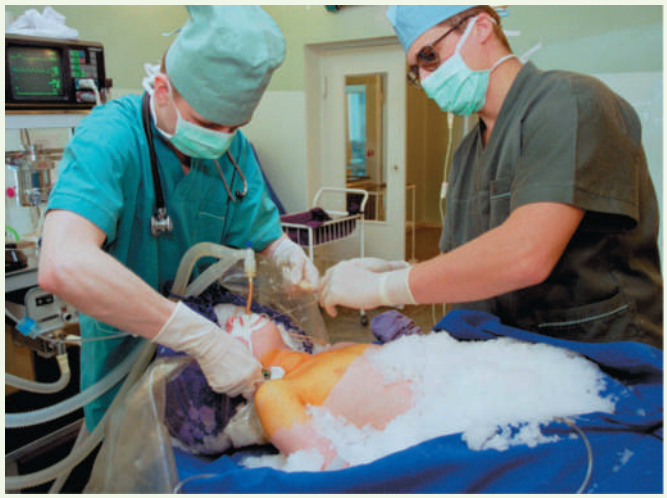
Regulation of Body Temperature

Living organisms are highly complex systems that use chemical reactions to produce the energy needed for daily activity. Many of these reactions occur very slowly—if at all—at normal body temperature, so organisms use several different strategies discussed in this chapter to obtain the energy they need and to function optimally. For example, the rates of slow reactions are increased by using biocatalysts, otherwise known as enzymes (Chapter 19). Le Châtelier's principle is used for regulation of critical processes, including oxygen transport (Chemistry in Action "Breathing and Oxygen Transport," p. 298) and blood pH (Chemistry in Action "Buffers in the Body: Acidosis and Alkalosis," p. 355). As mentioned in the beginning of the chapter, maintaining "normal" body temperature is crucial for mammals and other warm-blooded animals and is one of the conditions regulated by homeostasis. If the body's thermostat is unable to maintain a temperature of 310 K, the rates of the many thousands of chemical reactions that take place constantly in the body will change accordingly, with potentially disastrous consequences.

If, for example, a skater fell through the ice of a frozen lake, *hypothermia* could soon result. Hypothermia is a dangerous state that occurs when the body is unable to generate enough heat to maintain normal temperature. All chemical reactions in the body slow down because of the lower temperature, energy production drops, and death can result. Slowing the body's reactions can also be used to advantage, however. During open-heart surgery, the heart is stopped and maintained at about 288 K, while the body, which receives oxygenated blood from an external pump, is cooled to 288–305 K. In this case, the body is receiving oxygenated blood from an external pump in an operating chamber under medical supervision. If hypothermia occurred due to some other environmental condition, the heart would slow down, respiration would decrease, and the body would not receive sufficient oxygen and death would result.

Conversely, a marathon runner on a hot, humid day might become overheated, and *hyperthermia* could result. Hyperthermia, also called *heat stroke,* is an uncontrolled rise in temperature as the result of the body's inability to lose sufficient heat. Chemical reactions in the body are accelerated at higher temperatures, the heart struggles to pump blood faster to supply increased oxygen, and brain damage can result if the body temperature rises above 314 K.

Body temperature is maintained both by the thyroid gland and by the hypothalamus region of the brain, which act together to regulate metabolic rate. When the body's environment changes, temperature receptors in the skin, spinal cord, and abdomen send signals to the hypothalamus, which contains both heat-sensitive and cold-sensitive neurons.



▲ The body is cooled to 288–305 K by immersion in ice prior to open-heart surgery to slow down metabolism.

Stimulation of the heat-sensitive neurons on a hot day causes a variety of effects: Impulses are sent to stimulate the sweat glands, dilate the blood vessels of the skin, decrease muscular activity, and reduce metabolic rate. Sweating cools the body through evaporation; approximately 2260 J is removed by evaporation of 1.0 g of sweat. Dilated blood vessels cool the body by allowing more blood to flow close to the surface of the skin, where heat is removed by contact with air. Decreased muscular activity and a reduced metabolic rate cool the body by lowering internal heat production. Stimulation of the cold-sensitive neurons on a cold day also causes a variety of effects: The hormone epinephrine is released to stimulate metabolic rate; peripheral blood vessels contract to decrease blood flow to the skin and prevent heat loss; and muscular contractions increase to produce more heat, resulting in shivering and "goosebumps."

CIA Problem 7.3 Which body organs help to regulate body temperature?

CIA Problem 7.4 What is the purpose of blood vessel dilation?

The effects of changing reaction conditions on equilibria are summarized in Table 7.4.

Table 7.4 Effects of Changes in Reaction Conditions on Equilibria

Change	Effect
Concentration	Increase in reactant concentration or decrease in product concentration favors forward reaction. Increase in product concentration or decrease in reactant concentration favors reverse reaction.
Temperature	Increase in temperature favors endothermic reaction. Decrease in temperature favors exothermic reaction.
Pressure	Increase in pressure favors side with fewer moles of gas. Decrease in pressure favors side with more moles of gas.
Catalyst added	Equilibrium reached more quickly; value of *K* unchanged.

In Chapter 21, we will see how Le Châtelier's principle is exploited to keep chemical "traffic" moving through the body's metabolic pathways. It often happens that one reaction in a series is prevented from reaching equilibrium because its product is continuously consumed in another reaction.

Worked Example 7.9 Le Châtelier's Principle and Equilibrium Mixtures

Nitrogen reacts with oxygen to give NO:

$$N_2(g) + O_2(g) \rightleftharpoons 2\,NO(g) \quad \Delta H = +180\ kJ/mol$$

Explain the effects of the following changes on reactant and product concentrations:

(a) Increasing temperature

(b) Increasing the concentration of NO

(c) Adding a catalyst

SOLUTION

(a) The reaction is endothermic (positive ΔH), so increasing the temperature favors the forward reaction. The concentration of NO will be higher at equilibrium.

(b) Increasing the concentration of NO, a product, favors the reverse reaction. At equilibrium, the concentrations of both N_2 and O_2, as well as that of NO, will be higher.

(c) A catalyst accelerates the rate at which equilibrium is reached, but the concentrations at equilibrium do not change.

PROBLEM 7.15

Is the yield of SO_3 at equilibrium favored by a higher or lower pressure? By a higher or lower temperature?

$$2\,SO_2(g) + O_2(g) \rightleftharpoons 2\,SO_3(g) \quad \Delta H = -197\ kJ/mol$$

PROBLEM 7.16

What effect do the listed changes have on the position of the equilibrium in the reaction of carbon with hydrogen?

$$C(s) + 2\,H_2(g) \rightleftharpoons CH_4(g) \quad \Delta H = -75\ kJ/mol$$

(a) Increasing temperature

(b) Increasing pressure by decreasing volume

(c) Allowing CH_4 to escape continuously from the reaction vessel

PROBLEM 7.17

As we exercise, our bodies metabolize glucose, converting it to CO_2 and H_2O, to supply the energy necessary for physical activity. The simplified reaction is:

$$C_6H_{12}O_6(aq) + 6\,O_2(g) \longrightarrow 6\,CO_2(g) + 6\,H_2O(l) + 2840\ kJ$$

An individual weighing 68 kg jogging at 8 km/h for 30 minutes would burn 1138 kJ. How many moles of glucose would need to be metabolized to generate this required energy?

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Distinguish between potential and kinetic energy.** Energy can be classified as *potential energy* (energy that is stored) or as *kinetic energy* (energy in motion). Energy can be interconverted from one form to another.
- **Identify chemical reactions as endothermic or exothermic, and explain how the heats of reaction relate to the law of conservation of energy.** The law of conservation of energy states that energy can neither be created nor destroyed during a reaction. Energy can be converted from chemical or potential energy to heat and vice versa. Reactions that absorb heat (convert thermal energy to bond energies) are called *endothermic,* whereas reactions that release heat (convert bond energies to heat) are called *exothermic (see Problems 26–30, 67, 68, and 77).*
- **Use bond energies and stoichiometric relationships to calculate the enthalpy of a reaction and the total amount of heat consumed or produced.** The strength of a covalent bond is measured by its *bond dissociation energy,* the amount of energy that must be supplied to break the bond in an isolated gaseous molecule. For any reaction, the heat released or absorbed by changes in bonding is called the *heat of reaction* or *enthalpy change* (ΔH). If the total strength of the bonds formed in a reaction is greater than the total strength of the bonds broken, then heat is released (negative ΔH) and the reaction is *exothermic.* If the total strength of the bonds formed in a reaction is less than the total strength of the bonds broken, then heat is absorbed (positive ΔH) and the reaction is *endothermic (see Problems 23–26, 67–69, 72, 74, 76–78, and 80).*
- **Use enthalpy, entropy, and free energy to determine the spontaneity of a chemical reaction or process.** *Spontaneous reactions* are those that, once started, continue without external influence; nonspontaneous reactions require a continuous external influence. Spontaneity depends on two factors: the amount of heat absorbed or released in a reaction (ΔH) and the *entropy change* (ΔS), which measures the change in molecular disorder in a reaction. Spontaneous reactions are favored by a release of heat (negative ΔH) and/or an increase in disorder (positive ΔS). The *free-energy change* ΔG takes both factors into account, according to the equation $\Delta G = \Delta H - T\,\Delta S$. A negative value for ΔG indicates spontaneity, and a positive value for ΔG indicates nonspontaneity *(see Problems 18–20, 22, and 31–40).*
- **Use collision theory and reaction diagrams to explain the activation energy and free-energy change of a chemical reaction.** A chemical reaction occurs when reactant particles collide with proper orientation and sufficient energy to break bonds in reactants. The exact amount of collision energy necessary is called the *activation energy* ($\mathcal{E}_{act}$). A high activation energy results in a slow reaction because few collisions occur with sufficient force, whereas a low activation energy results in a fast reaction. The relationship between activation energy and the relative energies of reactants and products is illustrated using a *reaction diagram (see Problems 21, 41–43, 46–48, and 75).*
- **Explain how temperature, concentration of reactants, and presence of a catalyst affect the rate of a reaction.** Reaction rates can be increased by raising the temperature, by raising the concentrations of reactants, or by adding a *catalyst,* which accelerates a reaction without itself undergoing any change *(see Problems 44–48, 57, and 80).*
- **Define chemical equilibrium for reversible reactions.** A reaction that can occur in either the forward or reverse direction is *reversible* and will ultimately reach a state of *chemical equilibrium.* At equilibrium, the forward and reverse reactions occur at the same rate, and the concentrations of reactants and products are constant *(see Problems 49 and 50).*
- **Define the equilibrium constant *(K),* and use the value of *K* to predict the extent of reaction.** Every reversible reaction has a characteristic *equilibrium constant (K),* given by an *equilibrium equation* that can be derived from the balanced chemical equation as shown:

For the reaction: $aA + bB + \cdots \rightleftharpoons mM + nN + \cdots$

$$K = \frac{[M]^m[N]^n \cdots}{[A]^a[B]^b \cdots}$$

Product concentrations raised to powers equal to coefficients

Reactant concentrations raised to powers equal to coefficients

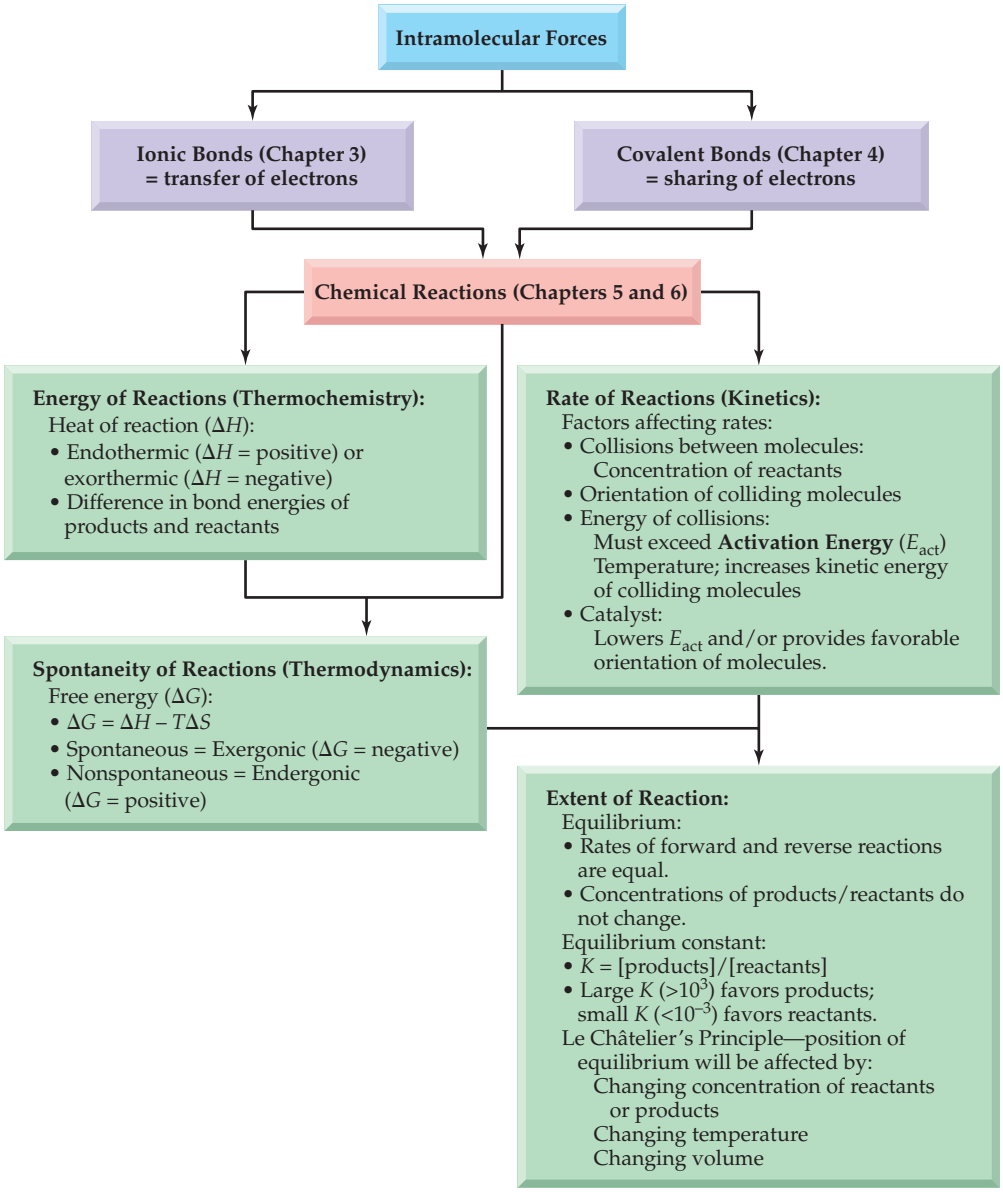
(see Problems 51–58 and 69).

- **Use Le Châtelier's principle to predict the effect of changes in temperature, pressure, and concentrations on an equilibrium reaction.** Le Châtelier's principle states that when a stress is applied to a system in equilibrium, the equilibrium shifts so that the stress is relieved. Applying this principle allows prediction of the effects of changes in temperature, pressure, and concentration *(see Problems 59–66, 70, 73, 79, and 80).*

KEY WORDS

Activation energy (E_{act}), *p. 230*
Bond dissociation energy, *p. 219*
Catalyst, *p. 232*
Chemical equilibrium, *p. 234*
Concentration, *p. 232*
Endergonic, *p. 228*
Endothermic, *p. 220*
Enthalpy (*H*), *p. 221*
Enthalpy change (ΔH), *p. 221*
Entropy (*S*), *p. 227*
Entropy change (ΔS), *p. 227*
Equilibrium constant (*K*), *p. 236*
Exergonic, *p. 228*
Exothermic, *p. 220*
Free-energy change (ΔG), *p. 228*
Heat, *p. 219*
Heat of reaction, *p. 221*
Kinetic energy, *p. 219*
Law of conservation of energy, *p. 220*
Le Châtelier's principle, *p. 239*
Potential energy, *p. 219*
Reaction rate, *p. 230*
Reversible reaction, *p. 234*
Spontaneous process, *p. 226*

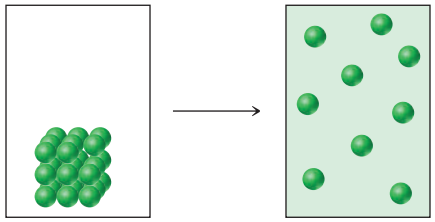
CONCEPT MAP: CHEMICAL REACTIONS: ENERGY, RATES, AND EQUILIBRIUM



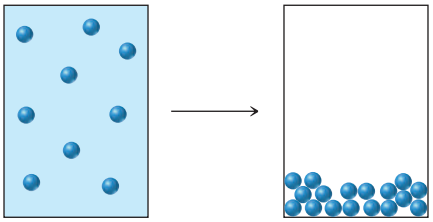
▲ **Figure 7.7 Concept Map.** We discussed the fundamentals of chemical reactions in Chapters 5 and 6. In this chapter, we looked at the heats of reaction, rates of reaction, spontaneity of reactions, and the extent of reaction as indicated by the equilibrium constant, *K*. These concepts, and the connections between them and previous concepts, are shown here.

UNDERSTANDING KEY CONCEPTS

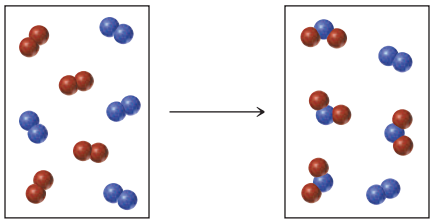
7.18 What are the signs of ΔH, ΔS, and ΔG for the spontaneous conversion of a crystalline solid into a gas? Explain.



7.19 What are the signs of ΔH, ΔS, and ΔG for the spontaneous condensation of a vapor to a liquid? Explain.



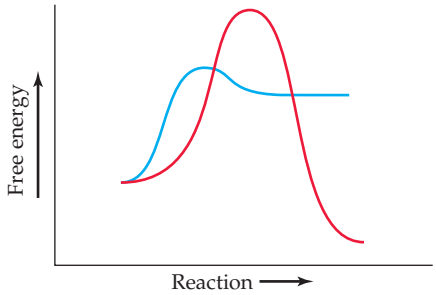
7.20 Consider the following spontaneous reaction of A_2 molecules (red) and B_2 molecules (blue):



(a) Write a balanced equation for the reaction.

(b) What are the signs of ΔH, ΔS, and ΔG for the reaction? Explain.

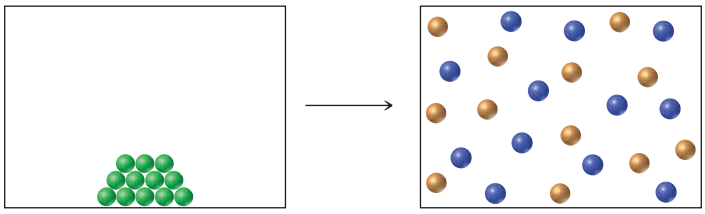
7.21 Two curves are shown in the following energy diagram:



(a) Which curve represents the faster reaction, and which the slower?

(b) Which curve represents the spontaneous reaction, and which the nonspontaneous?

7.22 The following diagram portrays a reaction of the type $A(s) \longrightarrow B(g) + C(g)$, where the different-colored spheres represent different molecular structures. Assume that the reaction has $\Delta H = +38.1$ kJ/mol.



(a) What is the sign of ΔS for the reaction?

(b) Is the reaction likely to be spontaneous at all temperatures, nonspontaneous at all temperatures, or spontaneous at some but nonspontaneous at others?

ADDITIONAL PROBLEMS

ENTHALPY AND HEAT OF REACTION (SECTIONS 7.1–7.3)

7.23 Is the total enthalpy *(H)* of the reactants for an endothermic reaction greater than or less than the total enthalpy of the products?

7.24 What is meant by the term *heat of reaction*? What other name is a synonym for this term?

7.25 The vaporization of Br_2 from the liquid to the gas state requires 31.0 kJ/mol.

(a) What is the sign of ΔH for this process? Write a reaction showing heat as a product or reactant.

(b) How many kilocalories are needed to vaporize 5.8 mol of Br_2?

(c) How many kilojoules are needed to evaporate 82 g of Br_2?

7.26 Converting liquid water to solid ice releases 6.02 kJ/mol.

(a) What is the sign of ΔH for this process? Write a reaction showing heat as a product or reactant.

(b) How many kilojoules are released by freezing 2.5 mol of H_2O?

(c) How many kilojoules are released by freezing 32 g of H_2O?

(d) How many kilojoules are absorbed by melting 1 mol of ice?

7.27 Ethyne $(H{-}C{\equiv}C{-}H)$ is the fuel used in welding torches.

(a) Write the balanced chemical equation for the combustion reaction of 1 mol of ethyne with $O_2(g)$ to produce $CO_2(g)$ and water vapor.

(b) Estimate ΔH for this reaction (in kJ/mol) using the bond energies listed in Table 7.1.

(c) Calculate the energy value (in kJ/g) for ethyne. How does it compare to the energy values for other fuels in Table 7.2?

7.28 Nitrogen in air reacts at high temperatures to form NO_2 according to the following reaction: $N_2 + 2\,O_2 \longrightarrow 2\,NO_2$

(a) Draw structures for the reactant and product molecules indicating single, double, and triple bonds.

(b) Estimate ΔH for this reaction (in kJ) using the bond energies from Table 7.1.

7.29 Glucose, also known as "blood sugar" when measured in blood, has the formula $C_6H_{12}O_6$.

(a) Write the equation for the combustion of glucose with O_2 to give CO_2 and H_2O.

(b) If 3.8 kcal (16 kJ) is released by combustion of each gram of glucose, how many kilojoules are released by the combustion of 1.50 mol of glucose?

(c) What is the minimum amount of energy (in kJ) a plant must absorb to produce 15.0 g of glucose?

7.30 During the combustion of 5.00 g of octane, C_8H_{18}, 1002 kJ is released.

(a) Write a balanced equation for the combustion reaction.

(b) What is the sign of ΔH for this reaction?

(c) How much energy (in kJ) is released by the combustion of 1.00 mol of C_8H_{18}?

(d) How many grams and how many moles of octane must be burned to release 1.90×10^3 kJ?

(e) How many kilojoules are released by the combustion of 17.0 g of C_8H_{18}?

ENTROPY AND FREE ENERGY (SECTION 7.4)

7.31 Which of the following processes results in an increase in entropy of the system?

(a) A drop of ink spreading out when it is placed in water

(b) Steam condensing into drops on windows

(c) Constructing a building from loose bricks

7.32 For each of the following processes, specify whether entropy increases or decreases. Explain each of your answers.

(a) Assembling a jigsaw puzzle

(b) $I_2(s) + 3\,F_2(g) \longrightarrow 2\,IF_3(g)$

(c) A precipitate forming when two solutions are mixed

(d) $C_6H_{12}O_6(aq) + 6\,O_2(g)6 \longrightarrow CO_2(g) + 6\,H_2O(g)$

(e) $CaCO_3(s) \longrightarrow CaO(s) + CO_2(g)$

(f) $Pb(NO_3)_2(aq) + 2\,NaCl(aq) \longrightarrow PbCl_2(s) + 2\,NaNO_3(aq)$

7.33 What two factors affect the spontaneity of a reaction?

7.34 What is the difference between an exothermic reaction and an exergonic reaction?

7.35 Why are most spontaneous reactions exothermic?

7.36 Under what conditions might a reaction be endothermic but exergonic? Explain.

7.37 For the reaction

$$NaCl(s) \xrightarrow{Water} Na^+(aq) + Cl^-(aq), \quad \Delta H = +4.184\ kJ/mol$$

(a) Is this process endothermic or exothermic?

(b) Does entropy increase or decrease in this process?

(c) Table salt (NaCl) readily dissolves in water. Explain, based on your answers to parts (a) and (b).

7.38 For the reaction $2\,Hg(l) + O_2(g) \longrightarrow 2\,HgO(s)$, $\Delta H = -180\ kJ/mol$.

(a) Does entropy increase or decrease in this process? Explain.

(b) Under what conditions would you expect this process to be spontaneous?

7.39 The reaction of gaseous H_2 and liquid Br_2 to give gaseous HBr has $\Delta H = -72.8\ kJ/mol$ and $\Delta S = 114\ J/(mol \cdot K)$.

(a) Write the balanced equation for this reaction.

(b) Does entropy increase or decrease in this process?

(c) Is this process spontaneous at all temperatures? Explain.

(d) What is the value of ΔG (in kJ) for the reaction at 300 K?

7.40 The following reaction is used in the industrial synthesis of polyvinyl chloride (PVC) polymer:

$$Cl_2(g) + H_2C{=}CH_2(g) \longrightarrow ClCH_2CH_2Cl(l), \quad \Delta H = -218\ kJ/mol$$

(a) Is ΔS positive or negative for this process?

(b) Is this process spontaneous at all temperatures? Explain.

RATES OF CHEMICAL REACTIONS (SECTIONS 7.5 AND 7.6)

7.41 What is the activation energy of a reaction?

7.42 Which reaction is faster, one with $E_{act} = +41.8\ kJ/mol$ or one with $E_{act} = +20.9\ kJ/mol$? Explain.

7.43 How does the rate of the forward reaction compare to the rate of the reverse reaction for an endergonic reaction? For an exergonic reaction? Explain.

7.44 Why does increasing concentration generally increase the rate of a reaction?

7.45 What is a catalyst, and what effect does it have on the activation energy of a reaction?

7.46 If a catalyst changes the activation energy of a forward reaction from 117 kJ/mol to 96 kJ/mol, what effect does it have on the reverse reaction?

7.47 For the reaction $C(s, \text{diamond}) \longrightarrow C(s, \text{graphite})$, $\Delta G = -2.90\ kJ/mol$ at 298 K.

(a) According to this information, do diamonds spontaneously turn into graphite?

(b) In light of your answer to part (a), why can diamonds be kept unchanged for thousands of years?

7.48 The reaction between hydrogen gas and carbon to produce the gas known as ethene is:

$$2\,H_2(g) + 2\,C(s) \longrightarrow H_2C{=}CH_2(g), \quad \Delta G = +68.2\ kJ/mol \text{ at } 298\ K$$

(a) Is this reaction spontaneous at 298 K?

(b) Would it be reasonable to try to develop a catalyst for the reaction run at 298 K? Explain.

CHEMICAL EQUILIBRIA (SECTIONS 7.7 AND 7.8)

7.49 What is meant by the term "chemical equilibrium"? Must amounts of reactants and products be equal at equilibrium?

7.50 Why do catalysts not alter the amounts of reactants and products present at equilibrium?

7.51 Write the equilibrium constant expressions for the following reactions:

(a) $2\,CO(g) + O_2(g) \rightleftharpoons 2\,CO_2(g)$

(b) $Mg(s) + HCl(aq) \rightleftharpoons MgCl_2(aq) + H_2(g)$

(c) $HF(aq) + H_2O(l) \rightleftharpoons H_3O^+(aq) + F^-(aq)$

(d) $S(s) + O_2(g) \rightleftharpoons SO_2(g)$

7.52 Write the equilibrium constant expressions for the following reactions.

(a) $S_2(g) + 2\,H_2(g) \rightleftharpoons 2\,H_2S(g)$

(b) $H_2S(aq) + Cl_2(aq) \rightleftharpoons S(s) + 2\,HCl(aq)$

(c) $Br_2(g) + Cl_2(g) \rightleftharpoons 2\,BrCl(g)$

(d) $C(s) + H_2O(g) \rightleftharpoons CO(g) + H_2(g)$

7.53 For the reaction $N_2O_4(g) \rightleftharpoons 2\,NO_2(g)$, the equilibrium concentrations at 298 K are $[NO_2] = 0.0325\ mol/L$ and $[N_2O_4] = 0.147\ mol/L$.

(a) What is the value of K at 298 K? Are reactants or products favored?

7.54 For the reaction $2\,CO(g) + O_2(g) \rightleftharpoons 2\,CO_2(g)$, the equilibrium concentrations at a certain temperature are $[CO_2] = 0.11$ mol/L, $[O_2] = 0.015$ mol/L, and $[CO] = 0.025$ mol/L.

(a) Write the equilibrium constant expression for the reaction.

(b) What is the value of K at this temperature? Are reactants or products favored?

7.55 Use your answer from Problem 7.53 to calculate the following:

(a) $[N_2O_4]$ at equilibrium when $[NO_2] = 0.0250$ mol/L

(b) $[NO_2]$ at equilibrium when $[N_2O_4] = 0.0750$ mol/L

7.56 Use your answer from Problem 7.54 to calculate the following:

(a) $[O_2]$ at equilibrium when $[CO_2] = 0.18$ mol/L and $[CO] = 0.0200$ mol/L

(b) $[CO_2]$ at equilibrium when $[CO] = 0.080$ mol/L and $[O_2] = 0.520$ mol/L

7.57 Would you expect to find relatively more reactants or more products for the reaction in Problem 7.53 if the pressure is raised by decreasing the volume? Explain.

7.58 Would you expect to find relatively more reactants or more products for the reaction in Problem 7.54 if the pressure is lowered by increasing the volume?

LE CHÂTELIER'S PRINCIPLE (SECTION 7.9)

7.59 Oxygen can be converted into ozone by the action of lightning or electric sparks:

$$3\,O_2(g) \rightleftharpoons 2\,O_3(g)$$

For this reaction, $\Delta H = +285$ kJ/mol and $K = 2.68 \times 10^{-29}$ at 298 K.

(a) Is the reaction exothermic or endothermic?

(b) Are the reactants or the products favored at equilibrium?

(c) Explain the effect on the equilibrium of

(1) Increasing pressure by decreasing volume

(2) Increasing the concentration of $O_2(g)$

(3) Increasing the concentration of $O_3(g)$

(4) Adding a catalyst

(5) Increasing the temperature

7.60 Hydrogen chloride can be made from the reaction of chlorine and hydrogen:

$$Cl_2(g) + H_2(g) \longrightarrow 2\,HCl(g)$$

For this reaction, $K = 26 \times 10^{33}$ and $\Delta H = -184$ kJ/mol at 298 K.

(a) Is the reaction endothermic or exothermic?

(b) Are the reactants or the products favored at equilibrium?

(c) Explain the effect on the equilibrium of

(1) Increasing pressure by decreasing volume

(2) Increasing the concentration of $HCl(g)$

(3) Decreasing the concentration of $Cl_2(g)$

(4) Increasing the concentration of $H_2(g)$

(5) Adding a catalyst

7.61 When the following equilibria are disturbed by increasing the pressure, does the concentration of reaction products increase, decrease, or remain the same?

(a) $2\,CO_2(g) \rightleftharpoons 2\,CO(g) + O_2(g)$

(b) $N_2(g) + O_2(g) \rightleftharpoons 2\,NO(g)$

(c) $Si(s) + 2\,Cl_2(g) \rightleftharpoons SiCl_4(g)$

7.62 For the following equilibria, use Le Châtelier's principle to predict the direction of the reaction when the pressure is increased by decreasing the volume of the equilibrium mixture.

(a) $C(s) + H_2O(g) \rightleftharpoons CO(g) + H_2(g)$

(b) $2\,H_2(g) + O_2(g) \rightleftharpoons 2\,H_2O(g)$

(c) $2\,Fe(s) + 3\,H_2O(g) \rightleftharpoons Fe_2O_3(s) + 3\,H_2(g)$

7.63 The reaction $CO(g) + H_2O(g) \rightleftharpoons CO_2(g) + H_2(g)$ has $\Delta H = -41$ kJ/mol. Does the amount of H_2 in an equilibrium mixture increase or decrease when the temperature is decreased?

7.64 The reaction $3\,O_2(g) \rightleftharpoons 2\,O_3(g)$ has $\Delta H = +285$ kJ/mol. Does the equilibrium constant for the reaction increase or decrease when the temperature increases?

7.65 The reaction $H_2(g) + I_2(g) \rightleftharpoons 2\,HI(g)$ has $\Delta H = -9.2$ kJ/mol. Will the equilibrium concentration of HI increase or decrease when

(a) I_2 is added?

(b) H_2 is removed?

(c) A catalyst is added?

(d) The temperature is increased?

7.66 The reaction $Fe^{3+}(aq) + Cl^-(aq) \rightleftharpoons FeCl^{2+}(aq)$ is endothermic. How will the equilibrium concentration of $FeCl^{2+}$ change when

(a) $Fe(NO_3)_3$ is added?

(b) Cl^- is precipitated by addition of $AgNO_3$?

(c) The temperature is increased?

(d) A catalyst is added?

CONCEPTUAL PROBLEMS

7.67 For the unbalanced combustion reaction shown, 1 mol of ethanol, C_2H_5OH, releases 1370 kJ:

$$C_2H_5OH + O_2 \longrightarrow CO_2 + H_2O$$

(a) Write a balanced equation for the combustion reaction.

(b) What is the sign of ΔH for this reaction?

(c) How much heat (in kilocalories) is released from the combustion of 5.00 g of ethanol?

(d) How many grams of C_2H_5OH must be burned to raise the temperature of 500.0 mL of water from 20.0 °C to 100.0 °C? (The specific heat of water is 4.184 J/g · °C. See Section 1.11.)

(e) If the density of ethanol is 0.789 g/mL, calculate the combustion energy of ethanol in kilojoules/milliliter.

7.68 For the production of ammonia from its elements, $\Delta H = -92$ kJ/mol.

(a) Is this process endothermic or exothermic?

(b) How much energy (in kilocalories and kilojoules) is involved in the production of 0.700 mol of NH_3?

7.69 Magnetite, an iron ore with formula Fe_3O_4, can be reduced by treatment with hydrogen to yield iron metal and water vapor.

(a) Write the balanced equation.

(b) This process requires 151 kJ for every 1.00 mol of Fe_3O_4 reduced. How much energy (in kilojoules) is required to produce 55 g of iron?

(c) How many grams of hydrogen are needed to produce 75 g of iron?

(d) This reaction has $K = 2.3 \times 10^{-18}$. Are the reactants or the products favored?

7.70 Hemoglobin (Hb) reacts reversibly with O_2 to form HbO_2, a substance that transfers oxygen to tissues:

$$Hb(aq) + O_2(aq) \rightleftharpoons HbO_2(aq)$$

Carbon monoxide (CO) is attracted to Hb 140 times more strongly than O_2 and establishes another equilibrium.

(a) Explain, using Le Châtelier's principle, why inhalation of CO can cause weakening and eventual death.

(b) Still another equilibrium is established when both O_2 and CO are present:

$$Hb(CO)(aq) + O_2(aq) \rightleftharpoons HbO_2(aq) + CO(aq)$$

Explain, using Le Châtelier's principle, why pure oxygen is often administered to victims of CO poisoning.

7.71 Urea is a metabolic waste product that decomposes to ammonia and water according to the following reaction:

$$NH_2CONH_2 + H_2O \longrightarrow 2\,NH_3 + CO_2.$$

(a) Draw the Lewis structure for urea.

(b) Estimate ΔH (in kJ) for this reaction using the bond energies from Table 7.1.

7.72 For the evaporation of water, $H_2O(l) \longrightarrow H_2O(g)$, at 373 K, $\Delta H = +40.7$ kJ/mol.

(a) How many kilojoules are needed to vaporize 10.0 g of $H_2O(l)$?

(b) How many kilojoules are released when 10.0 g of $H_2O(g)$ is condensed?

7.73 Ammonia reacts slowly in air to produce nitrogen monoxide and water vapor:

$$NH_3(g) + O_2(g) \rightleftharpoons NO(g) + H_2O(g) + \text{Heat}$$

(a) Balance the equation.

(b) Write the equilibrium equation.

(c) Explain the effect on the equilibrium of

(1) Raising the pressure

(2) Adding $NO(g)$

(3) Decreasing the concentration of NH_3

(4) Lowering the temperature

7.74 Methanol, CH_3OH, is used as race car fuel.

(a) Write the balanced equation for the combustion reaction of methanol with O_2 to form CO_2 and H_2O.

(b) $\Delta H = -728$ kJ/mol methanol for the process. How many kilojoules are released by burning 1.85 mol of methanol?

(c) How many kilojoules are released by burning 50.0 g of methanol?

7.75 Sketch an energy diagram for a system in which the forward reaction has $E_{act} = +105$ kJ/mol and the reverse reaction has $E_{act} = +146$ kJ/mol.

(a) Is the forward process endergonic or exergonic?

(b) What is the value of ΔG for the reaction?

7.76 The thermite reaction (photograph, p. 221), in which aluminum metal reacts with iron(III) oxide to produce a spectacular display of sparks, is so exothermic that the product (iron) is in the molten state:

$$2\,Al(s) + Fe_2O_3(s) \longrightarrow 2\,Al_2O_3(s) + 2\,Fe(l) \qquad \Delta H = -848.9\ \text{kJ/mol}$$

(a) How much heat is released (in kilojoules) when 0.255 mol of Al is used in this reaction?

(b) How much heat (in kilocalories) is released when 5.00 g of Al is used in the reaction?

7.77 How much heat (in kilocalories) is evolved or absorbed in the reaction of 1.00 g of Na with H_2O? Is the reaction exothermic or endothermic?

$$2\,Na(s) + 2\,H_2O(l) \longrightarrow 2\,NaOH(aq) + H_2(g) \qquad \Delta H = -368\ \text{kJ/mol}$$

GROUP PROBLEMS

7.78 Obtain a package of your favorite snack food and examine the nutritional information on the label. Confirm the caloric value listed by using the conversions listed in the table in the Chemistry in Action feature "Energy from Food" (p. 225). Alternatively, you can use the estimates for caloric value for a given food as provided in the table.

(a) Do some research to find out the amount of calories associated with typical physical activities (e.g., walking or jogging, riding a bicycle, swimming laps).

(b) How long would you have to engage in each of the physical activities to burn the calories contained in your snack?

7.79 Most living organisms use glucose in cellular metabolism to produce energy, but blood glucose levels that are too high can be toxic. Do a little research on the role of insulin in the regulation of blood glucose. Explain the process in terms of Le Châtelier's principle.

7.80 Ammonia is an important chemical used in the production of fertilizer. Industrial production of ammonia from atmospheric nitrogen is difficult because of the energy required to cleave the N–N triple bond. Consider the balanced reaction of ammonia: $N_2(g) + 3\,H_2(g) \longrightarrow 2\,NH_3(g)$. This reaction has a value of $K = 4.3 \times 10^{-2}$ at 298 K.

(a) Estimate the ΔH for this reaction using bond energies. Is the process endothermic or exothermic?

(b) Using Le Châtelier's principle, identify three ways you might increase the production of ammonia.

(c) Do some research on the Haber–Bosch process, developed in the early 1900s. What methods did this process use to increase production of ammonia (i.e., shift the equilibrium to the right)?

8

Gases, Liquids, and Solids

CONTENTS

CONCEPTS TO REVIEW

A. Specific Heat (Section 1.11)

B. Ionic Bonds (Section 3.7)

C. Polar Covalent Bonds and Polar Molecules (Sections 4.9 and 4.10)

D. Enthalpy, Entropy, and Free Energy (Sections 7.2–7.4)

▲ Aloe vera gel, extracted from the leaves of the succulent ornamental plant using supercritical fluid extraction, has many uses in cosmetics and alternative medicine.

Carbon dioxide is a gas at room temperature and is a significant component of the Earth's atmosphere. You may also be familiar with "dry ice," which is solid CO_2, and which evaporates directly to the gas phase. But have you ever seen "liquid" carbon dioxide? As a matter of fact, CO_2 can exist in a liquid-like state, known as a supercritical fluid, under conditions of elevated pressures and temperature. As you will learn in more detail in the Chemistry in Action on page 280 of this chapter, this unique state of matter has physical properties that make it particularly well suited for applications such as extracting potentially therapeutic natural products from plants—such as aloe vera, featured in the photo above. Supercritical fluid is also used for removing caffeine from coffee beans, cleaning and sterilizing medical implants, and for processing drugs to produce microencapsulated drug delivery systems. But what are the

characteristic properties of supercritical fluids and the other different states of matter, and how are those properties related to molecular structure?

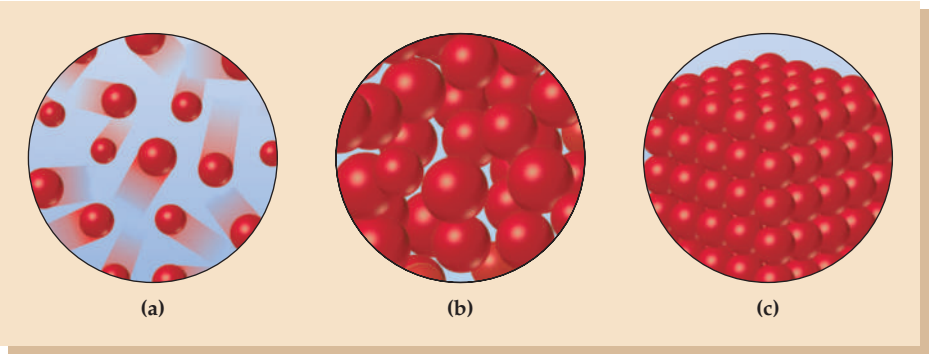
In the previous seven chapters, we dealt with matter at the atomic level. We have seen that all matter is composed of atoms, ions, or molecules; these particles are in constant motion; atoms combine to make compounds using chemical bonds; and physical and chemical changes are accompanied by the release or absorption of energy. Furthermore, we have distinguished between ionic and covalent compounds and between polar and nonpolar substances. In this chapter, we will concentrate on the large-scale behavior of visible amounts of matter, and how that behavior is related to molecular structure and affected by external factors such as temperature and pressure.

8.1 States of Matter and Their Changes

Learning Objective:

- Identify phase changes as endothermic or exothermic, and predict how a change in temperature will affect a phase change.

Matter exists in any of three phases, or *states*—solid, liquid, or gas. The state in which a compound exists under a given set of conditions depends on the relative strength of the attractive forces between particles compared to the kinetic energy of the particles. Kinetic energy (Section 7.1) is energy associated with motion and is related to the temperature of the substance. In gases, the attractive forces between particles are very weak compared to their kinetic energy, so the particles move about freely, are far apart, and have almost no influence on one another. In liquids, the attractive forces between particles are stronger, pulling the particles close together but still allowing them considerable freedom to move about. In solids, the attractive forces are much stronger than the kinetic energy of the particles, so the atoms, molecules, or ions are held in a specific arrangement and can only vibrate in place (Figure 8.1).



◀ **Figure 8.1**
A molecular comparison of gases, liquids, and solids.
(a) In gases, the particles feel little attraction for one another and are free to move about randomly. (b) In liquids, the particles are held close together by attractive forces but are free to slide over one another. (c) In solids, the particles are strongly attracted to one another. They can move slightly but are held in a fairly rigid arrangement with respect to one another.

The transformation of a substance from one state to another is called a *phase change* or a **change of state.** Every change of state is reversible and, like all chemical and physical processes, is characterized by changes in enthalpy and entropy.

Change of state The change of a substance from one state of matter (gas, liquid, or solid) to another.

The enthalpy change ΔH is a measure of the heat absorbed or released during a given change of state. The magnitude of ΔH depends on the attractive forces between molecules; as heat is absorbed, the kinetic energy of molecules increases until it is sufficient to overcome the forces of attraction. In the melting of a solid to a liquid, for example, heat is absorbed and ΔH is positive (endothermic). In the reverse process—the freezing of a liquid to a solid—the potential energy of attractive forces between molecules is converted to thermal energy; heat is released and ΔH is negative (exothermic). Look at the change between ice and water, for instance:

CONCEPTS TO REVIEW Review Sections 7.3 and 7.4 to brush up on these concepts.

$$\textbf{Melting:}\quad H_2O(s) \longrightarrow H_2O(l) \qquad \Delta H = +6.02\ \text{kJ/mol}$$

$$\textbf{Freezing:}\quad H_2O(l) \longrightarrow H_2O(s) \qquad \Delta H = -6.02\ \text{kJ/mol}$$

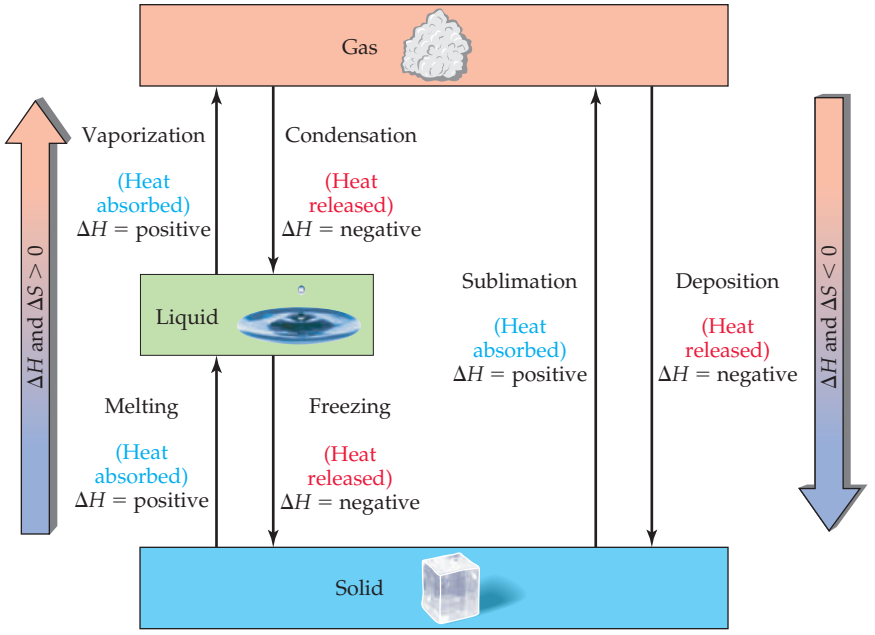
The entropy change ΔS is a measure of the change in molecular disorder or freedom that occurs during a process. In the melting of a solid to a liquid, for example, disorder increases because particles gain freedom of motion, so ΔS is positive. In the reverse process—the freezing of a liquid to a solid—disorder decreases as particles are locked into position, so ΔS is negative. Look at the change between ice and water:

$$\textbf{Melting:}\ H_2O(s) \longrightarrow H_2O(l) \quad \Delta S = +22.0\ \text{J}/(\text{mol}\cdot\text{K})$$
$$\textbf{Freezing:}\ H_2O(l) \longrightarrow H_2O(s) \quad \Delta S = -22.0\ \text{J}/(\text{mol}\cdot\text{K})$$

Melting point (mp) The temperature at which solid and liquid are in equilibrium.

Boiling point (bp) The temperature at which liquid and gas are in equilibrium.

The enthalpy and entropy associated with phase changes are contrary; the melting of ice, for instance, is unfavored by a positive ΔH but favored by a positive ΔS. Similarly, the freezing of water is favored by a negative ΔH but is unfavored by a negative ΔS. The exact temperature at which these two factors (ΔH and ΔS) exactly balance out is called the **melting point (mp)** and represents the temperature at which solid and liquid coexist in equilibrium. In the corresponding change from a liquid to a gas, the two states are in equilibrium at the **boiling point (bp).**



▶ **Figure 8.2**
Changes of state.
The changes are endothermic from bottom to top and exothermic from top to bottom.

The names and enthalpy changes associated with the different changes of state are summarized in Figure 8.2. Note that a solid can change directly to a gas without going through the liquid state—a process called *sublimation*. Dry ice (solid CO_2) at atmospheric pressure, for example, changes directly to a gas without melting.

PROBLEM 8.1

The change of state from liquid H_2O to gaseous H_2O has $\Delta H = +40.7\ \text{kJ/mol}$ and $\Delta S = -109\ \text{J}/(\text{mol}\cdot\text{K})$.

(a) Is the change from liquid to gaseous H_2O favored or unfavored by ΔH? By ΔS?

(b) What are the values of ΔH and ΔS (in kJ/mol) for the change from gaseous to liquid H_2O?

8.2 Intermolecular Forces

Learning Objective:

- Identify the different types of intermolecular attractive forces, and predict the predominant forces responsible for the physical properties of a given substance.

What determines whether a substance is a gas, a liquid, or a solid at a given temperature? Why does rubbing alcohol evaporate much more readily than water? Why do molecular compounds have lower melting points than ionic compounds? To answer these and a great many other such questions, we need to look into the nature of **intermolecular forces**—the forces that act *between different molecules* rather than within an individual molecule.

Intermolecular forces Forces that act between molecules or discrete atoms and hold them close to one another. Also called **van der Waals forces**.

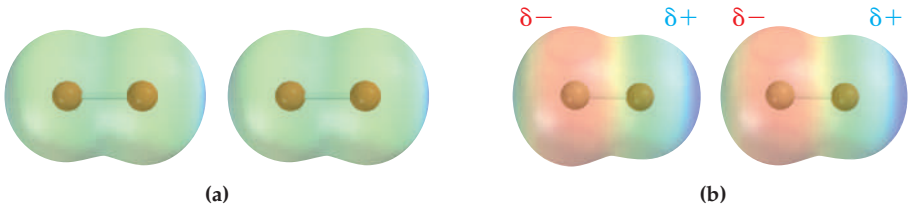
In gases, the intermolecular forces are negligible, so the gas molecules act independently of one another. In liquids and solids, however, intermolecular forces are strong enough to hold the molecules in close contact. As a general rule, the stronger the intermolecular forces in a substance, the more difficult it is to separate the molecules, and the higher the melting and boiling points of the substance.

There are three major types of intermolecular forces: *London dispersion, dipole–dipole,* and *hydrogen bonding.* Collectively, these attractive forces are also known as **van der Waals forces,** and we will discuss each in turn.

London Dispersion Forces

All molecules, regardless of structure, experience *London dispersion forces.* **London dispersion forces** are caused by the constant motion of electrons within molecules. Take even a simple nonpolar molecule like Br_2, for example. Averaged over time, the distribution of electrons throughout the molecule is uniform, but at any given *instant* there may be more electrons at one end of the molecule than at the other (Figure 8.3). At that instant, the molecule has a short-lived polarity. Electrons in neighboring molecules are attracted to the positive end of the polarized molecule, resulting in a polarization of the neighbor and creation of an attractive London dispersion force that holds the molecules together. As a result, Br_2 is a liquid at room temperature rather than a gas.

London dispersion force The short-lived attractive force due to the constant motion of electrons within molecules.



◄ Figure 8.3
(a) Averaged over time, the electron distribution in a Br_2 molecule is symmetrical. (b) At any given instant, however, the electron distribution may be unsymmetrical, resulting in a temporary polarity that induces a complementary polarity in neighboring molecules.

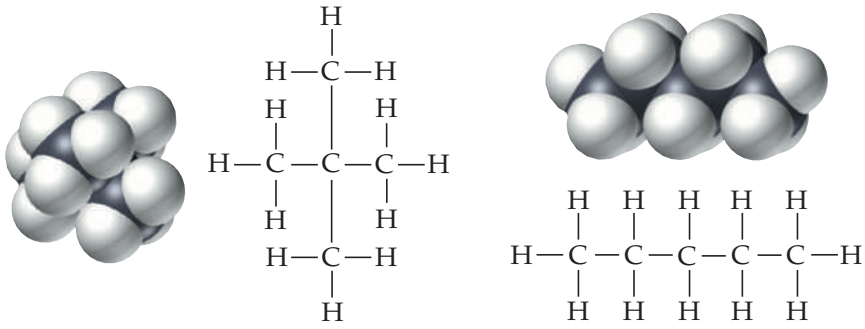
London dispersion forces are the only intermolecular force available to nonpolar molecules; they are relatively weak—in the range 2–10 kJ/mol—but they increase with molecular mass and amount of surface area available for interaction between molecules. The larger the molecular mass, the more electrons there are moving about and the greater the temporary polarization of a molecule. The larger the amount of surface contact, the greater the close interaction between different molecules.

The effect of surface area on the magnitude of London dispersion forces can be seen by comparing a roughly spherical molecule with a flatter, more linear one having the same molecular mass. Both 2,2-dimethylpropane and pentane, for instance, have the same formula (C_5H_{12}), but the nearly spherical shape of 2,2-dimethylpropane allows for less surface contact with neighboring molecules than does the more linear shape of pentane (Figure 8.4). As a result, London dispersion forces are smaller for 2,2-dimethylpropane, molecules are held together less tightly, and the boiling point is correspondingly lower: 9.5 °C for 2,2-dimethylpropane versus 36 °C for pentane.

Dipole–Dipole Forces

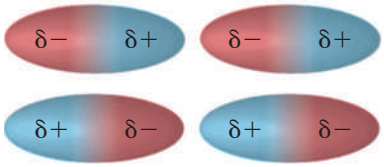
Many molecules contain polar covalent bonds and may therefore have a permanent net molecular polarity. In such cases, the positive and negative ends of different molecules are attracted to one another by what is called a **dipole–dipole force** (Figure 8.5).

Dipole–dipole force The attractive force between positive and negative ends of polar molecules.



(a) 2,2-Dimethylpropane (bp = 9.5 °C) **(b)** Pentane (bp = 36 °C)

▲ **Figure 8.4**
London dispersion forces.
More compact molecules like 2,2-dimethylpropane have smaller surface areas, weaker London dispersion forces, and lower boiling points. By comparison, flatter, less compact molecules like pentane have larger surface areas, stronger London dispersion forces, and higher boiling points.

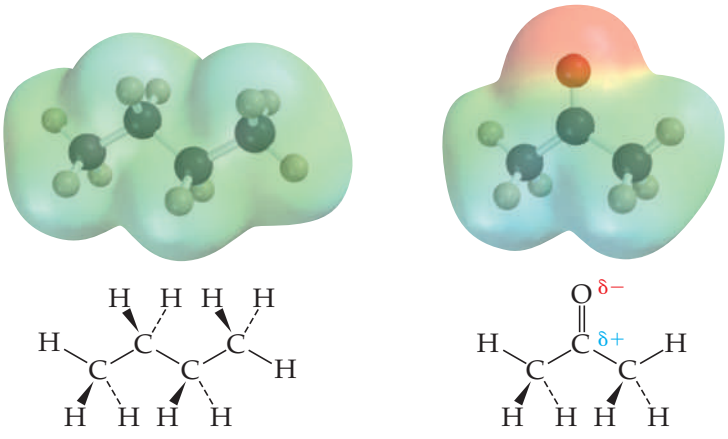


▲ **Figure 8.5**
Dipole–dipole forces.
The positive and negative ends of polar molecules are attracted to one another by dipole–dipole forces. As a result, polar molecules have higher boiling points than nonpolar molecules of similar size.

Recall from Sections 4.9 and 4.10 that a polar covalent bond is one in which the electrons are attracted more strongly by one atom than by the other.

Recall from Section 4.9 how molecular polarities can be visualized using electrostatic potential maps.

Dipole–dipole forces are typically stronger than London dispersion forces, with average strengths on the order of 4 kJ/mol. Although still significantly weaker than covalent bonds, which have bond strengths on the order of 300–400 kJ/mol, see Table 7.1, the effects of dipole–dipole forces are, nevertheless, important. This is demonstrated by observing the difference in boiling points between polar and nonpolar molecules. Butane, for instance, is a nonpolar molecule with a molecular mass of 58 amu and a boiling point of −0.5 °C, whereas acetone has the same molecular mass yet boils 57 °C higher because it is polar.



Butane (C_4H_{10})
Mol wt = 58 amu
bp = −0.5 °C

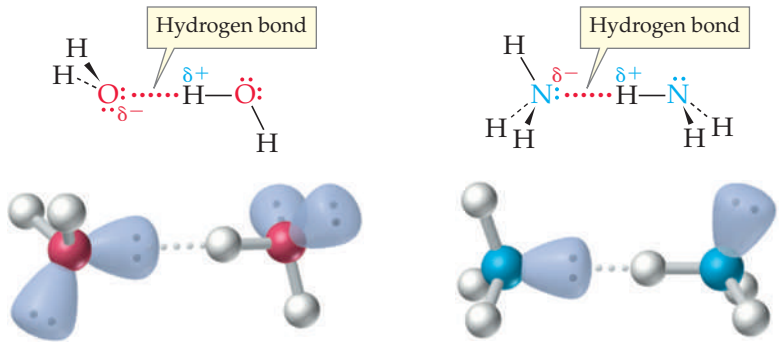
Acetone (C_3H_6O)
Mol wt = 58 amu
bp = 56.2 °C

Hydrogen Bonds

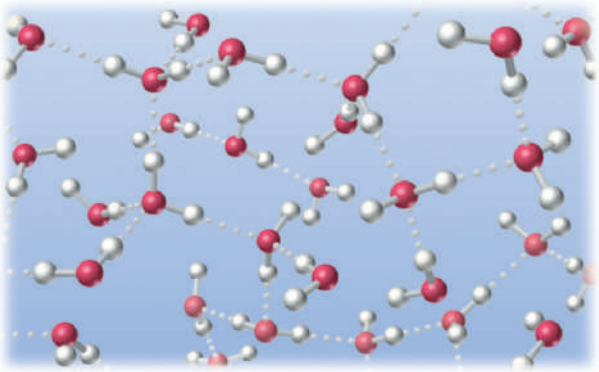
Hydrogen bond The attraction between a hydrogen atom bonded to an electronegative atom (N, O, or F) and another nearby electronegative N or O atom. While O and N atoms bonded to C can act as H-bond acceptors, F atoms bonded to C rarely act as H-bond acceptors.

In many ways, hydrogen bonding is responsible for life on earth. It causes water to be a liquid rather than a gas at ordinary temperatures, and it is the primary intermolecular force that holds huge biomolecules in the shapes needed to play their essential roles in biochemistry. Deoxyribonucleic acid (DNA) and keratin (Figure 8.6), for instance, are long molecular chains that form an α-helix, held in place largely due to hydrogen bonding.

A **hydrogen bond** is an attractive interaction between an H-bond acceptor (an electronegative O or N atom having unshared electron pairs) and an H-bond donor (a positively polarized hydrogen atom bonded to another electronegative atom (N, O, or F). For example, hydrogen bonds occur in both water and ammonia (see example at top of next page).



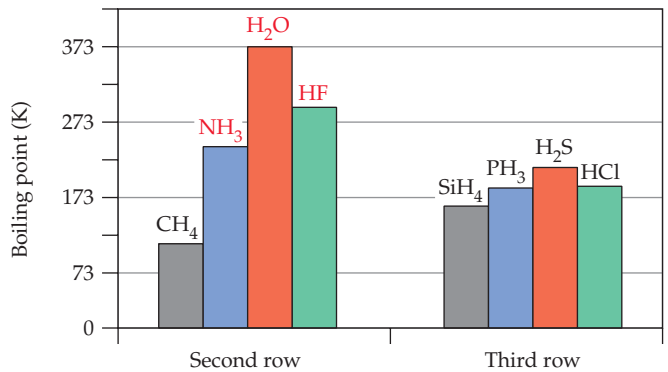
Hydrogen bonding is really just a special kind of dipole–dipole interaction. The O—H, N—H, and F—H bonds are highly polar, with a partial positive charge on the hydrogen and a partial negative charge on the electronegative atom. In addition, the hydrogen atom has no inner-shell electrons to act as a shield around its nucleus, and it is small, so it can be approached closely. As a result, the dipole–dipole attractions involving positively polarized hydrogens are unusually strong, and hydrogen bonds result. Water, in particular, is able to form a vast three-dimensional network of hydrogen bonds because each H_2O molecule has two hydrogens and two electron pairs (Figure 8.7).



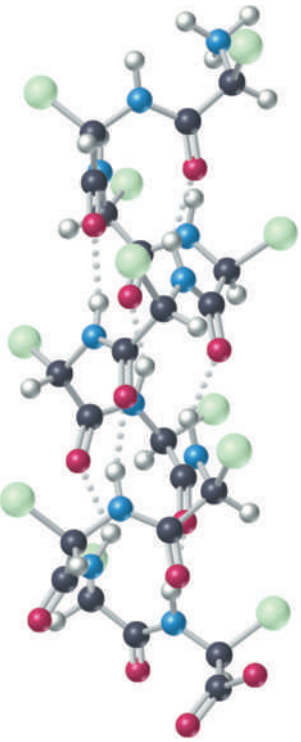
▲ Figure 8.7
Hydrogen bonding in water.
The intermolecular attraction in water is especially strong because each oxygen atom has two lone pairs and two hydrogen atoms, allowing the formation of as many as four hydrogen bonds per molecule. Individual hydrogen bonds are constantly being formed and broken.

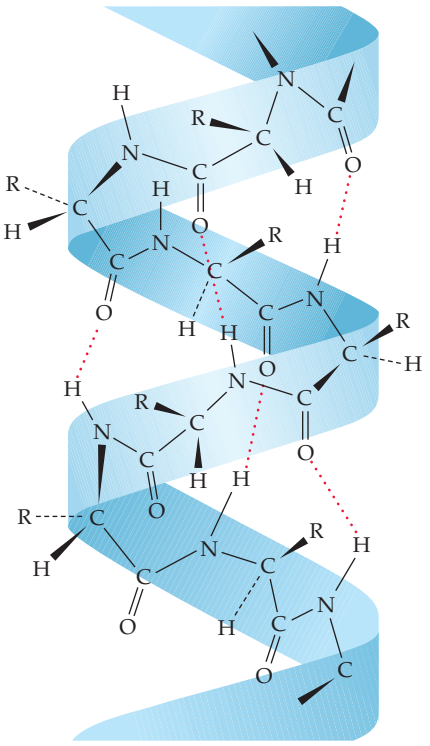
Hydrogen bonds can be quite strong, with energies up to 40 kJ/mol. To see the effect of hydrogen bonding, look at Table 8.1, which compares the boiling

Table 8.1 Boiling Points for Binary Hydrogen Compounds of Some Second-Row and Third-Row Elements



Compound	bp (K)
CH_4	111.5
NH_3	239.7
H_2O	373.2
HF	292.7
SiH_4	161.3
PH_3	185.5
H_2S	213.6
HCl	188.9





▲ Figure 8.6
The α-helical structure of keratin results from hydrogen bonding along the amino acid backbone of the molecule. Hydrogen bonding is represented by gray dots in the ball-and-stick model on the left and red dots in the molecular structure on the right.

points of binary hydrogen compounds of second-row elements with their third-row counterparts. Because NH_3, H_2O, and HF molecules are held tightly together by hydrogen bonds, an unusually large amount of energy must be added to separate them in the boiling process. As a result, the boiling points of NH_3, H_2O, and HF are much higher than the boiling points of their second-row neighbor CH_4 and of related third-row compounds.

A summary and comparison of the various kinds of intermolecular forces are shown in Table 8.2.

LOOKING AHEAD Dipole–dipole forces, London dispersion forces, and hydrogen bonds are traditionally called "intermolecular forces" because of their influence on the properties of molecular compounds. But these same forces can also operate between different parts of a very large molecule. In this context, they are often referred to as "noncovalent interactions." In later chapters, we will see how noncovalent interactions determine the shapes of biologically important molecules such as proteins and nucleic acids.

Table 8.2 A Comparison of Intermolecular Forces

	Strength	Characteristics
London dispersion	Weak (2–10 kJ/mol)	Occurs between all molecules; strength depends on size
Dipole–dipole	Weak (14 kJ/mol)	Occurs between polar molecules
Hydrogen bond	Moderate (8–40 kJ/mol)	Occurs between molecules with O—H, N—H, and/or F—H bonds

Worked Example 8.1 Identifying Intermolecular Forces: Polar vs. Nonpolar

Identify the intermolecular forces that influence the properties of the following compounds. Based on your answers, arrange the three molecules in order of increasing boiling point.

(a) Methane, CH_4 **(b)** HCl **(c)** CH_3COOH

ANALYSIS The intermolecular forces will depend on the molecular structure, what type of bonds are in the molecule (polar or non-polar), and how the bonds are arranged. The boiling point will depend on the relative strength of the predominant intermolecular forces for each compound.

SOLUTION

(a) Since methane contains only C—H bonds, it is a nonpolar molecule; it has only London dispersion forces, which are relatively weak since methane is a small molecule.

(b) The H—Cl bond is polar, so this is a polar molecule; it has both dipole–dipole forces and London dispersion forces.

(c) Acetic acid is a polar molecule with an O—H bond. Thus, it has dipole–dipole forces, London dispersion forces, and hydrogen bonds.

Based on the relative strengths of the predominant intermolecular forces for each compound, we would expect the boiling point to increase from $CH_4 < HCl < CH_3COOH$.

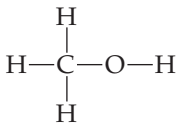
PROBLEM 8.2

Would you expect the boiling points to increase or decrease in the following series? Explain.

(a) Kr, Ar, Ne **(b)** Cl_2, Br_2, I_2

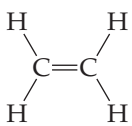
PROBLEM 8.3

Which of the following compounds form hydrogen bonds?



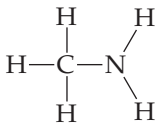
Methanol

(a)



Ethene

(b)



Methanamine

(c)

PROBLEM 8.4

Identify the intermolecular forces (dipole–dipole, London dispersion, hydrogen bonding) that influence the properties of the following compounds:

(a) Ethane, CH_3CH_3

(b) Ethanol, CH_3CH_2OH

(c) Chloroethane, CH_3CH_2Cl

8.3 Gases and the Kinetic–Molecular Theory

Learning Objective:

- Use the kinetic–molecular theory to explain the behavior of gases.

Gases behave quite differently from liquids and solids. Gases, for instance, have low densities and are easily compressed to a smaller volume when placed under pressure, a property that allows them to be stored in large tanks. Liquids and solids, by contrast, are much more dense and much less compressible. Furthermore, gases undergo a far larger expansion or contraction when their temperature is changed than do liquids and solids.

The behavior of gases can be explained by a group of assumptions known as the **kinetic–molecular theory of gases.** We will see in the next several sections how the following assumptions account for the observable properties of gases:

Kinetic–molecular theory of gases A group of assumptions that explain the behavior of gases.

- **A gas consists of many particles, either atoms or molecules, moving about at random with no attractive forces between them.** Because of this random motion, different gases mix together quickly.
- **The amount of space occupied by the gas particles themselves is much smaller than the amount of space between particles.** Most of the volume taken up by gases is empty space, accounting for the ease of compression and low densities of gases.
- **The average kinetic energy of gas particles is proportional to the Kelvin temperature.** Thus, gas particles have more kinetic energy and move faster as the temperature increases. (In fact, gas particles move much faster than you might suspect. The average speed of a helium atom at room temperature and atmospheric pressure is approximately 1.36 km/s, nearly that of a rifle bullet.)
- **Collisions of gas particles, either with other particles or with the wall of their container, are elastic; that is, no energy is lost during collisions so the total kinetic energy of the particles is constant.** The pressure of a gas against the walls of its container is the result of collisions of the gas particles with the walls. The more collisions and the more forceful each collision, the higher the pressure.

A gas that obeys all the assumptions of the kinetic–molecular theory is called an **ideal gas.** In practice, though, there is no such thing as a perfectly ideal gas. All gases behave somewhat differently than predicted when, at very high pressures or very low temperatures, their particles get closer together and interactions between particles become significant. As a rule, however, most real gases display nearly ideal behavior under normal conditions.

Ideal gas A gas that obeys all the assumptions of the kinetic–molecular theory.

8.4 Pressure

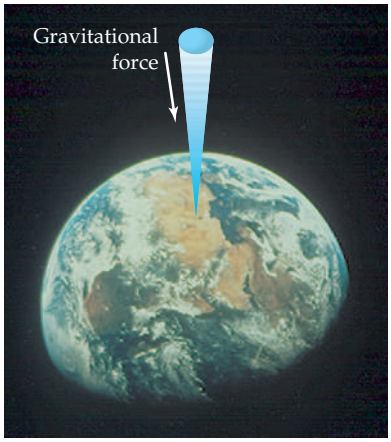
Learning Objective:

- Define pressure, and convert between units of pressure.

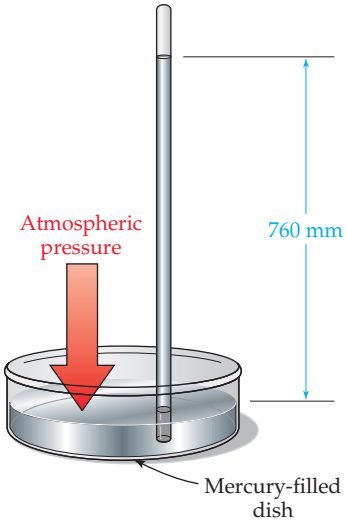
We are all familiar with the effects of air pressure. When you fly in an airplane, the change in air pressure against your eardrums as the plane climbs or descends can cause a painful "popping." When you pump up a bicycle tire, you increase the pressure of air against the inside walls of the tire until the tire feels hard.

In scientific terms, **pressure *(P)*** is defined as a force *(F)* per unit area *(A)* pushing against a surface; that is, $P = F/A$. In the bicycle tire, for example, the pressure you feel is the force of air molecules colliding with the inside walls of the tire. The units

Pressure *(P)* The force per unit area pushing against a surface.



▲ **Figure 8.8**
Atmospheric pressure.
A column of air weighing 1.03 kg presses down on each square centimeter of Earth's surface at sea level, resulting in what we call atmospheric pressure.



▲ **Figure 8.9**
Measuring atmospheric pressure.
A mercury barometer measures atmospheric pressure by determining the height of a mercury column in a sealed glass tube. The downward pressure of the mercury in the column is exactly balanced by the outside atmospheric pressure, which presses down on the mercury in the dish and pushes it up into the column.

you probably use for tire pressure are pounds per square inch (psi), where 1 psi is equal to the pressure exerted by a 1-pound object resting on a 1-square inch surface.

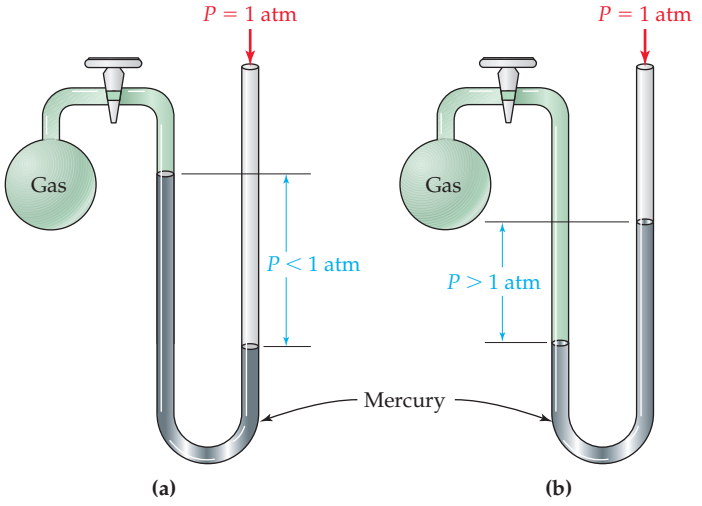
On Earth, we are under pressure from the atmosphere, the blanket of air pressing down on us (Figure 8.8). Atmospheric pressure is not constant, however; it varies slightly from day to day depending on the weather, and it also varies with altitude. Due to gravitational forces, the density of air is greatest at the earth's surface and decreases with increasing altitude. As a result, air pressure is greatest at the surface: It is about 101,325 Pa (1 atm) at sea level but only about 32,424 Pa (0.32 atm) on the summit of Mt. Everest.

One of the most commonly used units of pressure is the *millimeter of mercury,* abbreviated *mmHg* and often called a *torr* (after the Italian physicist Evangelista Torricelli). This unusual unit dates back to the early 1600s when Torricelli made the first mercury *barometer.* As shown in Figure 8.9, a barometer consists of a long, thin tube that is sealed at one end, filled with mercury, and then inverted into a dish of mercury. Some mercury runs from the tube into the dish until the downward pressure of the mercury in the column is exactly balanced by the outside atmospheric pressure, which presses down on the mercury in the dish and pushes it up into the column. The height of the mercury column varies depending on the altitude and weather conditions, but standard atmospheric pressure at sea level is defined to be exactly 760 mm.

Gas pressure inside a container is often measured using an open-ended *manometer,* a simple instrument similar in principle to the mercury barometer. As shown in Figure 8.10, an open-ended manometer consists of a U-tube filled with mercury, with one end connected to a gas-filled container and the other end open to the atmosphere. The difference between the heights of the mercury levels in the two arms of the U-tube indicates the difference between the pressure of the gas in the container and the pressure of the atmosphere. If the gas pressure inside the container is less than atmospheric pressure, the mercury level is higher in the arm connected to the container (Figure 8.10a). If the gas pressure inside the container is greater than atmospheric, the mercury level is higher in the arm open to the atmosphere (Figure 8.10b).

In the Systéme International (SI) system, (Section 2.1) the unit for pressure is named the *pascal* (Pa), where 1 Pa = 0.007500 mmHg (or 1 mmHg = 133.32 Pa). Measurements in pascals are becoming more common, and many clinical laboratories have made the switchover. Higher pressures are often still given in *atmospheres* (atm), where 1 atm = 760 mmHg exactly.

$$\text{Pressure units: } 1 \text{ atm} = 760 \text{ mmHg} = 14.7 \text{ psi} = 101{,}325 \text{ Pa}$$
$$1 \text{ mmHg} = 1 \text{ torr} = 133.32 \text{ Pa}$$



▲ **Figure 8.10**
Open-ended manometers for measuring pressure in a gas-filled bulb.
(a) When the pressure in the gas-filled container is lower than atmospheric pressure, the mercury level is higher in the arm open to the container. (b) When the pressure in the container is higher than atmospheric pressure, the mercury level is higher in the arm open to the atmosphere.

Worked Example 8.2 Unit Conversions (Pressure): psi, Atmospheres, and Pascals

A typical bicycle tire is inflated with air to a pressure of 55 psi. How many atmospheres is this? How many pascals?

ANALYSIS Using the starting pressure in psi, the pressure in atmospheres and pascals can be calculated using the equivalent values in appropriate units as conversion factors.

SOLUTION

STEP 1: Identify known information.

STEP 2: Identify answer and units.

STEP 3: Identify conversion factors. Using equivalent values in appropriate units, we can obtain conversion factors to convert to atmospheres and pascals.

STEP 4: Solve. Use the appropriate conversion factors to set up an equation in which unwanted units cancel.

$$\text{Pressure} = 55 \text{ psi}$$

$$\text{Pressure} = ?? \text{ atm} = ?? \text{ pascals}$$

$$14.7 \text{ psi} = 1 \text{ atm} \rightarrow \frac{1 \text{ atm}}{14.7 \text{ psi}}$$

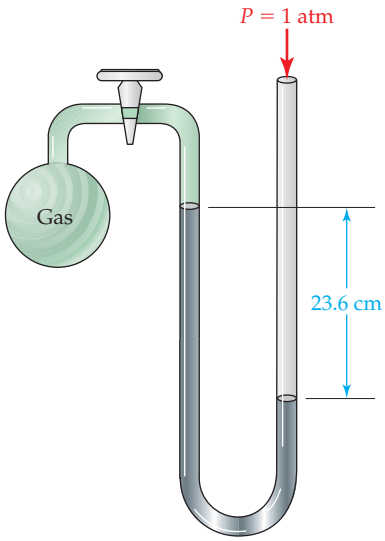
$$14.7 \text{ psi} = 101{,}325 \text{ Pa} \rightarrow \frac{101{,}325 \text{ Pa}}{14.7 \text{ psi}}$$

$$(55 \cancel{\text{psi}}) \times \left(\frac{1 \text{ atm}}{14.7 \cancel{\text{psi}}}\right) = 3.7 \text{ atm}$$

$$(55 \cancel{\text{psi}}) \times \left(\frac{101{,}325 \text{ Pa}}{14.7 \cancel{\text{psi}}}\right) = 3.8 \times 10^5 \text{ Pa}$$

Worked Example 8.3 Unit Conversions (Pressure): mmHg to Atmospheres

The pressure in a closed flask is measured using a manometer. If the mercury level in the arm open to the sealed vessel is 23.6 cm higher than the level of mercury in the arm open to the atmosphere, what is the gas pressure (in atm) in the closed flask?



ANALYSIS Since the mercury level is higher in the arm open to the flask, the gas pressure in the flask is lower than atmospheric pressure (1 atm = 760 mmHg). We can convert the difference in the level of mercury in the two arms of the manometer from mmHg to atmospheres to determine the difference in pressure.

BALLPARK ESTIMATE The height difference (23.6 cm) is about one-third the height of a column of Hg that is equal to 1 atm (or 76 cmHg). Therefore, the pressure in the flask should be about 0.33 atm lower than atmospheric pressure, or about 0.67 atm.

SOLUTION

Since the height difference is given in cmHg, we must first convert to mmHg, and then to atmospheres. The result is the difference in gas pressure between the flask and the open atmosphere (1 atm).

$$(23.6 \cancel{\text{cmHg}})\left(\frac{10 \cancel{\text{mmHg}}}{\cancel{\text{cmHg}}}\right)\left(\frac{1 \text{ atm}}{760 \cancel{\text{mmHg}}}\right) = 0.311 \text{ atm}$$

The pressure in the flask is calculated by subtracting this difference from 1 atm:

$$1 \text{ atm} - 0.311 \text{ atm} = 0.689 \text{ atm}$$

BALLPARK CHECK This result agrees well with our estimate of 0.67 atm.

PROBLEM 8.5

The air pressure outside a jet airliner flying at 10,670 m is about 0.289 atm. Convert this pressure to mmHg, psi, and pascals.

PROBLEM 8.6

A typical automobile tire is inflated with air to a pressure of 32 psi. Convert this pressure to atm, mmHg, and pascals.

CHEMISTRY IN ACTION

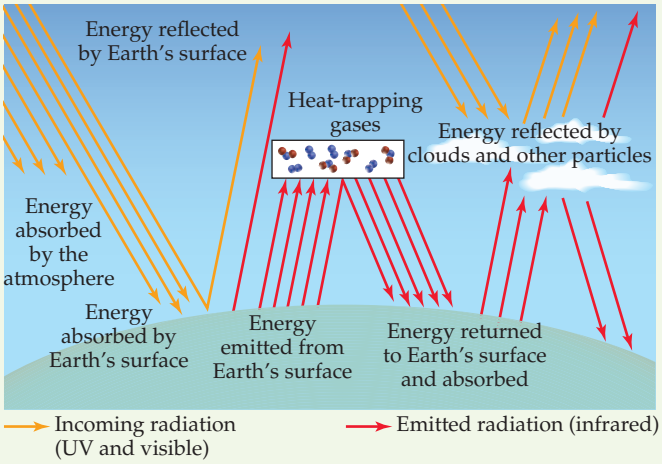
Greenhouse Gases and Global Warming

The mantle of gases surrounding the earth is far from the uniform mixture you might expect, consisting of layers that vary in composition and properties at different altitudes. The ability of the gases in these layers to absorb radiation is responsible for life on earth as we know it.

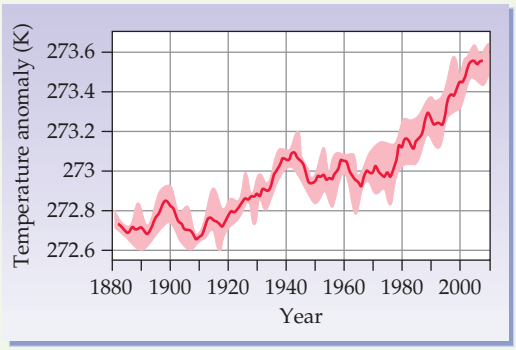
The *stratosphere*—the layer extending from about 12 km up to 50 km altitude—contains the ozone layer that is responsible for absorbing harmful ultraviolet (UV) radiation. The greenhouse effect refers to the warming that occurs in the *troposphere*, the layer extending from the surface of Earth up to about 12 km altitude, as gases absorb radiant energy. Much of the radiant energy reaching Earth's surface from the sun is reflected back into space, but some is absorbed by atmospheric gases, particularly those referred to as *greenhouse gases* (GHGs)—water vapor, carbon dioxide, and methane. This absorbed radiation warms the atmosphere and acts to maintain a relatively stable temperature of 288 K (15 °C) at Earth's surface. Without the greenhouse effect, the average surface temperature would be about 255 K (−18 °C)—a temperature so low that Earth would be frozen and unable to sustain life.

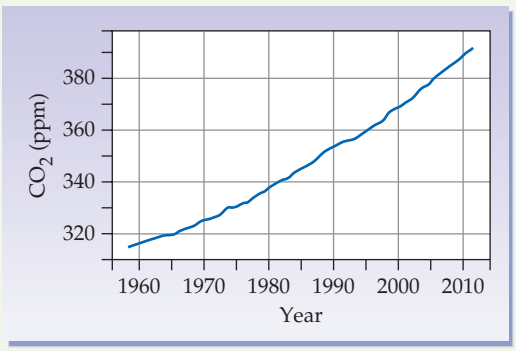
The basis for concern about the greenhouse effect is the fear that human activities over the past century have disturbed Earth's delicate thermal balance. Should increasing amounts of radiation be absorbed, increased atmospheric heating will result, and global temperatures will continue to rise.

Measurements show that the concentration of atmospheric CO_2 has been rising in the past 150 years, from an estimated 290 parts per million (ppm) in 1850 to current levels approaching 400 ppm. The increase in CO_2 levels is largely because of the increased burning of fossil fuels and correlates with a concurrent increase in average global temperatures. The latest Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) (AR5) approved at the 40th session of the IPCC in November 2014 concluded that "[W]arming of the climate system is unequivocal, and since the 1950s, many of the observed changes are unprecedented over decades to millennia. The atmosphere and ocean have warmed, the amounts of snow and ice have diminished, and sea levels have risen." With regard to future risks and impacts, they concluded, "Continued emission of greenhouse gases will cause further warming and long-lasting changes in all components of the climate system, increasing the likelihood of severe, pervasive, and irreversible impacts for people and ecosystems."[1] Increased international concerns about the political and economic impacts of global climate change prompted development of the Kyoto Protocol to the United Nations Framework Convention on Climate Change (UNFCCC). Under the protocol, countries commit to a reduction in the production and emission of GHGs, including CO_2, methane, and chlorofluorocarbons (CFCs). To date, however, many signatories to the original agreement have failed to reach their emission reduction targets due to economic and political pressures.



▲ GHGs trap heat reflected from the earth's surface, resulting in the increase in surface temperatures known as global warming.





▲ Concentrations of atmospheric CO_2 and global average temperatures have increased dramatically in the past 150 years because of increased fossil fuel use, causing serious changes in Earth's climate system.

However, environmental concerns have resulted in market pressures to develop sustainable and renewable energy sources as well as more efficient technologies, such as hybrid electric vehicles.

CIA Problem 8.1 What evidence is there that global warming is occurring

CIA Problem 8.2 What are the three most important GHGs?

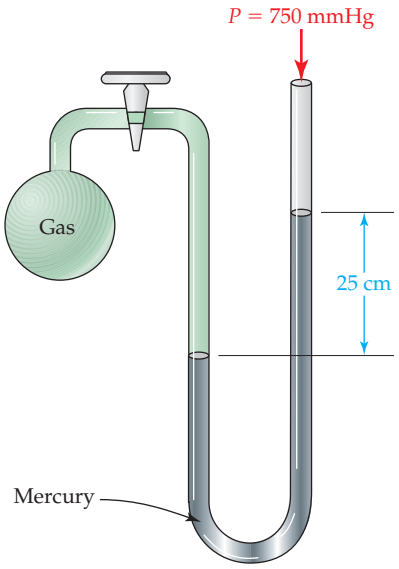
[1] *IPCC, 2014: Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II, and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Core Writing Team, R.K. Pachauri and L.A. Meyer (eds.)]. IPCC, Geneva, Switzerland, pp. 151.*

PROBLEM 8.7

A local weather station reports the barometric pressure as 74.9 cmHg (centimeters of Hg). Convert this pressure to torr and to atm.

KEY CONCEPT PROBLEM 8.8

Using the image in the margin, what is the pressure of the gas inside the following manometer (in mmHg) if outside pressure is 750 mmHg?



8.5 Boyle's Law: The Relation between Volume and Pressure

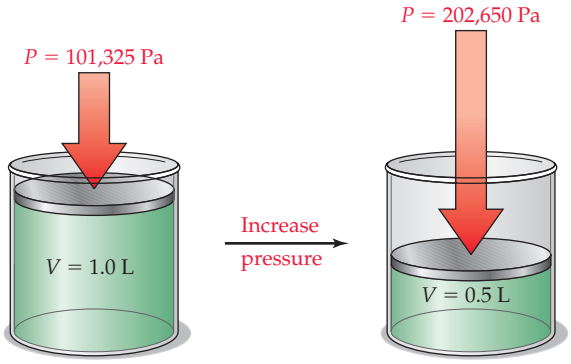
Learning Objective:

- Use Boyle's law to calculate the changes in pressure or volume of a gas at a given temperature.

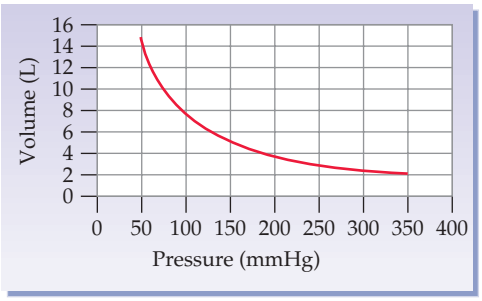
The physical behavior of all gases is much the same, regardless of identity. Helium and chlorine, for example, are completely different in their *chemical* behavior but are very similar in many of their physical properties. Observations of many different gases by scientists in the 1700s led to the formulation of the **gas laws,** which make it possible to predict the influence of pressure *(P),* volume *(V),* temperature *(T),* and molar amount *(n)* on any gas or mixture of gases. We will begin by looking at *Boyle's law,* which describes the relation between volume and pressure.

Gas laws A series of laws that predict the influence of pressure *(P),* volume *(V),* and temperature *(T)* on any gas or mixture of gases.

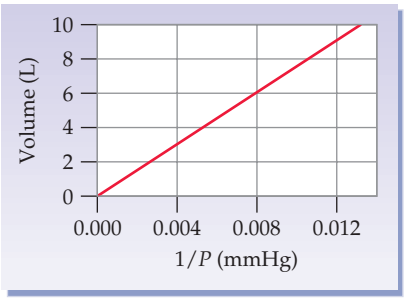
Imagine that you have a sample of gas inside a cylinder that has a movable plunger at one end (Figure 8.11). What happens if you double the pressure on the gas by pushing the plunger down, while keeping the temperature constant? Since the gas particles are forced closer together, the volume of the sample decreases.



▶ **Figure 8.11**
Boyle's law.
The volume of a gas decreases proportionately as its pressure increases. For example, if the pressure of a gas sample is doubled, the volume is halved.



(a)



(b)

▲ **Figure 8.12**
Boyle's law.
Pressure and volume are inversely related. Graph (a) demonstrates the decrease in volume as pressure increases, whereas graph (b) shows the linear relationship between V and $1/P$.

According to **Boyle's law,** the volume of a fixed amount of gas at a constant temperature is inversely proportional to its pressure, meaning that volume and pressure change in opposite directions. As pressure goes up, volume goes down; as pressure goes down, volume goes up (Figure 8.12). This observation is consistent with the kinetic–molecular theory. Since most of the volume occupied by gases is empty space, gases are easily compressed into smaller volumes. Since the average kinetic energy remains constant, the number of collisions must increase as the interior surface area of the container decreases, leading to an increase in pressure.

Boyle's law The volume of a gas is inversely proportional to its pressure for a fixed amount of gas at a constant temperature. That is, P times V is constant when the amount of gas n and the temperature T are kept constant. (The symbol $\propto$ means "is proportional to," and k denotes a constant value.)

$$\text{Volume } (V) \propto \frac{1}{\text{Pressure } (P)}$$

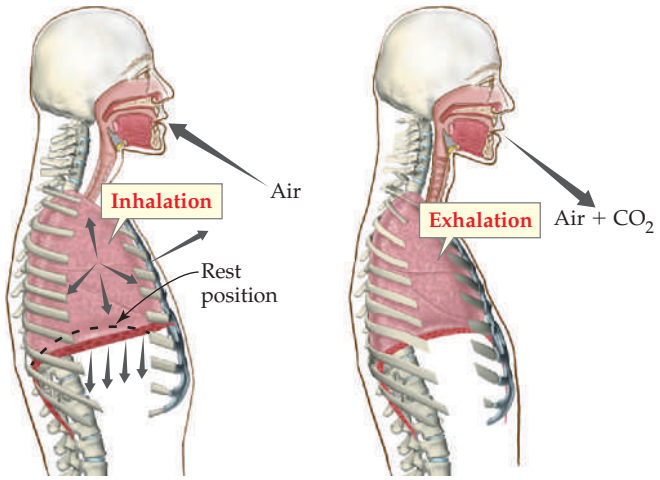
$$\text{or} \quad PV = k \quad (\text{A constant value})$$

Because $P \times V$ is a constant value for a fixed amount of gas at a constant temperature, the starting pressure (P_1) times the starting volume (V_1) must equal the

final pressure (P_2) times the final volume (V_2). Thus, Boyle's law can be used to find the final pressure or volume when the starting pressure or volume is changed.

$$\text{Since} \quad P_1V_1 = k \quad \text{and} \quad P_2V_2 = k$$
$$\text{then} \quad P_1V_1 = P_2V_2$$
$$\text{so} \quad P_2 = \frac{P_1V_1}{V_2} \quad \text{and} \quad V_2 = \frac{P_1V_1}{P_2}$$

As an example of Boyle's law behavior, think about what happens every time you breathe. Between breaths, the pressure inside your lungs is equal to atmospheric pressure. When inhalation takes place, your diaphragm lowers and the rib cage expands, increasing the volume of the lungs and thereby decreasing the pressure inside them (Figure 8.13). Air must then move into the lungs to equalize their pressure with that of the atmosphere. When exhalation takes place, the diaphragm rises and the rib cage contracts, decreasing the volume of the lungs and increasing pressure inside them. Now gases move out of the lungs until pressure is again equalized with the atmosphere.



Lung volume increases, causing pressure in lungs to *decrease.* Air flows *in.*

Lung volume decreases, causing pressure in lungs to *increase.* Air flows *out.*

▲ **Figure 8.13**
Boyle's law in breathing.
During inhalation, the diaphragm moves down and the rib cage moves up and out, thus increasing lung volume, decreasing pressure, and drawing in air. During exhalation, the diaphragm moves back up, lung volume decreases, pressure increases, and air moves out.

Worked Example 8.4 Using Boyle's Law: Finding Volume at a Given Pressure

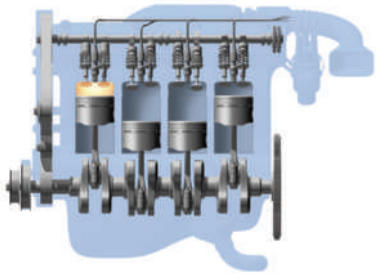
In a typical automobile engine, the fuel/air mixture in a cylinder is compressed from 10^5 Pa to 9.5×10^5 Pa. If the uncompressed volume of the cylinder is 0.750×10^{-3} m^3, what is the volume when fully compressed?

ANALYSIS This is a Boyle's law problem because the volume and pressure in the cylinder change but the amount of gas and the temperature remain constant. According to Boyle's law, the pressure of the gas times its volume is constant:

$$P_1V_1 = P_2V_2$$

Knowing three of the four variables in this equation, we can solve for the unknown.

BALLPARK ESTIMATE Since the pressure *increases* approximately 10-fold (from 10^5 Pa to 9.5×10^5 Pa), the volume must *decrease* to approximately one-tenth, from 0.750×10^{-3} m^3 to about 0.750×10^{-4} m^3.



▲ A cut-away diagram of an internal combustion engine shows movement of pistons during expansion and compression cycles.

SOLUTION

STEP 1: Identify known information. Of the four variables in Boyle's law, we know P_1, V_1, and P_2.

$P_1 = 10^5$ Pa
$V_1 = 0.750 \times 10^{-3}$ m^3
$P_2 = 9.5 \times 10^5$ Pa

STEP 2: Identify answer and units.

$V_2 = ??$ mL

STEP 3: Identify equation. In this case, we simply substitute the known variables into Boyle's law and rearrange to isolate the unknown.

$$P_1V_1 = P_2V_2 \Rightarrow V_2 = \frac{P_1V_1}{P_2}$$

STEP 4: Solve. Substitute the known information into the equation. Make sure units cancel so that the answer is given in the units of the unknown variable.

$$V_2 = \frac{P_1V_1}{P_2} = \frac{(10^5\ \cancel{\text{Pa}})(0.750 \times 10^{-3}\ \text{m}^3)}{(9.5 \times 10^5\ \cancel{\text{Pa}})} = 0.79 \times 10^{-4}\ \text{m}^3$$

BALLPARK CHECK Our estimate was 0.750×10^{-4} m^3

CHEMISTRY IN ACTION

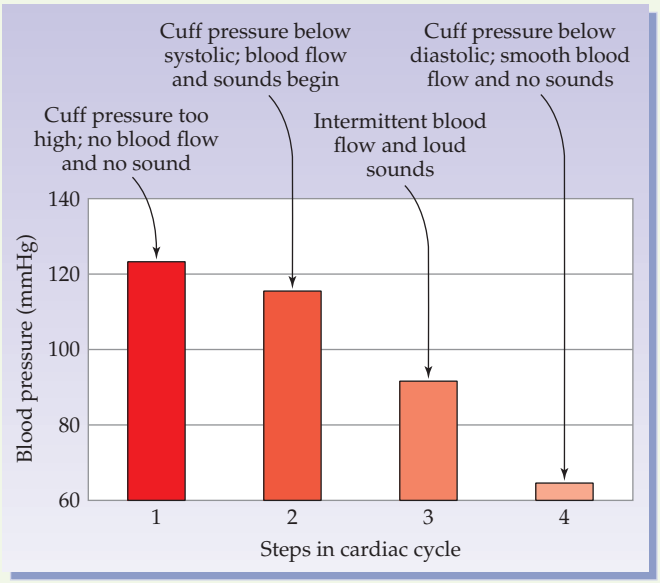
Blood Pressure

Having your blood pressure measured is a quick and easy way to get an indication of the state of your circulatory system. Although blood pressure varies with age, a normal adult male has a reading near 120/80 mmHg, and a normal adult female has a reading near 110/70 mmHg. Abnormally high values signal an increased risk of heart attack and stroke.

Pressure varies greatly in different types of blood vessels. Usually, though, measurements are carried out on arteries in the upper arm as the heart goes through a full cardiac cycle. *Systolic pressure* is the maximum pressure developed in the artery just after contraction, as the heart forces the maximum amount of blood into the artery. *Diastolic pressure* is the minimum pressure that occurs at the end of the heart cycle.

Blood pressure is most often measured by a *sphygmomanometer*, a device consisting of a squeeze bulb, a flexible cuff, and a mercury manometer. (1) The cuff is placed around the upper arm over the brachial artery and inflated by the squeeze bulb to about 200 mmHg pressure, an amount great enough to squeeze the artery shut and prevent blood flow. Air is then slowly released from the cuff, and pressure drops (2). As cuff pressure reaches the systolic pressure, blood spurts through the artery, creating a turbulent tapping sound that can be heard through a stethoscope. The pressure registered on the manometer at the moment the first sounds are heard is the systolic blood pressure.

(3) Sounds continue until the pressure in the cuff becomes low enough to allow diastolic blood flow. (4) At this point, blood flow becomes smooth, no sounds are heard, and a diastolic blood pressure reading is recorded on the manometer. Readings are usually recorded as systolic/diastolic, for example, 120/80. The accompanying figure shows the sequence of events during measurement.



▲ The sequence of events during blood pressure measurement, including the sounds heard.

CIA Problem 8.3 What is the difference between a systolic and a diastolic pressure reading? Is a blood pressure of 180/110 within the normal range?

CIA Problem 8.4 Convert the blood pressure reading in CIA Problem 8.3 to atm.

CIA Problem 8.5 Convert the blood pressure reading in CIA Problem 8.3 from mmHg to Pa. Now look up the ambient barometric pressure (Pa). How do they compare?

PROBLEM 8.9

An oxygen cylinder used for breathing has a volume of 5.0×10^{-3} m^3 at 90×10^5 Pa pressure. What is the volume of the same amount of oxygen at the same temperature if the pressure is 10^5 Pa? (Hint: Would you expect the volume of gas at this pressure to be greater than or less than the volume at 90×10^5 Pa?)

PROBLEM 8.10

A sample of hydrogen gas at 273 K has a volume of 3.2×10^{-3} m^3 at 4.0×10^5 Pa pressure. What is the volume if the pressure is increased to 10^6 Pa? If the pressure is decreased to 0.70×10^5 Pa?

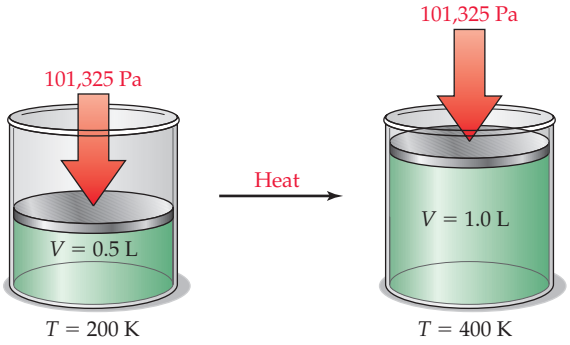
▲ The volume of the gas in the balloon increases as it is heated, causing a decrease in density and allowing the balloon to rise.

8.6 Charles's Law: The Relation between Volume and Temperature

Learning Objective:

- Use Charles's law to calculate changes in volume of a gas as a function of temperature.

Imagine that you again have a sample of gas inside a cylinder with a plunger at one end. What happens if you double the sample's kelvin temperature while letting the plunger move freely to keep the pressure constant? The gas particles move with twice as much energy and collide twice as forcefully with the walls. To maintain a constant pressure, the volume of the gas in the cylinder must double (Figure 8.14).



◀ **Figure 8.14**
Charles's law.
The volume of a gas is directly proportional to its kelvin temperature at constant n and P. If the kelvin temperature of the gas is doubled, its volume doubles.

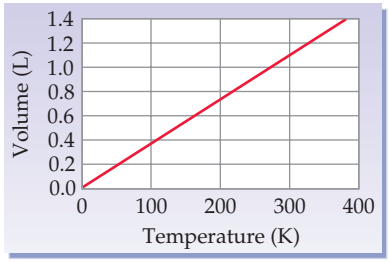
According to **Charles's law,** the volume of a fixed amount of gas at constant pressure is directly proportional to its kelvin temperature. Note the difference between *directly* proportional in Charles's law and *inversely* proportional in Boyle's law. Directly proportional quantities change in the same direction—as temperature goes up or down, volume also goes up or down (Figure 8.15).

Charles's law The volume of a gas is directly proportional to its kelvin temperature for a fixed amount of gas at a constant pressure. That is, V divided by T is constant when n and P are held constant.

$$V \propto T \quad \text{(In kelvins)}$$

$$\text{or } \frac{V}{T} = k \quad \text{(A constant value)}$$

$$\text{or } \frac{V_1}{T_1} = \frac{V_2}{T_2}$$



▲ **Figure 8.15**
Charles's law.
Volume is directly proportional to the kelvin temperature for a fixed amount of gas at a constant pressure. As the temperature goes up, the volume also goes up.

This observation is consistent with the kinetic–molecular theory. As temperature increases, the average kinetic energy of the gas molecules increases, as does the energy of molecular collisions with the interior surface of the container. The volume of the container must increase to maintain a constant pressure. As an example of Charles's law, think about what happens when a hot-air balloon is inflated. Heating causes the air inside to expand and fill the balloon. The air inside the balloon is less dense than the air outside the balloon, creating the buoyancy effect.

Worked Example 8.5 Using Charles's Law: Finding Volume at a Given Temperature

An average adult inhales a volume of 0.50×10^{-3} m^3 of air with each breath. If the air is warmed from room temperature (20 °C = 293 K) to body temperature (37 °C = 310 K) while in the lungs, what is the volume of the air exhaled?

ANALYSIS This is a Charles's law problem because the volume and temperature of the air change while the amount and pressure remain constant. Knowing three of the four variables, we can rearrange Charles's law to solve for the unknown.

BALLPARK ESTIMATE Charles's law predicts an increase in volume directly proportional to the increase in temperature from 273 K to 310 K. The increase of less than 20 K represents a relatively small change compared to the initial temperature of 273 K. A 10% increase, for example, would be equal to a temperature change of 27 K; so a 20-K change would be less than 10%. We would therefore expect the volume to increase by less than 10%, from 0.50×10^{-3} m^3 to a little less than 0.55×10^{-3} m^3.

SOLUTION

STEP 1: Identify known information. Of the four variables in Charles's law, we know T_1, V_1, and T_2.

STEP 2: Identify answer and units.

STEP 3: Identify equation. Substitute the known variables into Charles's law and rearrange to isolate the unknown.

STEP 4: Solve. Substitute the known information into Charles's law; check to make sure units cancel.

$$T_1 = 293 \text{ K}$$
$$V_1 = 0.50 \times 10^{-3} \text{ m}^3$$
$$T_2 = 310 \text{ K}$$
$$V_2 = ?? \text{ L}$$
$$\frac{V_1}{T_1} = \frac{V_2}{T_2} \quad \Rightarrow \quad V_2 = \frac{V_1 T_2}{T_1}$$
$$V_2 = \frac{V_1 T_2}{T_1} = \frac{(0.50 \times 10^{-3} \text{ m}^3)(310 \cancel{\text{K}})}{293 \cancel{\text{K}}} = 0.53 \times 10^{-3} \text{ m}^3$$

BALLPARK CHECK This is consistent with our estimate!

PROBLEM 8.11

A sample of chlorine gas has a volume of 0.30×10^{-3} m^3 at 273 K and 101,325 Pa pressure. What temperature (in °C) would be required to increase the volume to 1.0×10^{-3} m^3? To decrease the volume to 0.20×10^{-3} m^3?

HANDS-ON CHEMISTRY 8.1

Take a balloon and blow it up until it is about six inches in diameter. Then place it in the refrigerator or freezer. After about 10 minutes, remove it from the refrigerator and estimate its diameter. How much has it changed? Now run the balloon under hot water for a few minutes, and estimate its diameter. Explain the changes you observed in terms of the kinetic–molecular theory and using Charles's law. (Note: Instead of placing the balloon in the refrigerator/freezer, it can be run under cold water.)

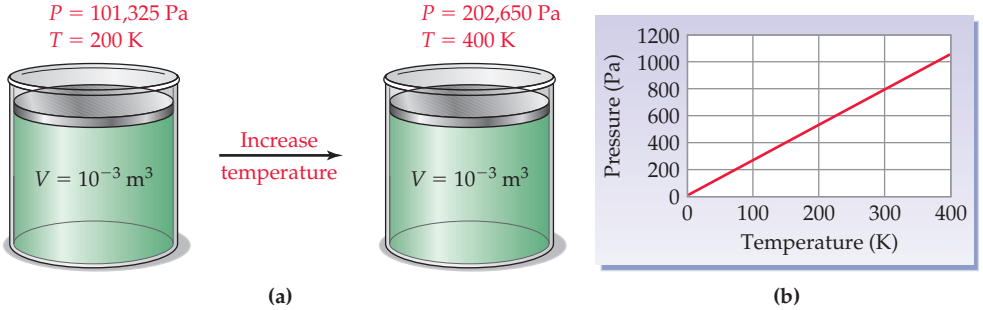
8.7 Gay-Lussac's Law: The Relation between Pressure and Temperature

Learning Objective:

- Use Gay-Lussac's law to calculate changes in pressure of a gas as a function of temperature.

Imagine next that you have a fixed amount of gas in a sealed container whose volume remains constant. What happens if you double the temperature (in kelvins)? The gas particles move with twice as much energy and collide with the walls of the container with twice as much force. Thus, the pressure in the container doubles. According to

Gay-Lussac's law, the pressure of a fixed amount of gas at constant volume is directly proportional to its Kelvin temperature. As temperature goes up or down, pressure also goes up or down (Figure 8.16).



▶ Figure 8.16
Gay-Lussac's law.
Pressure is directly proportional to the temperature in kelvins for a fixed amount of gas: (a) At a constant volume, doubling the absolute temperature would also double the pressure; (b) the increase in pressure is directly proportional to absolute temperature.

Gay-Lussac's law The pressure of a gas is directly proportional to its Kelvin temperature for a fixed amount of gas at a constant volume. That is, P divided by T is constant when n and V are held constant.

$$P \propto T \quad (\text{In kelvins})$$

$$\text{or } \frac{P}{T} = k \quad (\text{A constant value})$$

$$\text{or } \frac{P_1}{T_1} = \frac{P_2}{T_2}$$

According to the kinetic–molecular theory, the kinetic energy of molecules is directly proportional to absolute temperature. As the average kinetic energy of the molecules increases, the energy of collisions with the interior surface of the container increases, causing an increase in pressure. As an example of Gay-Lussac's law, think of what happens when an aerosol can is thrown into an incinerator. As the can gets hotter, pressure builds up inside and the can explodes (hence the warning statement on aerosol cans).

Worked Example 8.6 Using Gay-Lussac's Law: Finding Pressure at a Given Temperature

What does the inside pressure become if an aerosol can with an initial pressure of 4.5×10^5 Pa is heated in a fire from room temperature (20 °C) to 600 °C?

ANALYSIS This is a Gay-Lussac's law problem because the pressure and temperature of the gas inside the can change while its amount and volume remain constant. We know three of the four variables in the equation for Gay-Lussac's law and can find the unknown by substitution and rearrangement.

BALLPARK ESTIMATE Gay-Lussac's law states that pressure is directly proportional to temperature. Since the Kelvin temperature increases approximately threefold (from about 300 K to about 900 K), we expect the pressure to also increase by approximately threefold, from 4.5×10^5 Pa to about 14×10^5 Pa.

SOLUTION

STEP 1: Identify known information. Of the four variables in Gay-Lussac's law, we know P_1, T_1, and T_2. (Note that T must be in kelvins.)

$$P_1 = 4.5 \times 10^5 \text{ Pa}$$
$$T_1 = 20\ ^\circ\text{C} = 293 \text{ K}$$
$$T_2 = 600\ ^\circ\text{C} = 873 \text{ K}$$

STEP 2: Identify answer and units.

$$P_2 = \text{??} \text{ Pa}$$

STEP 3: Identify equation. Substituting the known variables into Gay-Lussac's law, we rearrange to isolate the unknown.

$$\frac{P_1}{T_1} = \frac{P_2}{T_2} \Rightarrow P_2 = \frac{P_1 T_2}{T_1}$$

STEP 4: Solve. Substitute the known information into Gay-Lussac's law; check to make sure units cancel.

$$P_2 = \frac{P_1 T_2}{T_1} = \frac{(4.5 \times 10^5 \text{ Pa})(873 \cancel{\text{K}})}{293 \cancel{\text{K}}} = 13 \times 10^5 \text{ Pa}$$

BALLPARK CHECK Our estimate was 14×10^5 Pa.

PROBLEM 8.12

Driving on a hot day causes tire temperature to rise. What is the pressure inside an automobile tire at 45 °C if the tire has a pressure of 2×10^5 Pa at 15 °C? Assume that the volume and amount of air in the tire remain constant.

8.8 The Combined Gas Law

Learning Objective:

- Use the combined gas law to determine changes in pressure, temperature, or volume of a gas.

Since PV, V/T, and P/T all have constant values for a fixed amount of gas, these relationships can be merged into a **combined gas law,** which holds true whenever the amount of gas is fixed.

Combined gas law

$$\frac{PV}{T} = k \quad (\text{A constant value})$$

$$\text{or } \frac{P_1V_1}{T_1} = \frac{P_2V_2}{T_2}$$

If any five of the six quantities in this equation are known, the sixth quantity can be calculated. Furthermore, if any of the three variables T, P, or V is constant, that variable drops out of the equation, leaving behind Boyle's law, Charles's law, or Gay-Lussac's law. As a result, *the combined gas law is the only equation you need to remember for a fixed amount of gas.* Worked Example 8.8 gives a sample calculation.

Since $\dfrac{P_1V_1}{T_1} = \dfrac{P_2V_2}{T_2}$

At constant T: $\dfrac{P_1V_1}{T} = \dfrac{P_2V_2}{T}$ gives $P_1V_1 = P_2V_2$ (Boyle's law)

At constant P: $\dfrac{PV_1}{T_1} = \dfrac{PV_2}{T_2}$ gives $\dfrac{V_1}{T_1} = \dfrac{V_2}{T_2}$ (Charles's law)

At constant V: $\dfrac{P_1V}{T_1} = \dfrac{P_2V}{T_2}$ gives $\dfrac{P_1}{T_1} = \dfrac{P_2}{T_2}$ (Gay-Lussac's law)

Worked Example 8.7 Using the Combined Gas Law: Finding Temperature

A 6.3×10^{-3} m^3 sample of helium gas stored at 298 K (25 °C) and 1.0×10^5 Pa pressure is transferred to a 2.0×10^{-3} m^3 tank and maintained at a pressure of 2.8×10^5 Pa. What temperature is needed to maintain this pressure?

ANALYSIS This is a combined gas law problem because pressure, volume, and temperature change while the amount of helium remains constant. Of the six variables in this equation, we know P_1, V_1, T_1, P_2, and V_2, and we need to find T_2.

BALLPARK ESTIMATE Since the volume goes down by a little more than a factor of about 3 (from 6.3×10^{-3} m^3 to 2.0×10^{-3} m^3) and the pressure goes up by a little less than a factor of about 3 (from 1.0×10^5 Pa to 2.8×10^5 Pa), the two changes roughly offset each other, and so the temperature should not change much. Since the volume-decrease factor (3.2) is slightly greater than the pressure-increase factor (2.8), the temperature will drop slightly ($T \propto V$).

SOLUTION

STEP 1: Identify known information. Of the six variables in the combined gas law, we know P_1, V_1, T_1, P_2, and V_2 (As always, T must be converted from Celsius degrees to kelvins.)

$P_1 = 1.0 \times 10^5$ Pa, $P_2 = 2.8 \times 10^5$ Pa
$V_1 = 6.3 \times 10^{-3}$ m^3, $V_2 = 2.0 \times 10^{-3}$ m^3
$T_1 = 25$ °C $= 298$ K

—continued on next page

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STEP 2: Identify answer and units.

STEP 3: Identify the equation. Substitute the known variables into the equation for the combined gas law and rearrange to isolate the unknown.

STEP 4: Solve. Solve the combined gas law equation for T_2, check to make sure units cancel.

$T_2 = ??$ kelvin

$$\frac{P_1V_1}{T_1} = \frac{P_2V_2}{T_2} \Rightarrow T_2 = \frac{P_2V_2T_1}{P_1V_1}$$

$$T_2 = \frac{P_2V_2T_1}{P_1V_1} = \frac{(2.8 \times 10^5 \cancel{\text{Pa}})(2.0 \times 10^{-3} \cancel{\text{m}^3})(298 \text{ K})}{(1.0 \times 10^5 \cancel{\text{Pa}})(6.3 \times 10^{-3} \cancel{\text{m}^3})} = 265 \text{ K} (\Delta T = 33 \text{ K})$$

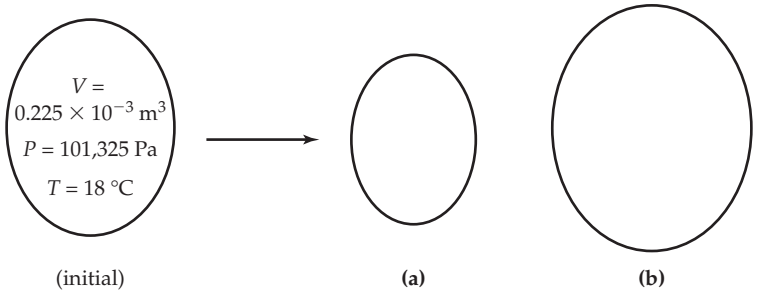
BALLPARK CHECK The relatively small decrease in temperature (33 K, or 13% compared to the original temperature) is consistent with our prediction.

PROBLEM 8.13

A weather balloon is filled with helium to a volume of 0.275 m^3 at 22 °C and 10^5 Pa. The balloon ascends to an altitude where the pressure is 0.64 × 10^5 Pa and the temperature is 241 K (−32 °C). What is the volume of the balloon at this altitude?

KEY CONCEPT PROBLEM 8.14

A balloon is filled under the initial conditions indicated in the following figure. If the pressure is then increased to 202,650 Pa while the temperature is increased to 50 °C, which balloon on the right, (a) or (b), represents the new volume of the balloon?



8.9 Avogadro's Law: The Relation between Volume and Molar Amount

Learning Objective:

- Use Avogadro's law to calculate the volume for a given number of moles of a gas.

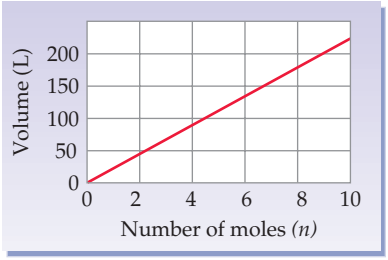
Here, we look at a gas law that takes changes in amount of gas into account. Imagine that you have two different volumes of a gas at the same temperature and pressure. How many moles does each sample contain? According to **Avogadro's law,** the volume of a gas is directly proportional to its molar amount at a constant pressure and temperature (Figure 8.17). A sample that contains twice the molar amount has twice the volume.

Avogadro's law The volume of a gas is directly proportional to its molar amount at a constant pressure and temperature. That is, V divided by n is constant when P and T are held constant.

$$\text{Volume } (V) \propto \text{Number of moles } (n)$$

$$\text{or } \frac{V}{n} = k \quad (\text{A constant value; the same for all gases})$$

$$\text{or } \frac{V_1}{n_1} = \frac{V_2}{n_2}$$



▲ **Figure 8.17**
Avogadro's law.
Volume is directly proportional to the molar amount, *n,* at a constant temperature and pressure. As the number of moles goes up, the volume also goes up.

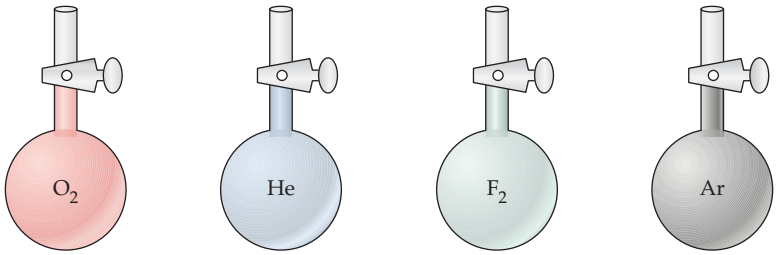
Because the particles in a gas are so tiny compared to the empty space surrounding them, there is no interaction among gas particles as proposed by the kinetic–molecular theory. As a result, the chemical identity of the particles does not matter and the value of the constant k in the equation $V/n = k$ is the same for all gases. It is therefore possible to compare the molar amounts of *any* two gases simply by comparing their volumes at the same temperature and pressure.

Notice that the *values* of temperature and pressure do not matter; it is only necessary that T and P be the same for both gases. To simplify comparisons of gas samples, however, it is convenient to define a set of conditions called **standard temperature and pressure (STP),** which specifies a temperature of 0 °C (273 K) and a pressure of 1 atm (760 mmHg).

At STP, 1 mol of any gas $(6.02 \times 10^{23}$ particles$)$ has a volume of 22.4 L, a quantity called the **standard molar volume** (Figure 8.18).

Standard temperature and pressure (STP) 0 °C (273.15 K); 1 atm (760 mmHg)

Standard molar volume Volume of one mole of any ideal gas at STP, 22.4 L/mol.



◀ **Figure 8.18**
Avogadro's law.
Each of these 22.4 L bulbs contains 1.00 mol of gas at 0 °C and 1 atm pressure. Note that the volume occupied by 1 mol of gas is the same even though the mass (in grams) of 1 mol of each gas is different.

Worked Example 8.8 Using Avogadro's Law: Finding Moles in a Given Volume at STP

Use the standard molar volume of a gas at STP (22.4 L) to find how many moles of air at STP are in a room measuring 4.11 m wide by 5.36 m long by 2.58 m high.

ANALYSIS We first find the volume of the room and then use standard molar volume as a conversion factor to find the number of moles.

SOLUTION

STEP 1: Identify known information. We are given the room dimensions.

$$\text{Length} = 5.36\ \text{m}$$
$$\text{Width} = 4.11\ \text{m}$$
$$\text{Height} = 2.58\ \text{m}$$

STEP 2: Identify answer and units.

$$\text{Moles of air} = ??\ \text{mol}$$

STEP 3: Identify the equation. The volume of the room is the product of its three dimensions. Once we have the volume (in m^3), we can convert to liters and use the molar volume at STP as a conversion factor to obtain moles of air.

$$\text{Volume} = (4.11\ \text{m})(5.36\ \text{m})(2.58\ \text{m}) = 56.8\ \text{m}^3$$
$$= 56.8\ \text{m}^3 \times \frac{1000\ \text{L}}{1\ \text{m}^3} = 5.68 \times 10^4\ \text{L}$$
$$1\ \text{mol} = 22.4\ \text{L} \rightarrow \frac{1\ \text{mol}}{22.4\ \text{L}}$$

STEP 4: Solve. Use the room volume and the molar volume at STP to set up an equation, making sure unwanted units cancel.

$$5.68 \times 10^4\ \cancel{\text{L}} \times \frac{1\ \text{mol}}{22.4\ \cancel{\text{L}}} = 2.54 \times 10^3\ \text{mol}$$

PROBLEM 8.15

How many moles of methane gas, CH_4, are in a 100 m^3 storage tank at STP? How many grams of methane is this? How many grams of carbon dioxide gas could the same tank hold?

8.10 The Ideal Gas Law

Learning Objective:

- Use the ideal gas law to calculate the pressure, temperature, volume, or number of moles of an ideal gas.

The relationships among the four variables *P, V, T,* and *n* for gases can be combined into a single expression called the **ideal gas law.** If you know the values of any three of the four quantities, you can calculate the value of the fourth.

Ideal gas law

$$\frac{PV}{nT} = R \quad (\text{A constant value})$$

$$\text{or } PV = nRT$$

Gas constant (*R*) The constant *R* in the ideal gas law, $PV = nRT$.

The constant *R* in the ideal gas law (instead of the usual *k*) is called the **gas constant.** Its value depends on the units chosen for pressure, with the two most common values being

$$\text{For } P \text{ in atmospheres:} \qquad R = 0.0821 \frac{\text{L} \cdot \text{atm}}{\text{mol} \cdot \text{K}}$$

$$\text{For } P \text{ in millimeters Hg:} \qquad R = 62.4 \frac{\text{L} \cdot \text{mmHg}}{\text{mol} \cdot \text{K}}$$

In using the ideal gas law, it is important to choose the value of *R* having pressure units that are consistent with the problem and, if necessary, to convert volume into liters and temperature into kelvins.

Table 8.3 summarizes the various gas laws, and Worked Examples 8.10 and 8.11 show how to use the ideal gas law.

Table 8.3 A Summary of the Gas Laws

	Gas Law	Variables	Constant
Boyle's law	$P_1V_1 = P_2V_2$	*P, V*	*n, T*
Charles's law	$V_1/T_1 = V_2/T_2$	*V, T*	*n, P*
Gay-Lussac's law	$P_1/T_1 = P_2/T_2$	*P, T*	*n, V*
Combined gas law	$P_1V_1/T_1 = P_2V_2/T_2$	*P, V, T*	*n*
Avogadro's law	$V_1/n_1 = V_2/n_2$	*V, n*	*P, T*
Ideal gas law	$PV = nRT$	*P, V, T, n*	*R*

Worked Example 8.9 Using the Ideal Gas Law: Finding Moles

How many moles of air are in the lungs of an average person with a total lung capacity of 3.8 L? Assume that the person is at 1.0 atm pressure and has a normal body temperature of 37 °C.

ANALYSIS This is an ideal gas law problem because it asks for a value of *n* when *P, V,* and *T* are known: $n = PV/RT$. The volume is given in the correct unit of liters, but temperature must be converted to kelvins.

SOLUTION

STEP 1: Identify known information. We know three of the four variables in the ideal gas law.

$P = 1.0 \text{ atm}$
$V = 3.8 \text{ L}$
$T = 37 \text{ °C} = 310 \text{ K}$

STEP 2: Identify answer and units.

Moles of air, $n =$?? mol

STEP 3: Identify the equation. Knowing three of the four variables in the ideal gas law, we can rearrange and solve for the unknown variable, *n*. Note: Because pressure is given in atmospheres, we use the value that is expressed in atm:

$$R = 0.0821 \frac{\text{L} \cdot \text{atm}}{\text{mol} \cdot \text{K}}$$

$$PV = nRT \Rightarrow n = \frac{PV}{RT}$$

STEP 4: Solve. Substitute the known information and the appropriate value of *R* into the ideal gas law equation and solve for *n*.

$$n = \frac{PV}{RT} = \frac{(1.0\ \cancel{\text{atm}})(3.8\ \cancel{\text{L}})}{\left(0.0821 \frac{\cancel{\text{L}} \cdot \cancel{\text{atm}}}{\text{mol} \cdot \cancel{\text{K}}}\right)(310\ \cancel{\text{K}})} = 0.15 \text{ mol}$$

Worked Example 8.10 Using the Ideal Gas Law: Finding Pressure

Methane gas is sold in steel cylinders with a volume of 43.8 L containing 5.54 kg. What is the pressure in atmospheres inside the cylinder at a temperature of 293.15 K (20.0 °C)? The molar mass of methane (CH_4) is 16.0 g/mol.

ANALYSIS This is an ideal gas law problem because it asks for a value of *P* when *V, T,* and *n* are given. Although not provided directly, enough information is given so that we can calculate the value of *n* (n = g/molar mass).

SOLUTION

STEP 1: Identify known information. We know two of the four variables in the ideal gas law—*V* and *T*—and can calculate the third, *n,* from the information provided.

$$V = 43.8 \text{ L}$$
$$T = 37\ ^\circ\text{C} = 310 \text{ K}$$

STEP 2: Identify answer and units.

Pressure, P = ?? atm

STEP 3: Identify equation. First, calculate the number of moles, *n,* of methane in the cylinder by using molar mass (16.0 g/mol) as a conversion factor. Then use the ideal gas law to calculate the pressure.

$$n = (5.54\ \cancel{\text{kg}} \text{ methane})\left(\frac{1000\ \cancel{\text{g}}}{1\ \cancel{\text{kg}}}\right)\left(\frac{1 \text{ mol}}{16.0\ \cancel{\text{g}}}\right) = 346 \text{ mol methane}$$

$$PV = nRT \Rightarrow P = \frac{nRT}{V}$$

STEP 4: Solve. Substitute the known information and the appropriate value of *R* into the ideal gas law equation and solve for *P*.

$$P = \frac{nRT}{V} = \frac{(346\ \cancel{\text{mol}})\left(0.0821 \frac{\cancel{\text{L}} \cdot \text{atm}}{\cancel{\text{mol}} \cdot \cancel{\text{K}}}\right)(293\ \cancel{\text{K}})}{43.8\ \cancel{\text{L}}} = 190 \text{ atm}$$

PROBLEM 8.16

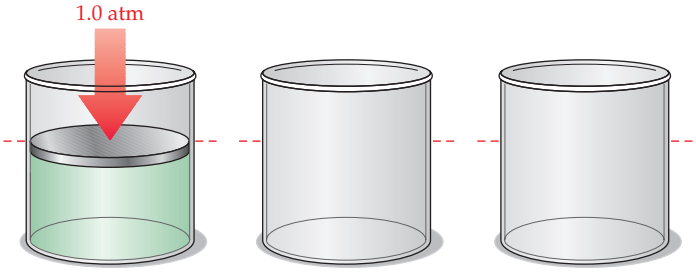
An aerosol spray can of deodorant with a volume of 350 mL contains 3.2 g of propane gas (C_3H_8) as propellant. What is the pressure (in Pa) in the can at 20 °C?

PROBLEM 8.17

A helium gas cylinder of the sort used to fill balloons has a volume of 0.180 m^3 and a pressure of 150 × 10^5 Pa (150 atm) at 298 K (25 °C). How many moles of helium are in the tank? How many grams?

KEY CONCEPT PROBLEM 8.18

Show the approximate level of the movable piston in drawings (a) and (b) after the indicated changes have been made to the initial gas sample (assume a constant pressure of 1 atm).



(initial)
$T = 300$ K
$n = 0.300$ mol

(a)
$T = 450$ K
$n = 0.200$ mol

(b)
$T = 200$ K
$n = 0.400$ mol

8.11 Partial Pressure and Dalton's Law

Learning Objective:

- Use Dalton's law to calculate the partial pressure or the number of moles of a gas in a mixture.

According to the kinetic–molecular theory, each particle in a gas acts independently of all others because there are no attractive forces between them and they are so far apart. To any individual particle, the chemical identity of its neighbors is irrelevant. Thus, *mixtures* of gases behave the same as pure gases and obey the same laws.

Dry air, for example, is a mixture of about 21% oxygen, 78% nitrogen, and 1% argon by volume, which means that 21% of atmospheric air pressure is caused by O_2 molecules, 78% by N_2 molecules, and 1% by Ar atoms. The contribution of each gas in a mixture to the total pressure of the mixture is called the **partial pressure** of that gas. According to **Dalton's law,** the total pressure exerted by a gas mixture (P_{total}) is the sum of the partial pressures of the components in the mixture.

Partial pressure The contribution of a given gas in a mixture to the total pressure.

Dalton's law: $P_{total} = P_{gas\ 1} + P_{gas\ 2} + P_{gas\ 3}$

In dry air at a total air pressure of 101,325 Pa, the partial pressure caused by the contribution of O_2 is $0.21 \times 101{,}325$ Pa $= 21{,}278$ Pa, the partial pressure of N_2 is 0.78×760 mmHg $= 79{,}034$ Pa, and that of argon is 1013 Pa. *The partial pressure exerted by each gas in a mixture is the same pressure that the gas would exert if it were alone.* Put another way, the pressure exerted by each gas depends on the frequency of collisions of its molecules with the walls of the container. However, this frequency does not change when other gases are present because the different molecules have no influence on one another.

To represent the partial pressure of a specific gas, we add the formula of the gas as a subscript to *P,* the symbol for pressure. You might see the partial pressure of oxygen represented as P_{O_2}, for instance. Moist air inside the lungs at 37 °C and atmospheric pressure has the following average composition at sea level. Note that P_{total} is equal to atmospheric pressure, 101,325 Pa.

$$\begin{aligned} P_{total} &= P_{N_2} + P_{O_2} + P_{CO_2} + P_{H_2O} \\ &= 76{,}394\ \text{Pa} + 13{,}332\ \text{Pa} + 5333\ \text{Pa} + 6266\ \text{Pa} \\ &= 101{,}325\ \text{Pa} \end{aligned}$$

The composition of air does not change appreciably with altitude, but the total pressure decreases rapidly. The partial pressure of oxygen in air therefore decreases with increasing altitude, and it is this change that leads to difficulty in breathing at high elevations.

Worked Example 8.11 Using Dalton's Law: Finding Partial Pressures

Humid air on a warm summer day is approximately 20% oxygen, 75% nitrogen, 4% water vapor, and 1% argon. What is the partial pressure of each component if the atmospheric pressure is 1.0×10^5 Pa?

ANALYSIS According to Dalton's law, the partial pressure of any gas in a mixture is equal to the percent concentration of the gas times the total gas pressure (750 mmHg). In this case,

$$P_{\text{total}} = P_{O_2} + P_{N_2} + P_{H_2O} + P_{Ar}$$

SOLUTION

Oxygen partial pressure (P_{O_2}):	0.20×10^5 Pa
Nitrogen partial pressure (P_{N_2}):	0.75×10^5 Pa
Water vapor partial pressure (P_{H_2O}):	0.04×10^5 Pa
Argon partial pressure (P_{Ar}):	0.01×10^5 Pa
Total pressure = 1.0×10^5 Pa	

Note that the sum of the partial pressures must equal the total pressure (within rounding error).

PROBLEM 8.19

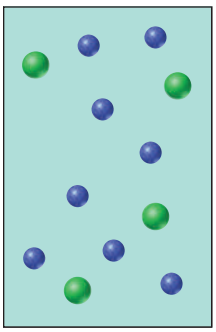
Assuming a total pressure of 9.5×10^5 Pa, what is the partial pressure of each component in the mixture of 98% helium and 2.0% oxygen breathed by deep-sea divers? How does the partial pressure of oxygen in diving gas compare with its partial pressure in normal air?

PROBLEM 8.20

Determine the percent composition of air in the lungs from the following composition in partial pressures: $P_{N_2} = 0.76 \times 10^5$ Pa, $P_{O_2} = 0.13 \times 10^5$ Pa, $P_{CO_2} = 0.050 \times 10^5$ Pa, and $P_{H_2O} = 0.060 \times 10^5$ Pa; all at 37 °C and 1.0×10^5 Pa pressure.

PROBLEM 8.21

The atmospheric pressure on the top of Mt. Everest, an altitude of 8850 m, is only 0.35×10^5 Pa. What is the partial pressure of oxygen in the lungs at this altitude (assuming that the percent O_2 is the same as in dry air)?



KEY CONCEPT PROBLEM 8.22

Using the image in the margin, assume that you have a mixture of He (blue spheres) and Xe (green spheres) at 300 K. The total pressure of the mixture is 10^5 Pa. What are the partial pressures of each of the gases?

8.12 Liquids

Learning Objective:

- Identify how the vapor pressure, boiling point, and surface tension of liquids are related to temperature and intermolecular forces.

Molecules are in constant motion in the liquid state, just as they are in gases. If a molecule happens to be near the surface of a liquid, and if it has enough energy, it can break free of the liquid and escape into the gas state, called **vapor.** In an open container, the now gaseous molecule will wander away from the liquid, and the process will continue until all the molecules escape from the container (Figure 8.19a). This, of course, is what happens during *evaporation*. We are all familiar with puddles of water evaporating after a rainstorm.

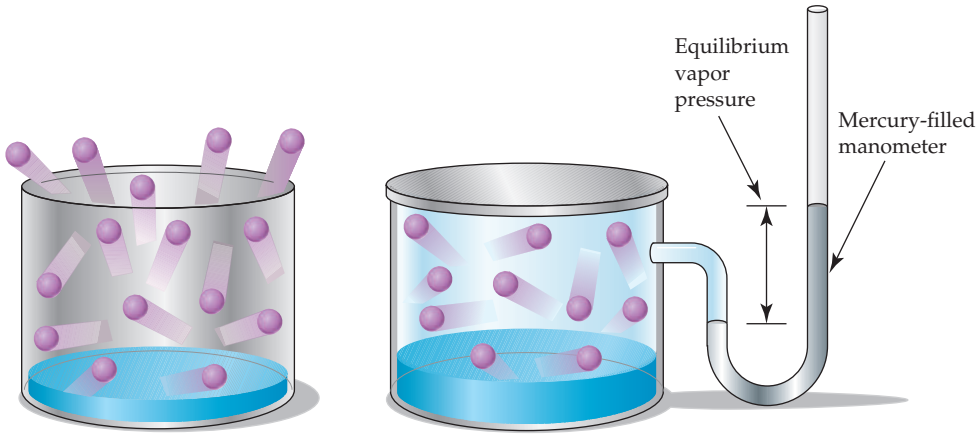
If the liquid is in a closed container, the situation is different because the gaseous molecules cannot escape. Thus, the random motion of the molecules occasionally brings them back into the liquid. After the concentration of molecules in the gas state has increased sufficiently, the number of molecules reentering the liquid becomes equal

Vapor The gas molecules are in equilibrium with a liquid.

to the number escaping from the liquid (Figure 8.19b). At this point, a dynamic equilibrium exists, exactly as in a chemical reaction at equilibrium. Evaporation and condensation take place at the same rate, and the concentration of vapor in the container is constant as long as the temperature does not change.

Once molecules have escaped from the liquid into the gas state, they are subject to all the gas laws previously discussed. In a closed container at equilibrium, for example, the vapor molecules will make their own contribution to the total pressure of gases above the liquid according to Dalton's law (Section 8.11). We call this contribution the **vapor pressure** of the liquid.

Vapor pressure The partial pressure of vapor molecules in equilibrium with a liquid.

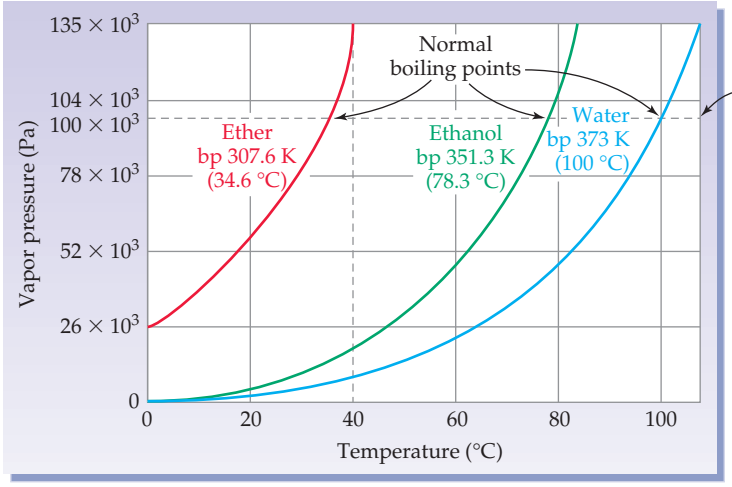


▶ **Figure 8.19**
The transfer of molecules between liquid and gas states.
(a) Molecules escape from an open container and drift away until the liquid has entirely evaporated. (b) Molecules in a closed container cannot escape. Instead, they reach an equilibrium in which the rates of molecules leaving the liquid and returning to the liquid are equal, and the concentration of molecules in the gas state is constant.

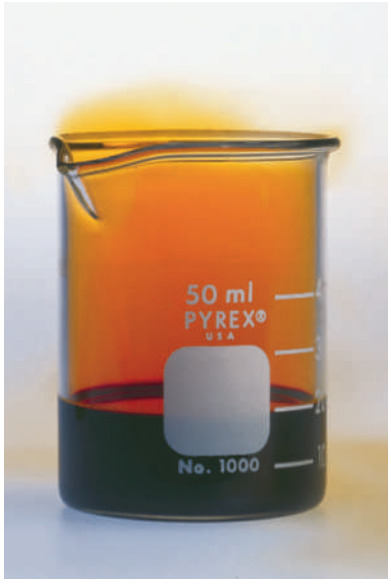
Vapor pressure depends on both temperature and the chemical identity of a liquid. As the temperature rises, molecules become more energetic and more likely to escape into the gas state. Thus, vapor pressure rises with increasing temperature until ultimately it becomes equal to the pressure of the atmosphere. At this point, bubbles of vapor form under the surface and force their way to the top, giving rise to the violent action observed during a vigorous boil. At an atmospheric pressure of exactly 760 mmHg, boiling occurs at the **normal boiling point.**

Normal boiling point The boiling point at a pressure of exactly 1 atm.

The vapor pressure and boiling point of a liquid will also depend on the intermolecular forces (discussed in Section 8.2) at work between liquid molecules. Ether molecules, for example, can engage in dipole–dipole interactions, which are weaker than the hydrogen bonds formed between water molecules. As a result, ether exhibits a higher vapor pressure at a given temperature and a lower boiling point than water, as seen in Figure 8.20.



▲ **Figure 8.20**
A plot of the change of vapor pressure with temperature for ethyl ether, ethanol, and water.
At a liquid's boiling point, its vapor pressure is equal to atmospheric pressure. Commonly reported boiling points are those at 100×10^3 Pa.



▲ Because bromine is colored, it is possible to see its gaseous reddish vapor above the liquid.

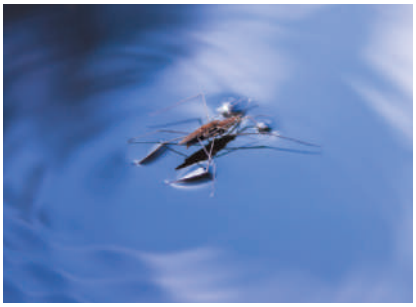
If atmospheric pressure is higher or lower than normal, the boiling point of a liquid changes accordingly. At high altitudes, for example, atmospheric pressure is lower than at sea level, and boiling points are also lower. On top of Mt. Everest (8850 m), atmospheric pressure is about 0.33×10^5 and the boiling temperature of water is only 344 K (71 °C). If the atmospheric pressure is higher than normal, the boiling point is also higher. This principle is used in strong vessels known as *autoclaves,* in which water at high pressure is heated to the temperatures needed for sterilizing medical and dental instruments (443 K/170 °C).

▲ A bench-top autoclave, used to sterilize medical and dental instruments.

Many familiar properties of liquids can be explained by the intermolecular forces just discussed. We all know, for instance, that some liquids, such as water or gasoline, flow easily when poured, whereas others, such as motor oil or maple syrup, flow sluggishly.

The measure of a liquid's resistance to flow is called its *viscosity.* Not surprisingly, viscosity is related to the ease with which individual molecules move around in the liquid and thus to the intermolecular forces present. Substances such as gasoline, which have small, nonpolar molecules, experience only weak intermolecular forces and have relatively low viscosities, whereas more polar substances such as glycerin $[C_3H_5(OH)_3]$ experience stronger intermolecular forces and so have higher viscosities.

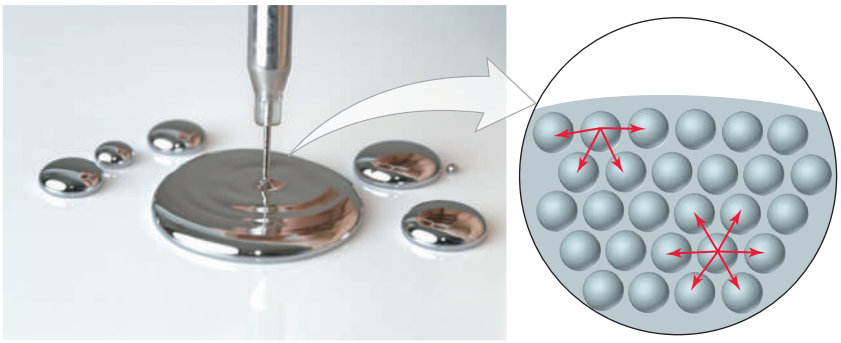
Another familiar property of liquids is *surface tension,* the resistance of a liquid to spreading out and increasing its surface area. Water beading up on a newly waxed car and the ability of a water strider to walk on water are both due to surface tension.



▲ Surface tension allows a water strider to walk on water without penetrating the surface.

The difference between the intermolecular forces experienced by molecules at the surface of the liquid and those experienced by molecules in the interior causes surface tension. Molecules in the interior of a liquid are surrounded and experience maximum intermolecular forces, whereas molecules at the surface have fewer neighbors and feel weaker forces. Surface molecules are therefore less stable, and the liquid acts to minimize their number by minimizing the surface area (Figure 8.21).

◀◀ Recall from Section 1.11 that specific heat is the amount of heat required to raise the temperature of 1g of a substance by 1 K/°C.



◀ **Figure 8.21**
Surface tension.
Surface tension is caused by the different forces experienced by molecules in the interior of a liquid and those on the surface. Molecules on the surface are less stable because they feel fewer attractive forces, so the liquid acts to minimize their number by minimizing surface area.

8.13 Solids

Learning Objective:

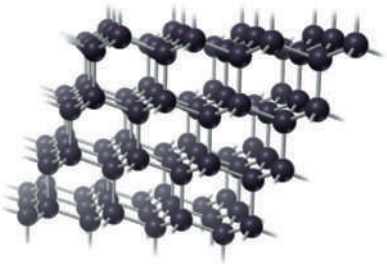
- Distinguish between the different types of solids and explain their physical properties.

A brief look around us reveals that most substances are solids rather than liquids or gases. It is also obvious that there are many different kinds of solids. Some, such as iron and aluminum, are hard and metallic; others, such as sugar and table salt, are crystalline and easily broken; and still others, such as rubber and many plastics, are soft and amorphous.

The most fundamental distinction between solids is that some are crystalline and some are amorphous. A **crystalline solid** is one whose particles—whether atoms, ions, or molecules—have an ordered arrangement extending over a long range. This order on the atomic level is also seen on the visible level because crystalline solids usually have flat faces and distinct angles.

Crystalline solid A solid whose atoms, molecules, or ions are rigidly held in an ordered arrangement.

▲ Crystalline solids, such as pyrite (left) and fluorite (right), have flat faces and distinct angles. The octahedral shape of pyrite and the cubic shape of fluorite reflect similarly ordered arrangements of particles at the atomic level.



▲ **Figure 8.22**
Diamond.
Diamond is a covalent network solid—one very large molecule of carbon atoms linked by covalent bonds.

Amorphous solid A solid whose particles do not have an orderly arrangement.

Crystalline solids can be further categorized as ionic, molecular, covalent network, or metallic. *Ionic solids* are those like sodium chloride, whose constituent particles are ions. A crystal of sodium chloride is composed of alternating Na^+ and Cl^- ions ordered in a regular three-dimensional arrangement held together by ionic bonds (see Figure 3.4). *Molecular solids* are those like sucrose or ice, whose constituent particles are molecules held together by the intermolecular forces discussed in Section 8.2. *Covalent network solids* are those like diamond (Figure 8.22) or quartz (SiO_2), whose atoms are linked together by covalent bonds into a giant three-dimensional array. In effect, a covalent network solid is one *very* large molecule.

Metallic solids, such as silver or iron, can be viewed as vast three-dimensional arrays of metal cations immersed in a sea of electrons that are free to move about. This continuous electron sea acts both as a glue to hold the cations together and as a mobile carrier of charge to conduct electricity. Furthermore, the fact that bonding attractions extend uniformly in all directions explains why metals are malleable rather than brittle. When a metal crystal receives a sharp blow, no spatially oriented bonds are broken; instead, the electron sea simply adjusts to the new distribution of cations.

An **amorphous solid,** by contrast with a crystalline solid, is one whose constituent particles are randomly arranged and have no ordered long-range structure. Amorphous solids often result when liquids cool before they can achieve internal order or when their molecules are large and tangled together, as happens in many polymers. Glass is an amorphous solid, as are tar, the gemstone opal, and some hard candies. Amorphous solids differ from crystalline solids by softening over a wide temperature range rather than having sharp melting points and by shattering to give pieces with curved rather than planar faces. Table 8.4 gives a summary of the different types of solids and their characteristics.

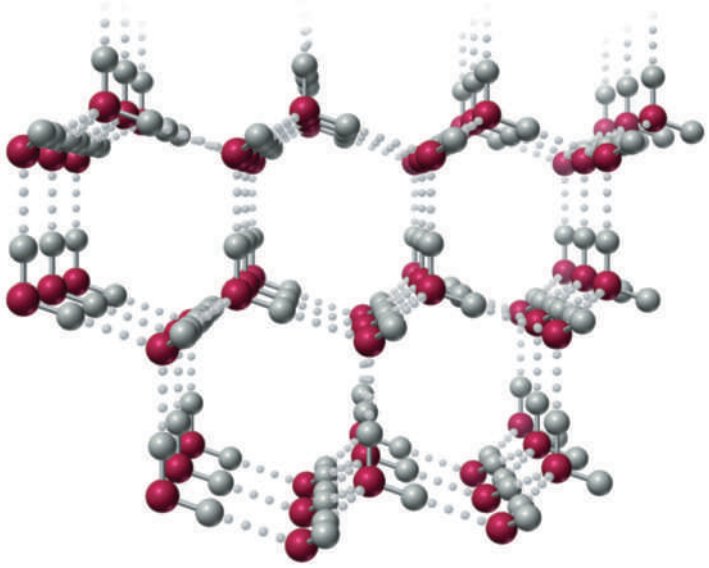
Table 8.4 Types of Solids

Substance	Smallest Unit	Interparticle Forces	Properties	Examples
Ionic solid	Ions	Attraction between positive and negative ions	Brittle and hard; high melting point; crystalline	NaCl, KI, $Ca_3(PO_4)_2$
Molecular solid	Molecules	Intermolecular forces	Soft; low to moderate melting point; crystalline	Ice, wax, frozen CO_2, all solid organic compounds
Covalent network	Atoms	Covalent bonds	Very hard; very high melting point; crystalline	Diamond, quartz (SiO_2), tungsten carbide (WC)
Metal or alloy	Metal atoms	Metallic bonding (attraction between metal ions and surrounding mobile electrons)	Lustrous; soft (Na) to hard (Ti); high melting point; crystalline	Elements (Fe, Cu, Sn, . . .), bronze (CuSn alloy), amalgams (Hg+ other metals)
Amorphous solid	Atoms, ions, or molecules (including polymer molecules)	Any of the above	Noncrystalline; no sharp melting point; able to flow (may be very slow); curved edges when shattered	Glasses, tar, some plastics

Most substances are more dense as solids than as liquids because molecules are more closely packed in the solid than in the liquid state. Water, however, is unique. Liquid water has a maximum density of 1.000 g/mL at 277.13 K (3.98 °C) but then becomes *less* dense as it cools. When it freezes, its density decreases still further to 0.917 g/mL.

As water freezes, each molecule is locked into position by hydrogen bonding to four other water molecules (Figure 8.23). The resulting structure has more open space than liquid water, accounting for its lower density. As a result, ice floats on liquid water, and lakes and rivers freeze from the top down. If the reverse were true, fish would be killed in winter as they became trapped in ice at the bottom.

Water has other unique properties, including a high heat of vaporization and the highest specific heat of any liquid. The high ΔH_{vap}, is of particular importance in regulating body temperature by dissipating heat generated by metabolic processes (Chapters 21 and 22).



◀ **Figure 8.23**
Ice.
Ice consists of individual H_2O molecules held rigidly together in an ordered manner by hydrogen bonds. The open, cage-like crystal structure shows why ice is less dense than liquid water.

8.14 Changes of State Calculations

Learning Objective:

- Calculate the total amount of heat associated with changes in physical states of a substance.

What happens when a solid is heated? As more and more energy is added, molecules begin to stretch, bend, and vibrate more vigorously, and atoms or ions wiggle about with more energy. Finally, if enough energy is added and the motions become vigorous enough, particles start to break free from one another and the substance starts to melt. Addition of more heat continues the melting process until all particles have broken free and are in the liquid phase. The quantity of heat required to completely melt a substance once it reaches its melting point is called its **heat of fusion.** After melting is complete, further addition of heat causes the temperature of the liquid to rise.

Heat of fusion The quantity of heat required to completely melt 1 g of a substance once it has reached its melting point.

The change of a liquid into a vapor proceeds in the same way as the change of a solid into a liquid. When you first put a pan of water on the stove, all the added heat goes into raising the temperature of the water. Once the water reaches its boiling point, further absorbed heat goes into freeing molecules from their neighbors as they escape into the gas state. The quantity of heat needed to completely vaporize a liquid once it reaches its boiling point is called its **heat of vaporization.** A liquid with a low heat of vaporization, like rubbing alcohol (isopropanol), evaporates rapidly and is said to be *volatile*. If you spill a volatile liquid on your skin, you will feel a cooling effect as it evaporates because it is absorbing heat from your body.

Heat of vaporization The quantity of heat needed to completely vaporize 1 g of a liquid once it has reached its boiling point.

It is important to know the difference between heat that is added or removed to change the *temperature* of a substance and heat that is added or removed to change the *phase* of a substance. Remember that temperature is a measure of the kinetic energy in a substance (see Section 7.1). When a substance is above or below its phase-change temperature (i.e., melting point or boiling point), adding or removing heat will simply change the kinetic energy and, hence, the temperature of the substance. The amount of heat needed to produce a given temperature change was presented previously (Section 1.11) but is worth presenting again here.

$$\text{Heat (J)} = \text{Mass (g)} \times \text{Temperature change (°C)} \times \text{Specific heat}\left(\frac{\text{J}}{\text{g} \times \text{°C}}\right)$$

In contrast, when a substance is at its phase-change temperature, heat that is added is being used to overcome the intermolecular forces holding particles in that phase. The temperature remains constant until *all* particles have been converted to the next phase. The energy needed to complete the phase change depends only on the amount of the substance and the heat of fusion (for melting) or the heat of vaporization (for boiling).

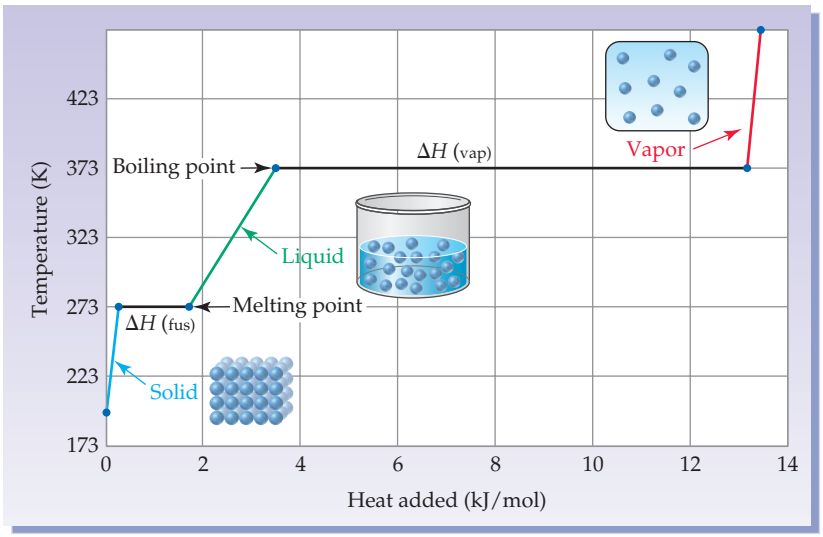
$$\text{Heat (J)} = \text{Mass (g)} \times \text{Heat of fusion}\left(\frac{\text{J}}{\text{g}}\right)$$

$$\text{Heat (J)} = \text{Mass (g)} \times \text{Heat of vaporization}\left(\frac{\text{J}}{\text{g}}\right)$$

If the intermolecular forces are strong then large amounts of heat must be added to overcome these forces and the heats of fusion and vaporization will be large. Table 8.5 gives a list of heats of fusion and heats of vaporization for some common substances. Butane, for example, has a small heat of vaporization since the predominant intermolecular forces in butane (dispersion) are relatively weak. Water, on the other hand, has a particularly high heat of vaporization because of its unusually strong hydrogen bonding interactions. Thus, water evaporates more slowly than many other liquids, takes a long time to boil away, and absorbs more heat in the process. A so-called *heating curve,* which indicates the temperature and state changes as heat is added, is shown in Figure 8.24.

Table 8.5 Melting Points, Boiling Points, Heats of Fusion, and Heats of Vaporization of Some Common Substances

Substance	Melting Point (K)	Boiling Point (K)	Heat of Fusion (J/g)	Heat of Vaporization (J/g)
Ammonia	195.3	239.6	351	1370
Butane	134.6	272.5	80.3	387
Ether	157	307.6	98.3	358
Ethanol	155.7	351.5	109	837
Isopropanol	183.5	355.4	89.5	665
Sodium	370.8	1156	113	4250
Water	273	373	333	2260



◀ Figure 8.24
A heating curve for water, showing the temperature and state changes that occur when heat is added. The horizontal lines at 273 K (0 °C) and 373 K (100 °C) represent the heat of fusion and heat of vaporization, respectively. The sloped lines represent temperature changes resulting from absorbed heat relative to the specific heat of the substance in a given phase.

Worked Example 8.12 Heat of Fusion: Calculating Total Heat of Melting

Naphthalene, an organic substance often used in mothballs, has a heat of fusion of 149 J/g and a molar mass of 128.0 g/mol. How much heat in kilojoules is required to melt 0.300 mol of naphthalene?

ANALYSIS The heat of fusion tells how much heat is required to melt 1 g. To find the amount of heat needed to melt 0.300 mol, we need a mole-to-mass conversion.

BALLPARK ESTIMATE Naphthalene has a molar mass of 128.0 g/mol, so 0.300 mol has a mass of about one-third this amount, or about 40 g. Approximately 150 J is required to melt 1 g, so we need about 40 times this amount of heat or $150 \times 40 = 6000\ \text{J} = 6.0\ \text{kJ}$.

SOLUTION

STEP 1: Identify known information. We know heat of fusion (cal/g) and the number of moles of naphthalene.

Heat of fusion = 149 J/g
Moles of naphthalene = 0.300 mol

STEP 2: Identify answer and units.

Heat = ?? cal or J

STEP 3: Identify conversion factors. First, convert moles of naphthalene to grams using the molar mass (128 g/mol) as a conversion factor. Then use the heat of fusion as a conversion factor to calculate the total heat necessary to melt the mass of naphthalene.

$$(0.300\ \cancel{\text{mol}}\ \text{naphthalene})\left(\frac{128.0\ \text{g}}{1\ \cancel{\text{mol}}}\right) = 38.4\ \text{g naphthalene}$$

Heat of fusion = 149 J/g

STEP 4: Solve. Multiplying the mass of naphthalene by the heat of fusion then gives the answer.

$$(38.4\ \cancel{\text{g naphthalene}})\left(\frac{149\ \text{J}}{1\ \cancel{\text{g naphthalene}}}\right) = 5720\ \text{J} = 5.72\ \text{kJ}$$

BALLPARK CHECK The calculated result agrees with our estimate (6.0 kJ)

PROBLEM 8.23

How much heat in kilojoules is required to (a) melt and (b) boil 1.50 mol of isopropanol (rubbing alcohol; molar mass = 60.0 g/mol)? The heat of fusion and heat of vaporization of isopropanol are given in Table 8.5.

PROBLEM 8.24

How much heat in kilojoules is released by the condensation of 2.5 mol of steam? The heat of vaporization is given in Table 8.5.

PROBLEM 8.25

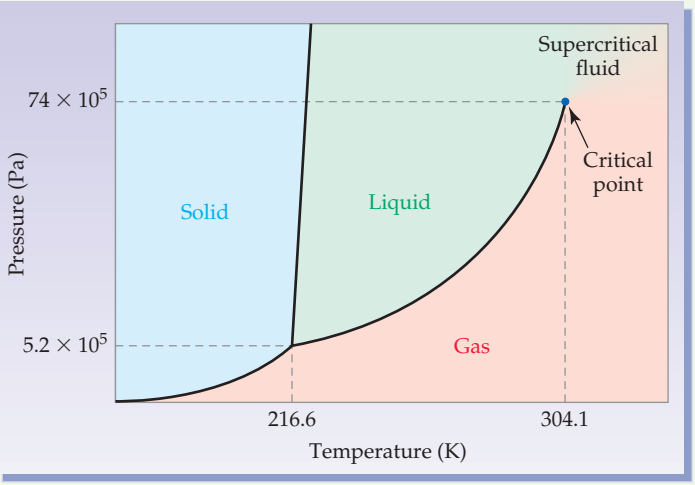
Compare the ΔH_{vap} values for water, isopropanol, ether, and ammonia, and order them from lowest to highest. Explain the rank order based on intermolecular attractive forces.

CHEMISTRY IN ACTION

CO_2 as an Environmentally Friendly Solvent

As noted in the chapter opener, most of us are familiar with CO_2 as an atmospheric gas, and as solid "dry ice," but how can CO_2 be a solvent?

Consider the two factors that determine the physical state of a substance: temperature and pressure. In the solid state, molecules are packed closely together and do not have enough kinetic energy to overcome the intermolecular forces. If we increase the temperature, however, we increase the kinetic energy so that the molecules can move apart and produce a phase change to either a liquid or a gas. In the gas state, molecules are too far apart to interact, but increasing the pressure will force molecules closer together and, eventually, intermolecular attractions between molecules will cause them to condense into a liquid or solid state. This dependence of the physical state on temperature and pressure is represented by a *phase diagram,* such as the one shown here for CO_2.



The *supercritical state* is intermediate between liquid and gas. The molecules are too far apart to be truly a liquid, yet they are too close together to be truly a gas. Supercritical CO_2 exists above the *critical point.* Above 74×10^5, the pressure is high enough to prevent molecules from expanding into the gas state; above 304.2 K (31.2 °C), the molecules have too much kinetic energy to condense into the liquid state.

Because open spaces already exist between CO_2 molecules, it is energetically easy for dissolved molecules to slip in, and supercritical CO_2 is therefore an extraordinarily good solvent. Among its many applications, supercritical CO_2 is used in the beverage and food-processing industries to decaffeinate coffee beans and to obtain spice extracts from vanilla, pepper, cloves, nutmeg, and other seeds. In the cosmetics and perfume industry, fragrant oils are extracted from flowers using supercritical CO_2. It is also used in the cleaning and sterilization of medical implants; because supercritical CO_2 has very low surface tension, it can permeate all the cracks and crevices in implant devices and afterward simply evaporates leaving no residue.

In the pharmaceutical industry, it can be used for both the extraction and processing of pharmacologically active compounds. Extraction of therapeutic natural products is accomplished without the use of organic solvents so the product contains no residual solvent impurities. Supercritical fluids (SCFs) are also used in processing of drugs; rapid recrystallization of drug compounds from SCF solvents produces much smaller particles with high surface areas, which can be absorbed more readily by the body and are more suitable for microencapsulated and aerosol delivery systems.

Perhaps the most impactful application is the use of carbon dioxide for dry-cleaning clothes, thereby replacing environmentally harmful chlorinated solvents with an alternative that is nontoxic and nonflammable. Industrial processes using CO_2 are designed as closed systems so that the CO_2 is recaptured after use and continually recycled. No organic solvent vapors are released into the atmosphere and no toxic liquids seep into groundwater supplies, as can occur with current procedures using chlorinated organic solvents. The future looks bright for this new "green" technology.

CIA Problem 8.6 What is a supercritical fluid?

CIA Problem 8.7 What are the environmental advantages of using supercritical CO_2 in place of chlorinated organic solvents?

CIA Problem 8.8 The physical state of CO_2 depends on the temperature and pressure. In what state would you expect to find CO_2 at 51×10^5 and 298 K (25 °C)?

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Identify phase changes as endothermic or exothermic, and predict how a change in temperature will affect a phase change.** Melting occurs when a solid is converted to a liquid; vaporization occurs when a liquid is converted to a gas; sublimation occurs when a solid is converted to a gas. These physical changes are endothermic (absorb heat, $\Delta H > 0$) and involve an increase in entropy ($\Delta S > 0$). Freezing occurs when a liquid is converted to a solid; condensation occurs when a gas is converted to a liquid; deposition occurs when a gas is converted to a solid. These physical changes are exothermic (release heat, $\Delta H < 0$) and involve a decrease in entropy ($\Delta S < 0$). Identify the different types of intermolecular forces, and predict the predominant forces responsible for the physical properties of a given compound *(see Problems 27, 28, 36, 37, and 114).*

- **Identify the different types of intermolecular attractive forces, and predict the predominant forces responsible for the physical properties of a given substance.** There are three major types of *intermolecular forces,* which act to hold molecules near one another in solids and liquids. *London dispersion forces* occur between all molecules as a result of temporary molecular polarities due to unsymmetrical electron distribution. These forces increase in strength with molecular mass and with the surface area of molecules. *Dipole–dipole forces* are the electrical attractions that occur between polar molecules. *Hydrogen bonding,* the strongest of the three intermolecular forces, occurs between a hydrogen atom bonded to O, N, or F and a nearby O, N, or F atom *(see Problems 34–37, 93, 109, and 113).*

- **Use the kinetic–molecular theory to explain the behavior of gases.** According to the *kinetic–molecular theory of gases,* the physical behavior of gases can be explained by assuming that they consist of particles moving rapidly at random, separated from other particles by great distances, and colliding without loss of energy. The kinetic energy of gas particles is directly proportional to absolute temperature (Kelvin scale). Gas pressure is the result of molecular collisions with a surface *(see Problems 29, 40, 41, and 100).*

- **Define pressure, and convert between units of pressure.** Pressure is defined as *force/area* ($P = F/A$). Common units for pressure are *pounds per square inch (psi), atmospheres (atm), torr (or mmHg),* and *pascals (Pa).* The relationship between these units is 1 atm = 760 mmHg = 14.7 psi = 101,325 Pa *(see Problems 30, 38, 39, and 42–45).*

- **Use Boyle's law to calculate the changes in pressure or volume of a gas at a given temperature.** *Boyle's law* says that the volume of a fixed amount of gas at constant temperature is inversely proportional to its pressure ($P_1V_1 = P_2V_2$) *(see Problems 26, 32, and 46–51).*

- **Use Charles's law to calculate changes in volume of a gas as a function of temperature.** *Charles's law* says that the volume of a fixed amount of gas at constant pressure is directly proportional to its Kelvin temperature ($V_1/T_1 = V_2/T_2$). *(see Problems 26, 27, and 52–57).*

- **Use Gay-Lussac's law to calculate changes in pressure of a gas as a function of temperature.** *Gay-Lussac's law* says that the pressure of a fixed amount of gas at constant volume is directly proportional to its Kelvin temperature ($P_1/T_1 = P_2/T_2$) *(see Problems 58–61).*

- **Use the combined gas law to determine changes in pressure, temperature, or volume of a gas.** Boyle's law, Charles's law, and Gay-Lussac's law together give the *combined gas law* ($P_1V_1/T_1 = P_2V_2/T_2$), which applies to changing conditions for a fixed quantity of gas *(see Problems 26, 32, and 62–67).*

- **Use Avogadro's law to calculate the volume for a given number of moles of a gas.** *Avogadro's law* says that equal volumes of gases at the same temperature and pressure contain the same number of moles ($V_1/n_1 = V_2/n_2$) *(see Problems 32, 68–75, 101, 107, and 111).*

- **Use the ideal gas law to calculate the pressure, temperature, volume, or number of moles of an ideal gas.** The four gas laws together give the *ideal gas law,* $PV = nRT$, which relates the effects of temperature, pressure, volume, and molar amount. If three of the four variables are specified, the fourth can be calculated using the ideal gas law. At 0 °C and 1 atm pressure, called *standard temperature and pressure (STP),* 1 mol of any gas (6.02×10^{23} molecules) occupies a volume of 22.4 L *(see Problems 76–85, 102–106, 108, and 110).*

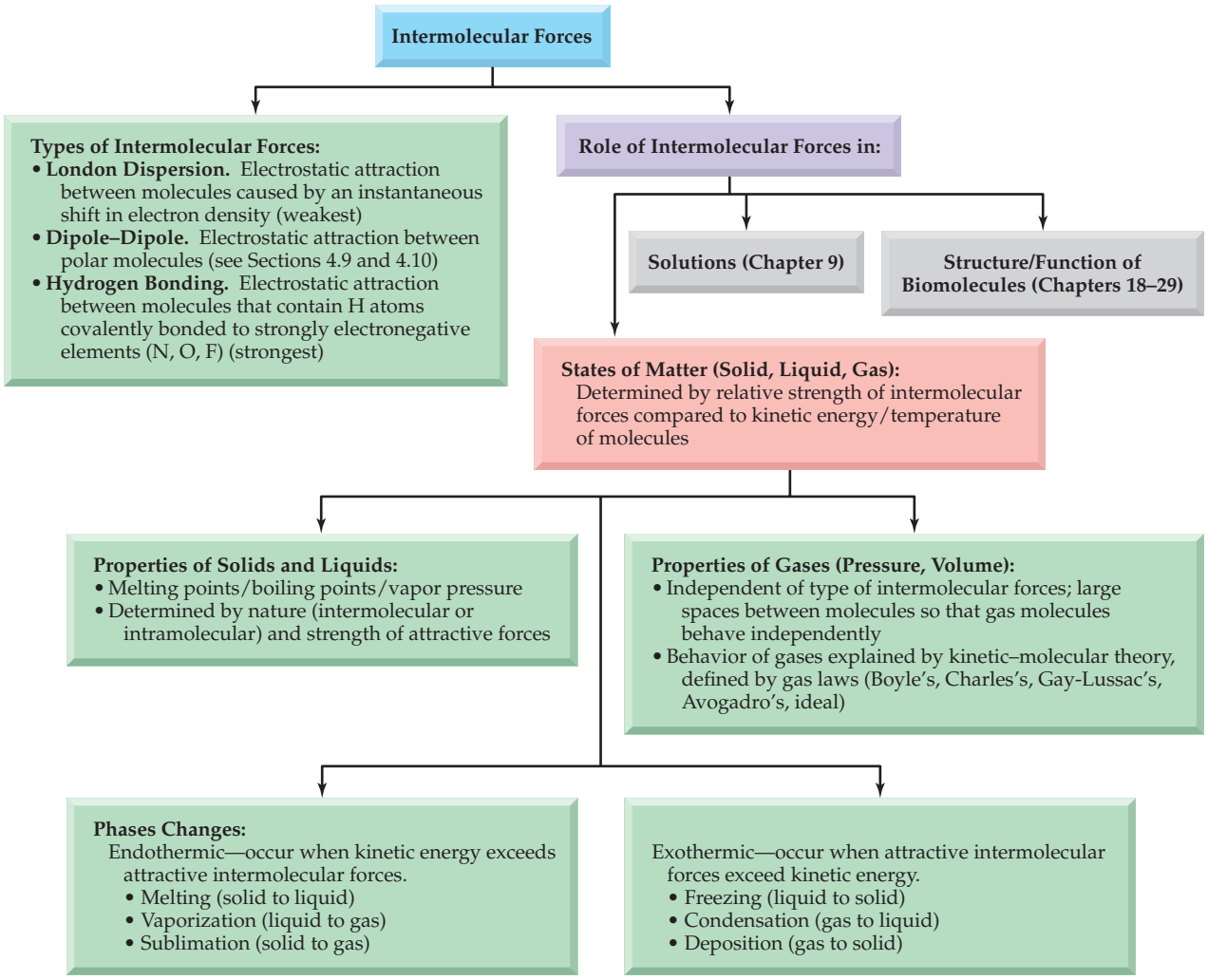
- **Use Dalton's law to calculate the partial pressure or the number of moles of a gas in a mixture.** The amount of pressure exerted by an individual gas in a mixture is called the *partial pressure* of the gas. According to *Dalton's law,* the total pressure exerted by the mixture is equal to the sum of the partial pressures of the individual gases and is proportional to the mole fraction of the gas in the mixture *(see Problems 33, 86–89, and 112).*

- **Identify how the vapor pressure, boiling point, and surface tension of liquids are related to temperature and intermolecular forces.** As a liquid is heated, molecules escape from the surface of a liquid until an equilibrium is reached between liquid and gas, resulting in a *vapor pressure* of the liquid. At a liquid's *boiling point,* its vapor pressure equals atmospheric pressure, and the entire liquid is converted into gas. The vapor pressure of a liquid is inversely related to the strength of the intermolecular forces of attraction between molecules; the boiling point of a liquid is directly related to the strength of the intermolecular forces *(see Problems 28, 90, 92, 93, and 109).*

- **Distinguish between the different types of solids and explain their physical properties.** Solids are either crystalline or amorphous. *Crystalline solids* are those whose constituent particles have an ordered arrangement; *amorphous solids* lack internal order and do not have sharp melting points. There are several kinds of crystalline solids: *Ionic solids* are those such as sodium chloride, whose constituent particles are ions. *Molecular solids* are those such as ice, whose constituent particles are molecules held together by intermolecular forces. *Covalent network solids* are those such as diamond, whose atoms are linked together by covalent bonds into a giant three-dimensional array. *Metallic solids,* such as silver or iron, also consist of large arrays of atoms, but their crystals have metallic properties such as electrical conductivity *(see Problems 96–99).*

- **Calculate the total amount of heat associated with changes in physical states of a substance.** When a solid is heated, particles begin to move around freely at the *melting point,* and the substance becomes liquid. The amount of heat necessary to melt a given amount of solid at its melting point is its *heat of fusion.* The amount of heat necessary to vaporize a given amount of liquid at its boiling point is called its *heat of vaporization (see Problems 31, 91, 94, 95, 98, and 99).*

CONCEPT MAP: GASES, LIQUIDS, AND SOLIDS



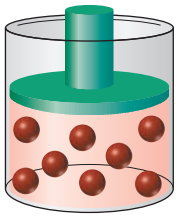
▲ **Figure 8.25 Concept Map.** The physical state of matter (solid, liquid, gas) depends on the strength of the intermolecular forces between molecules compared to the kinetic energy of the molecules. When the kinetic energy (i.e., temperature) is greater than the forces holding molecules in a given state, then a phase change occurs. Thus, the physical properties of matter (melting and boiling points, etc.) depend on the strength of the intermolecular forces between molecules, which depend on chemical structure and molecular shape. These relationships are reflected in the map above.

KEY WORDS

Amorphous solid, *p. 276*
Avogadro's law, *p. 268*
Boiling point (bp), *p. 252*
Boyle's law, *p. 261*
Change of state, *p. 251*
Charles's law, *p. 264*
Combined gas law, *p. 267*
Crystalline solid, *p. 275*
Dalton's law, *p. 272*
Dipole–dipole force, *p. 253*
Gas constant (*R*), *p. 270*
Gas laws, *p. 261*
Gay-Lussac's law, *p. 266*
Heat of fusion, *p. 277*
Heat of vaporization, *p. 277*
Hydrogen bond, *p. 254*
Ideal gas, *p. 257*
Ideal gas law, *p. 270*
Intermolecular forces, *p. 253*
Kinetic–molecular theory of gases, *p. 257*
London dispersion force, *p. 253*
Melting point (mp), *p. 252*
Normal boiling point, *p. 274*
Partial pressure, *p. 272*
Pressure (*P*), *p. 257*
Standard temperature and pressure (STP), *p. 269*
Standard molar volume, *p. 269*
Van der Waals forces, *p. 253*
Vapor, *p. 273*
Vapor pressure, *p. 274*

UNDERSTANDING KEY CONCEPTS

8.26 Assume that you have a sample of gas in a cylinder with a movable piston, as shown in the following drawing:



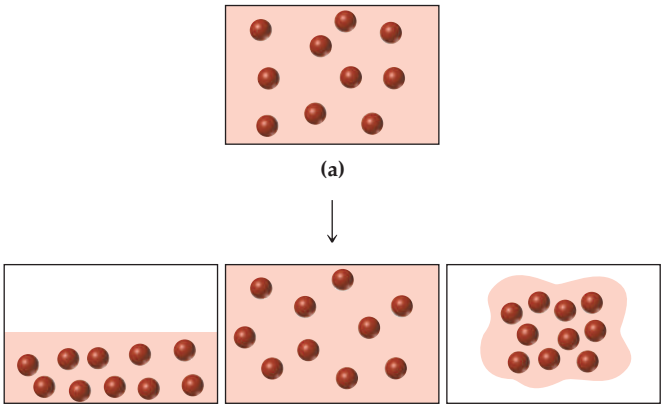
Redraw the apparatus to show what the sample will look like after the following changes:

(a) The temperature is increased from 300 K to 450 K at constant pressure.

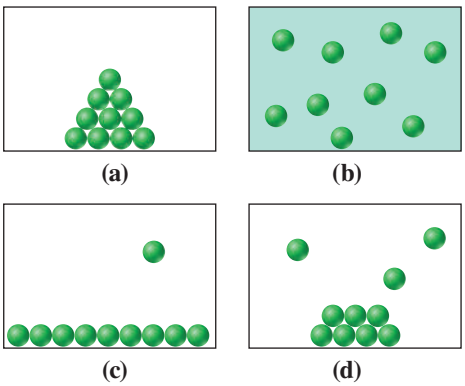
(b) The pressure is increased from 1.0×10^5 Pa to 2.0×10^5 Pa at constant temperature.

(c) The temperature is decreased from 300 K to 200 K and the pressure is decreased from 3.0×10^5 Pa to 2.0×10^5 Pa.

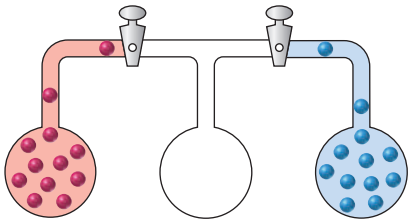
8.27 Assume that you have a sample of gas at 350 K in a sealed container, as represented in part (a). Which of the drawings (b)–(d) represents the gas after the temperature is lowered from 350 K to 150 K and if the gas has a boiling point of 200 K? Which drawing represents the gas at 150 K if the gas has a boiling point of 100 K?



8.28 Assume that drawing (a) represents a sample of H_2O at 200 K. Which of the drawings (b)–(d) represents what the sample will look like when the temperature is raised to 300 K?

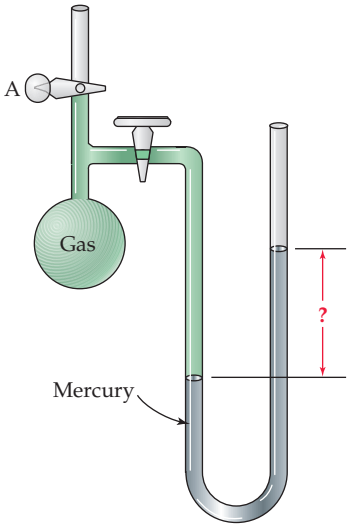


8.29 Three bulbs, two of which contain different gases and one of which is empty, are connected as shown in the following drawing:

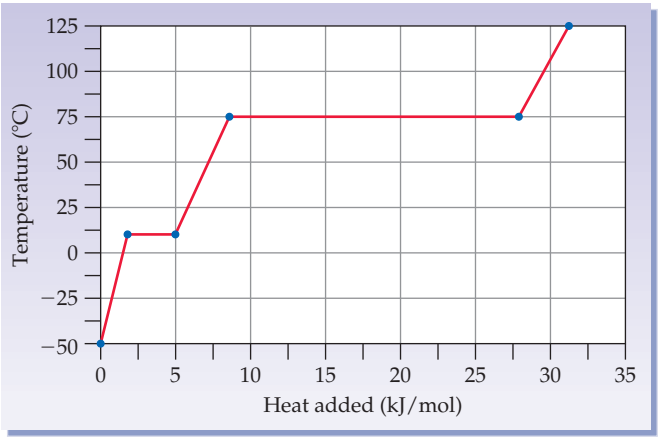


Redraw the apparatus to represent the gases after the stopcocks are opened and the system is allowed to come to equilibrium.

8.30 Redraw the following open-ended manometer to show what it would look like when stopcock A is opened.



8.31 The following graph represents the heating curve of a hypothetical substance:



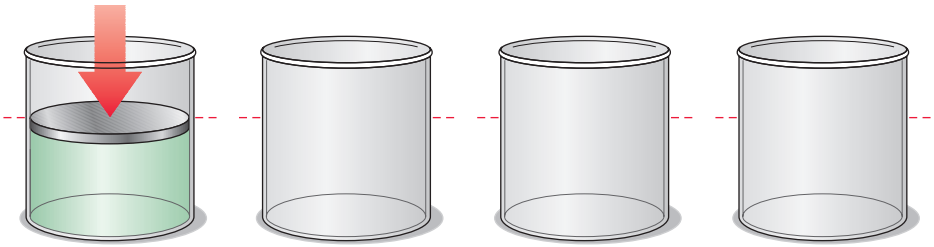
(a) What is the melting point of the substance?

(b) What is the boiling point of the substance?

(c) Approximately what is the heat of fusion for the substance in kJ/mol?

(d) Approximately what is the heat of vaporization for the substance in kJ/mol?

8.32 Show the approximate level of the movable piston in drawings (a)–(c) after the indicated changes have been made to the gas.



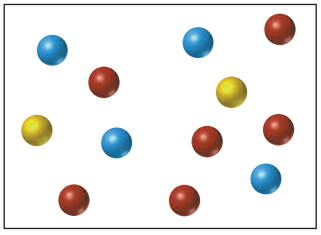
(initial)
$T = 25\ ^\circ C$
$n = 0.075$ mol
$P = 120$ Pa

(a)
$T = 50\ ^\circ C$
$n = 0.075$ mol
$P = 120$ Pa

(b)
$T = 175\ ^\circ C$
$n = 0.075$ mol
$P = 350$ Pa

(c)
$T = 25\ ^\circ C$
$n = 0.22$ mol
$P = 350$ Pa

8.33 The partial pressure of the blue gas in the container represented in the picture is 0.32×10^5 Pa. What are the partial pressures of the yellow and red gases? What is the total pressure inside the container?



ADDITIONAL PROBLEMS

INTERMOLECULAR FORCES (SECTIONS 8.1 AND 8.2)

8.34 What characteristic must a compound have to experience the following intermolecular forces?

(a) London dispersion forces

(b) Dipole–dipole forces

(c) Hydrogen bonding

8.35 Identify the predominant intermolecular force in each of the following substances.

(a) N_2 **(b)** HCN **(c)** CCl_4

(d) NH_3 **(e)** CH_3Cl **(f)** CH_3COOH

8.36 Dimethyl ether (CH_3OCH_3) and ethanol (C_2H_5OH) have the same formula (C_2H_6O), but the boiling point of dimethyl ether is $-25\ ^\circ C$ while that of ethanol is $78\ ^\circ C$. Explain this difference in boiling points.

8.37 Iodine is a solid at room temperature $(\text{mp} = 113.5\ ^\circ C)$ while bromine is a liquid $(\text{mp} = -7\ ^\circ C)$. Explain this difference in terms of intermolecular forces.

GASES AND PRESSURE (SECTIONS 8.3 AND 8.4)

8.38 How is 1 atm of pressure defined?

8.39 List four common units for measuring pressure.

8.40 What are the four assumptions of the kinetic–molecular theory of gases?

8.41 How does the kinetic–molecular theory of gases explain gas pressure?

8.42 Convert the following values into mmHg:

(a) Standard pressure **(b)** 25.3 psi

(c) 7.5 atm **(d)** 28.0 in. Hg

(e) 41.8 Pa

8.43 Atmospheric pressure at the top of the Mont Blanc in the Alps is 420 mmHg.

(a) How many atmospheres is this?

(b) How many pascals is this?

8.44 What is the pressure (in mmHg) inside a container of gas connected to a mercury-filled, open-ended manometer of the sort shown in Figure 8.10 when the level in the arm connected to the container is 17.6 cm lower than the level in the arm open to the atmosphere and the atmospheric pressure reading outside the apparatus is 754.3 mmHg? What is the pressure inside the container in atmospheres?

8.45 What is the pressure (in atmospheres) inside a container of gas connected to a mercury-filled, open-ended manometer of the sort shown in Figure 8.10 when the level in the arm connected to the container is 28.3 cm higher than the level in the arm open to the atmosphere, and the atmospheric pressure reading outside the apparatus is 1.021 atm? What is the pressure in mmHg?

BOYLE'S LAW (SECTION 8.5)

8.46 What is Boyle's law, and what variables must be kept constant for the law to hold?

8.47 Which assumptions of the kinetic–molecular theory explain the behavior of gases described by Boyle's law? Explain your answer.

8.48 The pressure of gas in a 600.0 mL cylinder is 86×10^2 Pa. What is the new volume when the pressure is increased to 51×10^3 Pa?

8.49 The volume of a balloon is 2.85 L at 1.00×10^5 Pa. What pressure is required to compress the balloon to a volume of 1.70 L?

8.50 The use of CFCs as refrigerants and propellants in aerosol cans has been discontinued as a result of concerns about the ozone layer. If an aerosol can contained 350 mL of CFC gas at a pressure of 5.0×10^5 Pa, what volume would this gas occupy at 101,325 Pa?

8.51 A balloon occupies a volume of 1.25 L at sea level where the ambient pressure is 1 atm. What volume would the balloon occupy at an altitude of 10,700 m, where the air pressure is only 220 mmHg?

CHARLES'S LAW (SECTION 8.6)

8.52 What is Charles's law, and what variables must be kept constant for the law to hold?

8.53 Which assumptions of the kinetic–molecular theory explain the behavior of gases described by Charles's law? Explain your answer.

8.54 A hot-air balloon has a volume of 0.96 m^3 at 291 K. To what temperature (in °C) must it be heated to raise its volume to 1.20 m^3, assuming the pressure remains constant?

8.55 A hot-air balloon has a volume of 0.875 m^3. What is the original temperature of the balloon if its volume changes to 0.955 m^3 when heated to 56 °C?

8.56 A gas sample has a volume of 0.185×10^{-6} m^3 at 38 °C. What is its volume at 97 °C?

8.57 A balloon has a volume of 0.0430 m^3 at 25 °C. What is its volume at 2.8 °C?

GAY-LUSSAC'S LAW (SECTION 8.7)

8.58 What is Gay-Lussac's law, and what variables must be kept constant for the law to hold?

8.59 Which assumptions of the kinetic–molecular theory explain the behavior of gases described by Gay-Lussac's law? Explain your answer.

8.60 A glass laboratory flask is filled with gas at 25 °C and 0.95 atm pressure, sealed, and then heated to 117 °C. What is the pressure inside the flask?

8.61 An aerosol can has an internal pressure of 3.85 atm at 25 °C. What temperature is required to raise the pressure to 18.0 atm?

COMBINED GAS LAW (SECTION 8.8)

8.62 A gas has a volume of 2.84 L at 1.00 atm and 0 °C. At what temperature does it have a volume of 7.50 L at 520 mmHg?

8.63 A compressed-air tank carried by scuba divers has a volume of 6.80 L and a pressure of 120 atm at 20 °C. What is the volume of air in the tank at 0 °C and 1.00 atm pressure (STP)?

8.64 When H_2 gas was released by the reaction of HCl with Zn, the volume of H_2 collected was 75.4 mL at 23 °C and 748 mmHg. What is the volume of the H_2 at 0 °C and 1.00 atm pressure (STP)?

8.65 What is the effect on the volume of a gas if you simultaneously:

(a) Halve its pressure and double its Kelvin temperature?

(b) Double its pressure and double its Kelvin temperature?

8.66 What is the effect on the pressure of a gas if you simultaneously:

(a) Halve its volume and double its Kelvin temperature?

(b) Double its volume and halve its Kelvin temperature?

8.67 A small cylinder of helium gas used for filling balloons has a volume of 2.30 L and a pressure of 1850 atm at 25 °C. How many balloons can you fill if each one has a volume of 1.5 L and a pressure of 1.25 atm at 25 °C?

AVOGADRO'S LAW AND STANDARD MOLAR VOLUME (SECTION 8.9)

8.68 Explain Avogadro's law using the kinetic–molecular theory of gases.

8.69 What conditions are defined as STP?

8.70 How many molecules are in 1.0 L of O_2 at STP? How may grams of O_2?

8.71 How many moles of gas are in a volume of 48.6 L at STP?

8.72 What is the mass of CH_4 in a sample that occupies a volume of 16.5 L at STP?

8.73 Assume that you have 1.75 g of the deadly gas hydrogen cyanide, HCN. What is the volume of the gas at STP?

8.74 A typical room is 4.0 m long, 5.0 m wide, and 2.5 m high. What is the total mass of the oxygen in the room assuming that the gas in the room is at STP and that air contains 21% oxygen and 79% nitrogen?

8.75 What is the total volume and number of moles of nitrogen in the room described in Problem 8.74?

IDEAL GAS LAW (SECTION 8.10)

8.76 What is the ideal gas law?

8.77 How does the ideal gas law differ from the combined gas law?

8.78 Which sample contains more molecules: 2.0 L of Cl_2 at STP or 3.0 L of CH_4 at 300 K and 1150 mmHg? Which sample weighs more?

8.79 Which sample contains more molecules: 2.0 L of CO_2 at 300 K and 500 mmHg or 1.5 L of N_2 at 57 °C and 760 mmHg? Which sample weighs more?

8.80 If 2.3 mol of He has a volume of 0.15 L at 294 K, what is the pressure in atm? In Pa?

8.81 If 3.5 mol of O_2 has a volume of 27.0 L at a pressure of 1.6 atm, what is its temperature in degrees Celsius?

8.82 If 15.0 g of CO_2 gas has a volume of 0.30 L at 310 K, what is its pressure in mmHg? In Pa?

8.83 If 20.0 g of N_2 gas has a volume of 4.00 L and a pressure of 6.0 atm, what is its temperature?

8.84 If 18.0 g of O_2 gas has a temperature of 350 K and a pressure of 550 mmHg, what is its volume?

8.85 How many moles of a gas will occupy a volume of 0.55 L at a temperature of 347 K and a pressure of 2.5 atm?

DALTON'S LAW AND PARTIAL PRESSURE (SECTION 8.11)

8.86 What is meant by *partial pressure*?

8.87 What is Dalton's law?

8.88 If the partial pressure of oxygen in air at 1.0 atm is 160 mmHg, what is its partial pressure on the summit of Mt. Whitney, where atmospheric pressure is 440 mmHg? Assume that the percent oxygen is the same.

8.89 Scuba divers who suffer from decompression sickness are treated in hyperbaric chambers using heliox (21% oxygen, 79% helium) at pressures up to 120 psi. Calculate the partial pressure of O_2 (in mmHg) in a hyperbaric chamber under these conditions.

LIQUIDS (SECTIONS 8.12 AND 8.14)

8.90 What is the vapor pressure of a liquid?

8.91 What is a liquid's heat of vaporization?

8.92 What is the effect of pressure on a liquid's boiling point?

8.93 Which of the following substances would you expect to have the higher vapor pressure: CH_3OH or CH_3Cl? Explain.

8.94 The heat of vaporization of water is 40.7 kJ/mol.

(a) How much heat (in kilojoules) is required to vaporize 3.00 mol of H_2O?

(b) How much heat (in kilojoules) is released when 320 g of steam condenses?

8.95 Patients with a high body temperature are often given "alcohol baths." The heat of vaporization of isopropanol (rubbing alcohol) is 665 J/g. How much heat is removed from the skin by the evaporation of 190 g (about half a cup) of isopropanol?

SOLIDS (SECTION 8.13)

8.96 What is the difference between an amorphous and a crystalline solid?

8.97 List three kinds of crystalline solids, and give an example of each.

8.98 The heat of fusion of acetic acid, the principal organic component of vinegar, is 192 J/g. How much heat (in kilojoules) is required to melt 1.75 mol of solid acetic acid?

8.99 The heat of fusion of sodium metal is 2.6 kJ/mol. How much heat (in kilojoules) is required to melt 262 g of sodium?

CONCEPTUAL PROBLEMS

8.100 Use the kinetic–molecular theory to explain why gas pressure increases if the temperature is raised and the volume is kept constant.

8.101 Hydrogen and oxygen react according to the equation $2\,H_2(g) + O_2(g) \longrightarrow 2\,H_2O(g)$. According to Avogadro's law, how many liters of hydrogen are required to react with 2.5 L of oxygen at STP?

8.102 If 3.0 L of hydrogen and 1.5 L of oxygen at STP react to yield water, how many moles of water are formed? What gas volume does the water have at a temperature of 100 °C and 1 atm pressure?

8.103 Approximately 240 mL/min of CO_2 is exhaled by an average adult at rest. Assuming a temperature of 37 °C and 1 atm pressure, how many moles of CO_2 is this?

8.104 How many grams of CO_2 are exhaled by an average resting adult in 24 hours? (See Problem 8.103.)

8.105 When fully inflated, a hot-air balloon has a volume of 1.6×10^5 L at an average temperature of 375 K and a pressure of 0.975 atm. Assuming that air has an average molar mass of 29 g/mol, what is the density of the air in the hot-air balloon? How does this compare with the density of air at STP?

8.106 A 10.0 g sample of an unknown gas occupies 1.47×10^{-2} m^3 at a temperature of 298 K (25 °C) and a pressure of 1.03×10^5 Pa. How many moles of gas are in the sample? What is the molar mass of the gas?

8.107 One mole of any gas has a volume of 22.4 L at STP. What are the molecular masses of the following gases, and what are their densities in grams per liter at STP?

(a) CH_4 **(b)** CO_2 **(c)** O_2

8.108 Gas pressure outside the space shuttle is approximately 1×10^{-14} mm Hg at a temperature of approximately 1 K. If the gas is almost entirely hydrogen atoms (H, not H_2), what volume of space is occupied by 1 mol of atoms? What is the density of H gas in atoms per liter?

8.109 Ethane-1,2-diol, $C_2H_6O_2$, has one OH bonded to each carbon.

(a) Draw the Lewis dot structure of ethane-1,2-diol.

(b) Draw the Lewis dot structure of chloroethane, C_2H_5Cl.

(c) Chloroethane has a slightly higher molar mass than ethane-1,2-diol but a much lower boiling point (3 °C versus 198 °C). Explain.

8.110 Isooctane, C_8H_{18}, is the component of gasoline from which the term *octane rating* derives.

(a) Write a balanced equation for the combustion of isooctane to yield CO_2 and H_2O.

(b) Assuming that gasoline is 100% isooctane and that the density of isooctane is 0.792 g/mL, what mass of CO_2 (in kilograms) is produced each year by the annual U.S. gasoline consumption of 4.6×10^{10} L?

(c) What is the volume (in liters) of this CO_2 at STP?

GROUP PROBLEMS

8.111 Imagine that you have two identical containers, one containing hydrogen at STP and the other containing oxygen at STP. How can you tell which is which without opening them?

8.112 A rule of thumb for scuba diving is that the external pressure increases by 1 atm for every 10 m of depth. A diver using a compressed air tank is planning to descend to a depth of 25 m.

(a) What is the external pressure at this depth? (Remember that the pressure at sea level is 1 atm.)

(b) Assuming that the tank contains 20% oxygen and 80% nitrogen, what is the partial pressure of each gas in the diver's lungs at this depth?

8.113 Obtain an aerosol can and read the list of ingredients. Some of the ingredients are "active" (e.g., the substance used as a deodorant or a lubricant) while others are listed as "inert." For aerosol products, one of the inert ingredients is typically used as a propellant to provide the pressure necessary to disperse the active ingredients as an aerosol.

(a) For your aerosol product, identify the inert ingredient used as the propellant and research its physical properties (melting point and boiling point).

(b) Discuss how the physical properties make it suitable for the aerosol application.

8.114 Obtain phase diagrams for water and carbon dioxide.

(a) Based on the phase diagram for water, explain how it is possible to skate on ice, that is, solid water.

(b) Would it be possible to skate on "dry ice," that is, solid CO_2?

8.115 The increase in atmospheric CO_2 levels has been correlated with the combustion of fossil fuels (see the Chemistry in Action "Greenhouse Gases and Global Warming" on p. 260). How would the atmospheric CO_2 levels be affected by a shift to corn-based ethanol or some other biomass-based fuel? Explain.

9

Solutions

CONTENTS

CONCEPTS TO REVIEW

A. Ions and Ionic Compounds (Sections 3.1 and 3.10)
B. Enthalpy Changes (Section 7.2)
C. Chemical Equilibrium (Section 7.7)
D. Le Châtelier's Principle (Section 7.9)
E. Intermolecular Forces and Hydrogen Bonds (Section 8.2)
F. Partial Pressure of Gases (Section 8.11)
G. Vapor Pressure (Section 8.12)

▲ Controlled-release medications provide significant benefits for the treatment of many conditions, including attention deficit-hyperactivity disorder (ADHD). Development of appropriate drug delivery systems requires consideration of many factors discussed in this chapter, including drug solubility and osmosis.

Have you ever taken medication for motion sickness or for allergy relief or to relieve chronic pain? While the biological activity of these drugs is often complex, and a topic for later chapters, the delivery systems used to control the release of these drugs in the body are equally complex. Some drugs taken for relief of acute asthma or extreme pain must be fast acting. Other pharmaceuticals, for treatment of conditions such as attention deficit hyperactivity disorder (ADHD) and diabetes, are more beneficial if delivered in controlled doses over extended periods of time. An effective drug delivery system must consider many factors: How soluble is it? What concentration of the drug in the blood is necessary to provide a therapeutic response without toxic side effects? How can the release of the drug be controlled to provide the optimal dose?

To date, we have discussed the properties of pure substances, but to answer the questions raised in the introduction we need to examine how different substances interact to form mixtures, which we call *solutions.* Specifically, we will address how solutions are formed, how we can express quantitatively the amounts of substances in the solution, and how the properties of solutions differ from those of pure substances.

9.1 Mixtures and Solutions

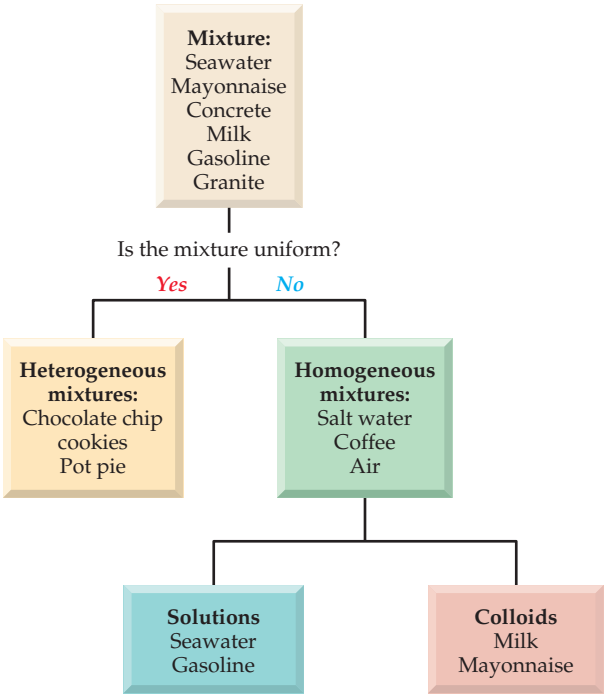
Learning Objective:

- Distinguish between heterogeneous and homogeneous mixtures and between solutions and colloids.

As we saw in Section 1.3, a *mixture* is an intimate combination of two or more substances, both of which retain their chemical identities. Mixtures can be classified as either *heterogeneous* or *homogeneous,* as indicated in Figure 9.1, depending on their appearance. In heterogeneous mixtures, the mixing is not uniform and the mixtures have regions of different composition. Rocky Road ice cream, for example, is a heterogeneous mixture, with something different in every spoonful. Mixing *is* uniform in homogenous mixtures, and they have the same composition throughout. Seawater, a homogeneous mixture of soluble ionic compounds in water, is an example.

Homogeneous mixtures are further classified as either *solutions* or *colloids,* according to the size of their particles. **Solutions,** the most important class of homogeneous mixtures, contain particles the size of a typical ion or small molecule—roughly 0.1–2 nm in diameter. **Colloids,** such as milk and fog, are also homogeneous in appearance but contain larger particles than solutions—in the range 2–500 nm diameter. Many common over-the-counter medications, such as Milk of Magnesia and PeptoBismol, are colloidal suspensions.

Liquid solutions, colloids, and heterogeneous mixtures can be distinguished in several ways. For example, liquid solutions are transparent (although they may be colored). Colloids may appear transparent if the particle size is small, but they have a murky or opaque appearance if the particle size is larger. Neither solutions nor small-particle colloids separate on standing, and the particles in both are too small to be removed by filtration. Heterogeneous mixtures and large-particle colloids, also known as "suspensions," are murky or opaque and their particles will slowly settle on prolonged standing. House paint is one example.



▲ **Figure 9.1**
Classification of mixtures.
The components in heterogeneous mixtures are not uniformly mixed, and the composition varies with location within the mixture. In homogeneous mixtures, the components are uniformly mixed at the molecular level.

Table 9.1 gives some examples of solutions, colloids, and heterogeneous mixtures. It is interesting to note that blood has characteristics of all three. About 45% by volume of blood consists of suspended red and white cells, which settle slowly on standing; the remaining 55% is *plasma,* which contains ions in solution and colloidal protein molecules.

Solution A homogeneous mixture that contains particles the size of a typical ion or small molecule.

Colloid A homogeneous mixture that contains particles that range in diameter from 2 to 500 nm.

Table 9.1 Some Characteristics of Solutions, Colloids, and Heterogeneous Mixtures

Type of Mixture	Particle Size	Examples	Characteristics
Solution	<2.0 nm	Air, seawater, gasoline, wine	Transparent to light; does not separate on standing; nonfilterable
Colloid	2.0–500 nm	Butter, milk, fog, pearl	Often murky or opaque to light; does not separate on standing; nonfilterable
Heterogeneous	>500 nm	Blood, paint, aerosol sprays	Murky or opaque to light; separates on standing; filterable

Although we usually think of solids dissolved in liquids when we talk about solutions, solutions actually occur in all three phases of matter (Table 9.2). Metal alloys like 14-karat gold (58% gold with silver and copper) and brass (10–40% zinc with copper), for instance, are solutions of one solid with another. For solutions in which a gas or solid is dissolved in a liquid, the dissolved substance is called the **solute** and the liquid is called the **solvent.** In seawater, for example, the dissolved salts would be the solutes and water would be the solvent. When one liquid is dissolved in another, the minor component is usually considered the solute and the major component is the solvent.

Solute A substance that is dissolved in a solvent.

Solvent The substance in which another substance (the solute) is dissolved.

Table 9.2 Some Different Types of Solutions

Type of Solution	Example
Gas in gas	Air (O_2, N_2, Ar, and other gases)
Gas in liquid	Seltzer water (CO_2 in water)
Gas in solid	H_2 in palladium metal
Liquid in liquid	Gasoline (mixture of hydrocarbons)
Liquid in solid	Dental amalgam (mercury in silver)
Solid in liquid	Seawater (NaCl and other salts in water)
Solid in solid	Metal alloys such as 14-karat gold (Au, Ag, and Cu)

PROBLEM 9.1

Classify the following liquid mixtures as heterogeneous or homogeneous. Further classify each homogeneous mixture as a solution or colloid.

(a) Orange juice with pulp **(b)** Apple juice

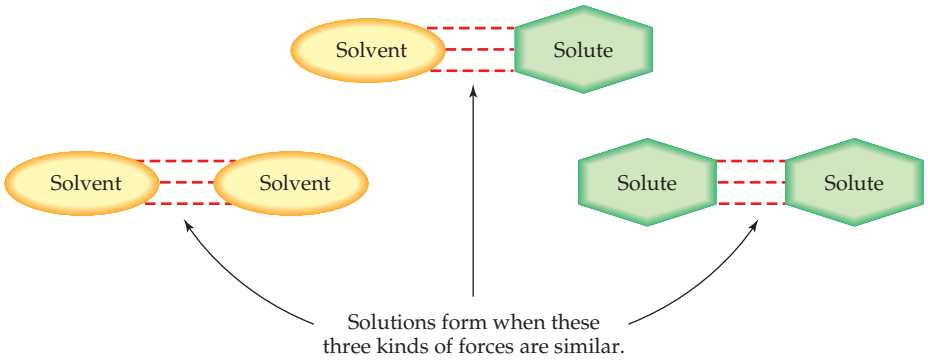
(c) Hand lotion **(d)** Tea

9.2 The Solution Process

Learning Objective:

- Predict whether a solution is likely to form based on the relative polarity and intermolecular forces between solute and solvent.

What determines whether a substance is soluble in a given liquid? Solubility depends primarily on the strength of the attractions between solute and solvent particles relative to the strengths of the attractions within the pure substances. Ethanol is soluble in water, for example, because hydrogen bonding (Section 8.2) is nearly as strong between water and ethanol molecules as it is between water molecules alone or ethanol molecules alone.



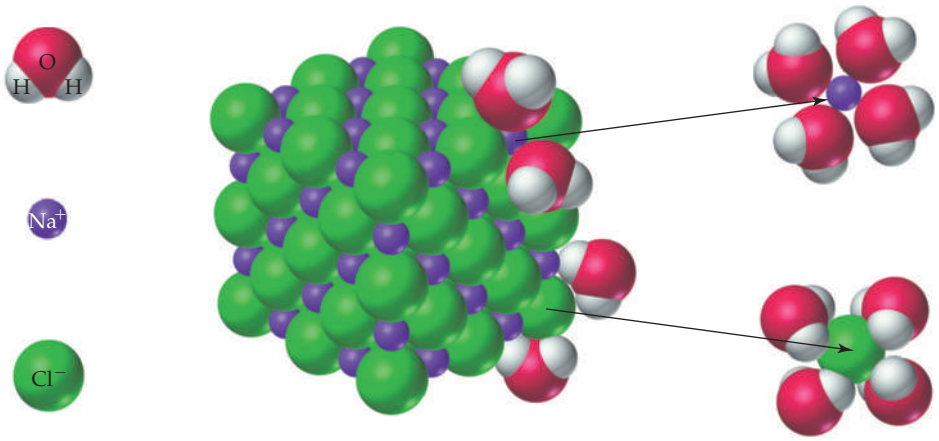
A good rule of thumb for predicting solubility is that "like dissolves like," meaning that substances with similar intermolecular forces form solutions with one another, whereas substances with different intermolecular forces do not (Section 8.2).

Polar solvents dissolve polar and ionic solutes; nonpolar solvents dissolve nonpolar solutes. Thus, a polar, hydrogen-bonding compound like water dissolves ethanol and sodium chloride, whereas a nonpolar organic compound like hexane (C_6H_{14}) dissolves other nonpolar organic compounds like fats and oils. Water and oil, however, do not dissolve one another, as summed up by the old saying, "Oil and water don't mix." The intermolecular forces between water molecules are so strong that after an oil–water mixture is shaken, the water layer re-forms, squeezing out the oil molecules.

LOOKING AHEAD Many compounds consisting largely of carbon, hydrogen, and oxygen are called organic compounds because they were originally derived from living organisms. We will study the chemistry of organic compounds in Chapters 12–18, 21, and 23.

Water solubility is not limited to ionic compounds and ethanol. Many polar organic substances, such as sugars, amino acids, and even some proteins, dissolve in water. In addition, small, moderately polar organic molecules such as chloroform ($CHCl_3$) are soluble in water to a limited extent. When mixed with water, a small amount of the organic compound dissolves, but the remainder forms a separate liquid layer. As the number of carbon atoms in organic molecules increases, though, water solubility decreases.

The process of dissolving an ionic solid in a polar liquid is shown in Figure 9.2 for sodium chloride. When NaCl crystals are put in water, ions at the crystal surface come into contact with polar water molecules. Positively charged Na^+ ions are attracted to the negatively polarized oxygen of water, and negatively charged Cl^- ions are attracted to the positively polarized hydrogens. The combined forces of attraction between an ion and several water molecules pull the ion away from the crystal, exposing a



◀ **Figure 9.2**
Dissolution of a NaCl crystal in water.
Polar water molecules surround the individual Na^+ and Cl^- ions at an exposed edge or corner, pulling them from the crystal surface into solution and surrounding them. Note how the negatively polarized oxygens of water molecules cluster around Na^+ ions and the positively polarized hydrogens cluster around Cl^- ions.

fresh surface, until ultimately the crystal dissolves. Once in solution, Na^+ and Cl^- ions are completely surrounded by solvent molecules, a phenomenon called **solvation** (or, specifically for water, *hydration*). The water molecules form a loose shell around the ions, stabilizing them by electrical attraction.

Solvation The clustering of solvent molecules around a dissolved solute molecule or ion.

The dissolution of a solute in a solvent is a physical change, because the solution components retain their chemical identities. When sugar dissolves in water, for example, the individual sugar and water molecules still have the same chemical formulas as in the pure or undissolved state. Like all chemical and physical changes, the dissolution of a substance in a solvent has associated with it a heat change, or *enthalpy* change (Section 7.2). Some substances dissolve exothermically, releasing heat and warming the resultant solution, whereas other substances dissolve endothermically, absorbing heat and cooling the resultant solution. Calcium chloride, for example, *releases* 81.2 kJ/mol of heat energy when it dissolves in water, but ammonium nitrate (NH_4NO_3) *absorbs* 25.5 kJ/mol of heat energy. Athletes and others take advantage of both situations when they use instant hot packs or cold packs to treat injuries. Both hot and cold packs consist of a pouch of water and a dry chemical, such as $CaCl_2$ or $MgSO_4$ for hot packs and NH_4NO_3 for cold packs. Squeezing the pack breaks the pouch and the solid dissolves, either raising or lowering the temperature.

▲ Instant cold packs used to treat muscle strains and sprains often take advantage of the endothermic enthalpy of a solution of salts such as ammonium nitrate.

Worked Example 9.1 Formation of Solutions

Which of the following pairs of substances would you expect to form solutions?
(a) Carbon tetrachloride (CCl_4) and hexane (C_6H_{14}).
(b) Octane (C_8H_{18}) and methanol (CH_3OH).

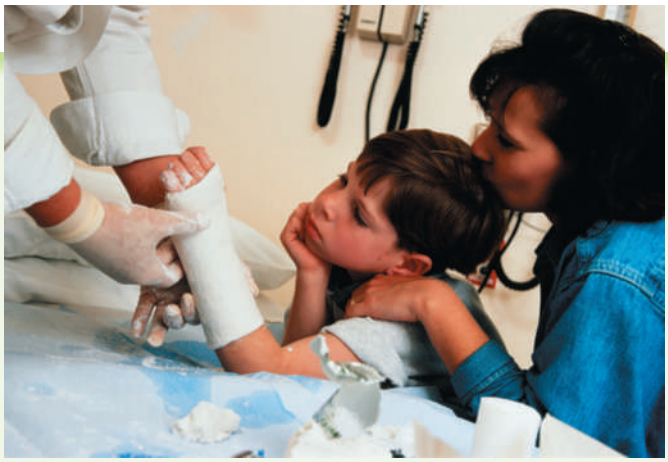
ANALYSIS Identify the kinds of intermolecular forces in each substance (Section 8.2). Substances with similar intermolecular forces tend to form solutions.

SOLUTION

(a) Hexane contains only C—H and C—C bonds, which are nonpolar. Carbon tetrachloride contains polar C—Cl bonds, but they are distributed symmetrically in the tetrahedral molecule so that it too is nonpolar. The major intermolecular force for both compounds is London dispersion forces, so they will form a solution.

(b) Octane contains only C—H and C—C bonds and so is nonpolar; the major intermolecular force is dispersion. Methanol contains polar C—O and O—H bonds; it is polar and forms hydrogen bonds. The intermolecular forces for the two substances are so dissimilar that they do not form a solution.

CHEMISTRY IN ACTION



Solid Hydrates—Salt + Water

If you add salt to water, you would expect it to dissolve and form a solution. But some ionic compounds attract water strongly enough to hold on to water molecules even when crystalline, forming what are called *solid hydrates.* For example, the plaster of Paris used to make decorative objects and casts for broken limbs is calcium sulfate hemihydrate, $CaSO_4 \cdot \frac{1}{2}H_2O$. The dot between $CaSO_4$ and $\frac{1}{2}H_2O$ in the formula indicates that for every two $CaSO_4$ formula units in the crystal there is also one water molecule present.

$CaSO_4 \cdot \frac{1}{2}H_2O$ A solid hydrate

After being ground up and mixed with water to make plaster, $CaSO_4 \cdot \frac{1}{2}H_2O$ gradually changes into the crystalline dihydrate $CaSO_4 \cdot 2H_2O$, known as *gypsum.*

During the change, the plaster hardens and expands in volume, causing it to fill a mold or shape itself closely around a broken limb. Still other ionic compounds attract water so strongly that they pull water vapor from humid air to become hydrated. Compounds that show this behavior, such as calcium chloride ($CaCl_2$), are called hygroscopic and are often used as drying agents. You might have noticed a small bag of a hygroscopic compound (probably silica gel, SiO_2) included in the packing material of a new MP3 player, camera, or other electronic device to keep humidity low during shipping. These and other ionic compounds that are handled primarily as hydrates are listed in the following table.

Some Common Solid Hydrates

Formula	Name	Uses
$AlCl_3 \cdot 6H_2O$	Aluminum chloride hexahydrate	Antiperspirant
$CaSO_4 \cdot 2H_2O$	Calcium sulfate dihydrate (gypsum)	Cements, wallboard molds
$CaSO_4 \cdot \frac{1}{2}H_2O$	Calcium sulfate hemihydrate (plaster of Paris)	Casts, molds
$CuSO_4 \cdot 5H_2O$	Copper(II) sulfate pentahydrate (blue vitriol)	Pesticide, germicide, topical fungicide
$MgSO_4 \cdot 7H_2O$	Magnesium sulfate heptahydrate (epsom salts)	Laxative, anticonvulsant
$NaB_4O_7 \cdot 10H_2O$	Sodium tetraborate decahydrate (borax)	Cleaning compounds, fireproofing agent
$Na_2S_2O_3 \cdot 5H_2O$	Sodium thiosulfate pentahydrate (hypo)	Photographic fixer

CIA Problem 9.1 Write the formula of sodium sulfate decahydrate, known as Glauber's salt and used as a laxative.

CIA Problem 9.2 What mass of Glauber's salt must be used to provide 1.00 mol of sodium sulfate?

PROBLEM 9.2

Which of the following pairs of substances would you expect to form solutions?

(a) CCl_4 and water
(b) Benzene (C_6H_6) and $MgSO_4$
(c) Hexane (C_6H_{14}) and heptane (C_7H_{16})
(d) Ethanol (C_2H_5OH) and heptanol $(C_7H_{15}OH)$

9.3 Solubility

Learning Objective:

- Define the properties of a solution, including miscibility, saturation, and solubility.

We learned in Section 9.2 that ethanol is soluble in water because hydrogen bonding is nearly as strong between water and ethanol molecules as it is between water molecules alone or ethanol molecules alone. So similar are the forces in this

particular case, in fact, that the two liquids are **miscible** or mutually soluble in all proportions. Ethanol will continue to dissolve in water no matter how much is added.

Miscible Mutually soluble in all proportions.

Most substances, however, reach a solubility limit beyond which no more will dissolve in solution. Imagine, for instance, that you are asked to prepare a saline solution (aqueous NaCl). You might measure out some water, add solid NaCl, and stir the mixture. Dissolution occurs rapidly at first but then slows down as more and more NaCl is added. Eventually the dissolution stops because an equilibrium is reached when the numbers of Na^+ and Cl^- ions leaving a crystal and going into solution are equal to the numbers of ions returning from solution to the crystal. At this point, the solution is said to be **saturated.** A maximum of 35.8 g of NaCl will dissolve in 100 mL of water at 20 °C (293 K). Any amount above this limit simply sinks to the bottom of the container and sits there.

Saturated solution A solution that contains the maximum amount of dissolved solute at equilibrium.

The equilibrium reached by a saturated solution is like the equilibrium reached by a reversible reaction (Section 7.7). Both are dynamic situations in which no *apparent* change occurs because the rates of forward and backward processes are equal. Solute particles leave the solid surface and reenter the solid from solution at the same rate.

$$\text{Solid solute} \underset{\text{Crystallize}}{\overset{\text{Dissolve}}{\rightleftharpoons}} \text{Solution}$$

The maximum amount of a substance that will dissolve in a given amount of a solvent at a given temperature, usually expressed in grams per 100 mL (g/100 mL), is called the substance's **solubility.** Solubility is a characteristic property of a specific solute–solvent combination, and different substances have greatly differing solubilities. Only 9.6 g of sodium hydrogen carbonate will dissolve in 100 mL of water at 20 °C (293 K), for instance, but 204 g of sucrose will dissolve under the same conditions.

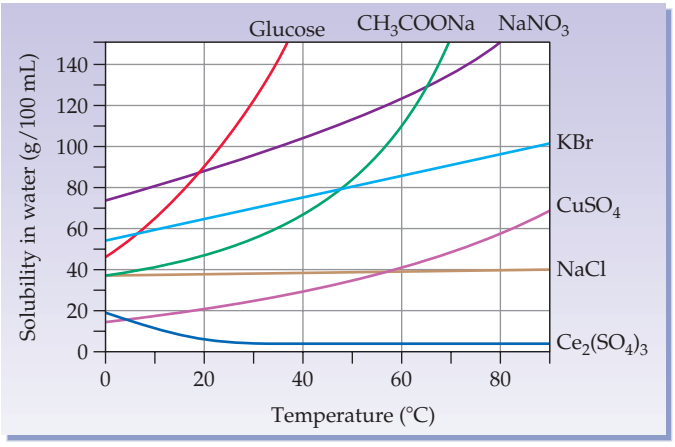
Solubility The maximum amount of a substance that will dissolve in a given amount of solvent at a specified temperature.

9.4 The Effect of Temperature on Solubility

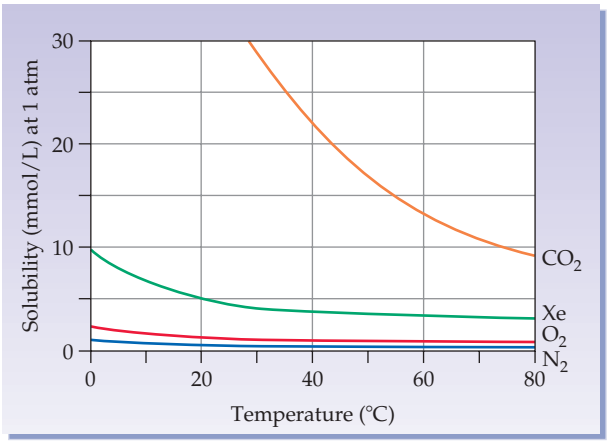
Learning Objective:

- Determine the effect of temperature changes on the solubility of a solute in a solution.

As anyone who has ever made tea or coffee knows, temperature often has a dramatic effect on solubility. The compounds in tea leaves or coffee beans, for instance, dissolve easily in hot water but not in cold water. The effect of temperature is different for every substance, however, and is usually unpredictable. As shown in Figure 9.3a, the solubilities of most molecular and ionic solids increase with increasing temperature, but the



(a)



(b)

▲ **Figure 9.3**

Solubilities of some (a) solids and (b) gases in water as a function of temperature.

Most solid substances become more soluble as temperature rises (although the exact relationship is usually complex), whereas the solubility of gases decreases.

▲ **Figure 9.4**
A supersaturated solution of sodium acetate in water.
When a tiny seed crystal is added, larger crystals rapidly grow and precipitate from the solution until equilibrium is reached.

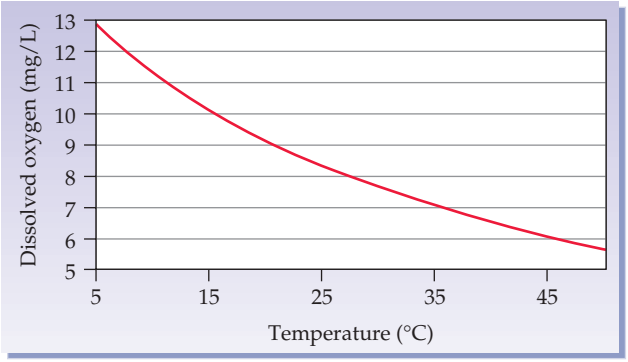
solubilities of others (NaCl) are almost unchanged, and the solubilities of still others [$Ce_2(SO_4)_3$] decrease with increasing temperature.

Solids that are more soluble at high temperature than at low temperature can sometimes form **supersaturated solutions,** which contain even more solute than a saturated solution. Suppose, for instance, that a large amount of a substance is dissolved at a high temperature. As the solution cools, the solubility decreases and the excess solute should precipitate to maintain equilibrium. But if the cooling is done very slowly, and if the container stands quietly, crystallization might not occur immediately and a supersaturated solution might result. Such a solution is unstable, however, and precipitation can occur dramatically when a tiny seed crystal is added to initiate crystal growth or when the container is disturbed (Figure 9.4).

Unlike solids, the influence of temperature on the solubility of gases *is* predictable: Addition of heat decreases the solubility of most gases, as seen in Figure 9.3b (helium is the only common exception). One result of this temperature-dependent decrease in gas solubility can sometimes be noted in a stream or lake near the outflow of warm water from an industrial operation. As water temperature increases, the concentration of dissolved oxygen in the water decreases, killing fish that cannot tolerate the lower oxygen levels.

Worked Example 9.2 Solubility of Gases: Effect of Temperature

From the following graph of solubility versus temperature for O_2, estimate the concentration of dissolved oxygen in water at 25 °C and at 35 °C. By what percentage does the concentration of O_2 change?



ANALYSIS The solubility of O_2 (on the *y*-axis) can be determined by finding the appropriate temperature (on the *x*-axis) and extrapolating. The percent change is calculated as

$$\frac{(\text{Solubility at 25 °C}) - (\text{Solubility at 35 °C})}{(\text{Solubility at 25 °C})} \times 100$$

SOLUTION
From the graph, we estimate that the solubility of O_2 at 25 °C is approximately 8.3 mg/L and at 35 °C is 7.0 mg/L. The percent change in solubility is

$$\frac{8.3 - 7.0}{8.3} \times 100 = 16$$

Supersaturated solution A solution that contains more than the maximum amount of dissolved solute; a nonequilibrium situation.

PROBLEM 9.3

A solution is prepared by dissolving 12.5 g of KBr in 20 mL of water at 60 °C (see Figure 9.3). Is this solution saturated, unsaturated, or supersaturated? What will happen if the solution is cooled to 10 °C?

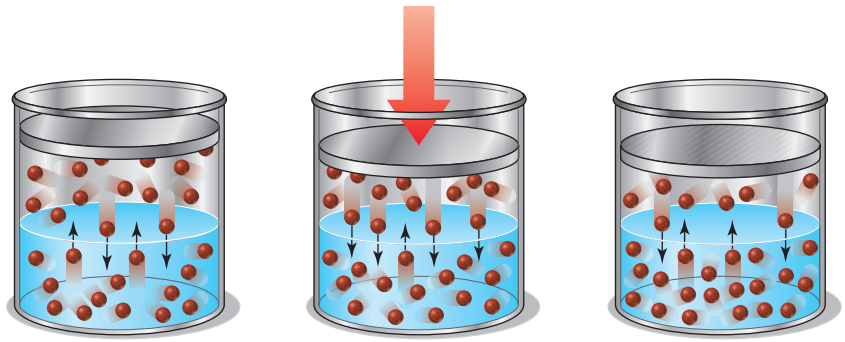
9.5 The Effect of Pressure on Solubility: Henry's Law

Learning Objective:

- Determine the effect of a change in pressure on the solubility of a gas in solution.

Pressure has virtually no effect on the solubility of a solid or liquid, but it has a strong effect on the solubility of a gas. According to **Henry's law,** the solubility (or concentration) of a gas in a liquid is directly proportional to the partial pressure of the gas over the liquid. If the partial pressure of the gas doubles, solubility doubles; if the gas pressure is halved, solubility is halved (Figure 9.5).

CONCEPTS TO REVIEW Recall from Section 8.11 that each gas in a mixture exerts a partial pressure independent of other gases present (Dalton's law of partial pressures).



(a) Equilibrium **(b)** Pressure increase **(c)** Equilibrium restored

Figure 9.5
Henry's law.
The solubility of a gas is directly proportional to its partial pressure. An increase in pressure causes more gas molecules to enter solution until equilibrium is restored between the dissolved and undissolved gas.

Henry's law The solubility (or concentration) of a gas is directly proportional to the partial pressure of the gas if the temperature is constant. That is, concentration *(C)* divided by pressure *(P)* is constant when *T* is constant, or

$$\frac{C}{P_{\text{gas}}} = k \quad \text{(At a constant temperature)}$$

Le Châtelier's principle states that when a system at equilibrium is placed under stress, the equilibrium shifts to relieve that stress (Section 7.9).

Henry's law can be explained using Le Châtelier's principle. In the case of a saturated solution of a gas in a liquid, an equilibrium exists whereby gas molecules enter and leave the solution at the same rate. When the system is stressed by increasing the pressure of the gas, more gas molecules go into solution to relieve that increase. Conversely, when the pressure of the gas is decreased, more gas molecules come out of solution to relieve the decrease.

[Pressure increases ⟶]
$$\text{Gas} + \text{Solvent} \rightleftharpoons \text{Solution}$$

As an example of Henry's law in action, think about the fizzing that occurs when you open a bottle of soft drink or champagne. The bottle is sealed under greater than 1 atm of CO_2 pressure, causing some of the CO_2 to dissolve. When the bottle is opened, however, CO_2 pressure drops and gas comes fizzing out of solution.

Writing Henry's law in the form $P_{\text{gas}} = C/k$ shows that partial pressure can be used to express the concentration of a gas in a solution, a practice especially common in health-related sciences. Table 9.3 gives some typical values and illustrates the convenience of having the same unit for concentration of a gas in both air and blood. Compare the oxygen partial pressures in saturated alveolar air (air in the lungs) and in arterial blood, for instance. The values are almost the same because the gases dissolved in blood come to equilibrium with the same gases in the lungs.

If the partial pressure of a gas over a solution changes while the temperature is constant, the new solubility of the gas can be found easily. Because C/P is a constant value at constant temperature, Henry's law can be restated to show how one variable changes if the other changes.

$$\frac{C_1}{P_1} = \frac{C_2}{P_2} = k \quad \text{(Where } k \text{ is constant at a fixed temperature)}$$

Worked Example 9.3 gives an illustration of how to use this equation.

Table 9.3 Partial Pressures and Normal Gas Concentrations in Body Fluids

Sample	Partial Pressure (Pa)			
	P_{N_2}	P_{O_2}	P_{CO_2}	P_{H_2O}
Inspired air (dry)	79.6×10^3	21.2×10^3	40.0	493
Alveolar air (saturated)	76.3×10^3	13.3×10^3	5.33×10^3	6.27×10^3
Expired air (saturated)	75.9×10^3	15.5×10^3	3.7×10^3	6.27×10^3
Arterial blood	76.4×10^3	12.7×10^3	5.33×10^3	
Venous blood	76.4×10^3	5.33×10^3	6.0×10^3	
Peripheral tissues	76.4×10^3	5.33×10^3	6.0×10^3	

Worked Example 9.3 Solubility of Gases: Henry's Law

At a partial pressure of oxygen in the atmosphere of 21.2×10^3 Pa, the solubility of oxygen in blood is 0.44 g/100 mL. What is the solubility of oxygen in blood at 7925 m, where the partial pressure of O_2 is 7.5×10^3 Pa?

ANALYSIS According to Henry's law, the solubility of the gas divided by its pressure is constant.

$$\frac{C_1}{P_1} = \frac{C_2}{P_2}$$

Of the four variables in this equation, we know P_1, C_1, and P_2, and we need to find C_2.

BALLPARK ESTIMATE The pressure drops by a factor of about 3 (from 21.2×10^3 Pa to 7.5×10^3 Pa). Since the ratio of solubility to pressure is constant, the solubility must also drop by a factor of 3 (from 0.44 g/100 mL to about 0.15 g/100 mL).

SOLUTION

STEP 1: Identify known information. We have values for P_1, C_1, and P_2.

$P_1 = 21.2 \times 10^3$ Pa
$C_1 = 0.44$ g/100 mL
$P_2 = 7.5 \times 10^3$ Pa

STEP 2: Identify answer and units. We are looking for the solubility of O_2 (C_2) at a partial pressure P_2.

Solubility of O_2, C_2 = ?? g/100 mL

STEP 3: Identify conversion factors or equations. In this case, we restate Henry's law to solve for C_2.

$$\frac{C_1}{P_1} = \frac{C_2}{P_2} \Rightarrow C_2 = \frac{C_1 P_2}{P_1}$$

STEP 4: Solve. Substitute the known values into the equation and calculate C_2.

$$C_2 = \frac{C_1 P_2}{P_1} = \frac{(0.44 \text{ g/100 mL})(7.5 \times 10^3 \cancel{\text{Pa}})}{21.2 \times 10^3 \cancel{\text{Pa}}} = 0.16 \text{ g/100 mL}$$

BALLPARK CHECK The calculated answer matches our estimate.

PROBLEM 9.4

At 20 °C (293 K) and a partial pressure of 10^5 Pa, the solubility of CO_2 in water is 0.169 g/100 mL. What is the solubility of CO_2 at 33.3×10^5 Pa?

PROBLEM 9.5

At a total atmospheric pressure of 10^5 Pa, the partial pressure of CO_2 in air is approximately 4.0×10^{29} Pa. Using the data in Problem 9.4, what is the solubility of CO_2 in an open bottle of seltzer water at 20 °C (293 K)?

9.6 Units of Concentration

Learning Objective:

- Define units of concentration, and calculate the concentration of a solute in solution.

Although we speak casually of a solution of, say, orange juice as either "dilute" or "concentrated," laboratory work usually requires an exact knowledge of a solution's concentration. As indicated in Table 9.4, there are several common methods for expressing concentration. The units differ, but all the methods describe how much solute is present in a given quantity of solution.

Table 9.4 Some Units for Expressing Concentration

Concentration Measure	Solute Measure	Solution Measure
Percent		
Mass/mass percent, (m/m)%	Mass (g)	Mass (g)
Volume/volume percent, (v/v)%	Volume*	Volume*
Mass/volume percent, (m/v)%	Mass (g)	Volume (mL)
Parts per million, ppm	Parts*	10^6 parts*
Parts per billion, ppb	Parts*	10^9 parts*
Molarity, M	Moles	Volume (L)

*Any units can be used as long as they are the same for both solute and solution.

Let us look at each of the concentration measures listed in Table 9.4 individually, beginning with *percent concentrations.*

Percent Concentrations

Percent concentrations express the amount of solute in 100 units of solution. The amount of solute and the amount of solution can be represented in units of mass or volume. For solid solutions, such as a metal alloy, concentrations are typically expressed as **mass/mass percent concentration, (m/m)%.**

mass/mass percent concentration, (m/m)% Concentration expressed as the number of grams of solute per 100 g of solution.

$$\textbf{(m/m)\% concentration} = \frac{\text{Mass of solute (g)}}{\text{Mass of solution (g)}} \times 100$$

For example, the mass percent of copper in a red-gold ring that contains 19.20 g of gold and 4.80 g of copper would be calculated as

$$\textbf{(m/m)\% Cu} = \frac{\text{mass of Cu (g)}}{\text{mass of Cu (g)} + \text{mass of Au (g)}} \times 100$$

$$= \frac{4.80\ \text{g}}{4.80\ \text{g} + 19.20\ \text{g}} \times 100 = 20.0$$

The concentration of a solution made by dissolving one liquid in another is often given by expressing the volume of solute as a percentage of the volume of final solution—the **volume/volume percent concentration, (v/v)%.**

volume/volume percent concentration, (v/v)% Concentration expressed as the number of milliliters of solute dissolved in 100 mL of solution.

$$\textbf{(v/v)\% concentration} = \frac{\text{Volume of solute (mL)}}{\text{Volume of solution (mL)}} \times 100$$

For example, if 10.0 mL of ethanol is dissolved in enough water to give 100.0 mL of solution, the ethanol concentration is $(10.0\ \text{mL}/100.0\ \text{mL}) \times 100 = 10.0\%\ (\text{v/v})$.

A third common method for expressing percent concentration is to give the number of grams (mass) as a percentage of the number of milliliters (volume) of the final solution—called the **mass/volume percent concentration, (m/v)%.**

mass/volume percent concentration, (m/v)% Concentration expressed as the number of grams of solute per 100 mL of solution.

CHEMISTRY IN ACTION

Breathing and Oxygen Transport

Like all other animals, humans need oxygen. When we breathe, the freshly inspired air travels through the bronchial passages and into the lungs. The oxygen then diffuses through the delicate walls of the approximately 150 million alveolar sacs of the lungs and into arterial blood, which transports it to all body tissues.

Only about 3% of the oxygen in blood is dissolved; the rest is chemically bound to *hemoglobin* molecules, large proteins with *heme* groups embedded in them. Each hemoglobin molecule contains four heme groups, and each heme group contains an iron atom that is able to bind one O_2 molecule. Thus, a single hemoglobin molecule can bind up to four molecules of oxygen. The entire system of oxygen transport and delivery in the body depends on the pickup and release of O_2 by hemoglobin (Hb) according to the following series of equilibria:

$$O_2(\text{lungs}) \rightleftharpoons O_2(\text{blood}) \quad (\text{Henry's law})$$
$$Hb + 4\,O_2(\text{blood}) \rightleftharpoons Hb(O_2)_4$$
$$Hb(O_2)_4 \rightleftharpoons Hb + 4O_2(\text{cell})$$

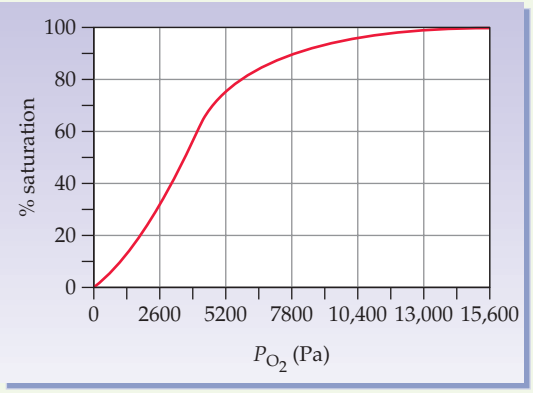
The delivery of oxygen depends on the concentration of O_2 in the various tissues, as measured by partial pressure (P_{O_2}, Table 9.3). The amount of oxygen carried by hemoglobin at any given value of P_{O_2} is usually expressed as a percent saturation and can be found from the curve shown in the accompanying figure. When $P_{O_2} = 13.3 \times 10^3$ Pa, the saturation in the lungs is 97.5%, meaning that each hemoglobin is carrying close to its maximum of four O_2 molecules. When $P_{O_2} = 3.5 \times 10^3$ Pa, however, the saturation drops to 50%.

So, how does the body ensure that enough oxygen is available to the various tissues? When large amounts of oxygen are needed—during a strenuous workout, for example—oxygen is released from hemoglobin to the hardworking, oxygen-starved muscle cells, where P_{O_2} is low. Increasing the supply of oxygen to the blood (by breathing harder and faster) shifts all the equilibria toward the right, according to Le Châtelier's principle (Section 7.9), to supply the additional O_2 needed by the muscles.

What about people living at high altitudes? In Leadville, CO, for example, where the altitude is 3095 m, the P_{O_2} in the lungs is only about 9.1×10^3 Pa. Hemoglobin is only 90% saturated with O_2 at this pressure, meaning that less oxygen is available for delivery to the tissues. The body responds by producing erythropoietin (EPO), a hormone that stimulates the bone marrow to produce more red blood cells and hemoglobin molecules. The increase in Hb provides more capacity for O_2 transport and drives the $Hb + O_2$ equilibria to the right.

World-class athletes use the mechanisms of increased oxygen transport associated with higher levels of hemoglobin to enhance their performance. High-altitude training centers have sprung up, with living and training regimens designed to increase blood EPO levels. Unfortunately, some athletes have also tried to "cheat" by using injections of EPO and synthetic analogs and "blood doping" to boost performance. This has led the governing bodies of many sports federations, including the Olympic Committee, to start testing for such abuse.

▲ At high altitudes, the partial pressure of oxygen in the air is too low to saturate hemoglobin sufficiently. Additional oxygen is therefore needed.



▲ An oxygen-carrying curve for hemoglobin. The percent saturation of the oxygen binding sites on hemoglobin depends on the partial pressure of oxygen P_{O_2}.

CIA Problem 9.3 How does the body increase oxygen availability at high altitude?

CIA Problem 9.4 The height of Mt. Kilimanjaro in Africa is 5895 m. The atmospheric pressure at this altitude is 50×10^3 Pa. Assuming that the atmosphere is 18% oxygen (by volume), calculate the partial pressure of O_2, and determine the percent saturation of O_2 in blood.

Mathematically, (m/v)% concentration is found by taking the number of grams of solute per milliliter of solution and multiplying by 100.

$$\textbf{(m/v)\% concentration} = \frac{\text{Mass of solute (g)}}{\text{Volume of solution (mL)}} \times 100$$

For example, if 15 g of glucose is dissolved in enough water to give 100 mL of solution, the glucose concentration is 15 g/100 mL or 15% (m/v).

$$\frac{15 \text{ g glucose}}{100 \text{ mL solution}} \times 100 = 15\% \text{ (m/v)}$$

To prepare 100 mL of a specific mass/volume solution, the weighed solute is dissolved in just enough solvent to give a final volume of 100 mL, not in an initial volume of 100 mL solvent. (If the solute is dissolved in 100 mL of solvent, the final volume of the solution will likely be a bit larger than 100 mL, since the volume of the solute is included.) In practice, the appropriate amount of solute is weighed and placed in a *volumetric flask,* as shown in Figure 9.6. Enough solvent is then added to dissolve the solute, and further solvent is added until an accurately calibrated final volume is reached. The solution is then shaken until it is uniformly mixed. Worked Examples 9.4–9.7 illustrate how percent concentrations can be calculated for a solution, or how the percent concentration can be used as a conversion factor to determine the amount of solute in a given amount of solution.

(a) (b) (c)

◀ Figure 9.6
Preparing a solution of known mass/volume percent concentration, (m/v)%.
(a) A measured number of grams of solute is placed in a volumetric flask. (b) Enough solvent is added to dissolve the solute by swirling. (c) Further solvent is carefully added until the calibration mark on the neck of the flask is reached, and the solution is shaken until uniform.

Worked Example 9.4 Mass Percent as Conversion Factor: Mass of Solution to Mass of Solute

The percentage of gold in jewelry is typically reported in carats, with 24 carats representing 100% gold. A sample of 18-carat gold would contain 18 g of gold in 24 g of metal, which would equal a (m/m)% of 75%. Calculate the mass of gold in a 5.05 g ring that is 18-carat gold.

ANALYSIS We are given a concentration and the total mass of the sample solution (the gold alloy in the ring), and we need to find the mass of gold by rearranging the equation for (m/m)% concentration.

BALLPARK ESTIMATE A 75% (m/m) solution contains 75 g for every 100 g of solution, so 10 g contains 7.5 g. The mass of the ring is a little more than 5 g (or half of 10 g) so the amount of gold in the ring will be slightly more than half of 7.5 g, or ~3.8 g gold.

SOLUTION

$$(5.05 \text{ g})\left(\frac{75 \text{ g Au}}{100 \text{ g solution}}\right) = 3.79 \text{ g Au}$$

BALLPARK CHECK The calculated answer is consistent with our estimate of 3.8 g gold.

Worked Example 9.5 Volume Percent as Conversion Factor: Volume of Solution to Volume of Solute

How many milliliters of methanol are needed to prepare 75 mL of a 5.0% (v/v) solution?

ANALYSIS We are given a solution volume (75 mL) and a concentration (5.0% (v/v), meaning 5.0 mL solute/100 mL solution). The concentration acts as a conversion factor for finding the amount of methanol needed.

BALLPARK ESTIMATE A 5% (v/v) solution contains 5 mL of solute in 100 mL of solution, so the amount of solute in 75 mL of solution must be about three-fourths of 5 mL, which means between 3 and 4 mL.

SOLUTION

$$(75 \text{ mL solution})\left(\frac{5.0 \text{ mL methanol}}{100 \text{ mL solution}}\right) = 3.8 \text{ mL methanol}$$

BALLPARK CHECK The calculated answer is consistent with our estimate of between 3 and 4 mL.

Worked Example 9.6 Solution Concentration: Mass/Volume Percent

A solution of heparin sodium, an anticoagulant for blood, contains 1.8 g of heparin sodium dissolved to make a final volume of 15 mL of solution. What is the mass/volume percent concentration of this solution?

ANALYSIS Mass/volume percent concentration is defined as the mass of the solute in grams divided by the volume of solution in milliliters and multiplied by 100.

BALLPARK ESTIMATE The mass of solute (1.8 g) is smaller than the volume of solvent (15 mL) by a little less than a factor of 10. The weight/volume percent should thus be a little greater than 10%.

SOLUTION

$$(\text{m/v})\% \text{ concentration} = \frac{1.8 \text{ g heparin sodium}}{15 \text{ mL}} \times 100 = 12\%(\text{m/v})$$

BALLPARK CHECK The calculated (m/v)% is reasonably close to our original estimate of 10%.

Worked Example 9.7 Mass/Volume Percent as Conversion Factor: Volume to Mass

How many grams of NaCl are needed to prepare 250 mL of a 1.5% (m/v) saline solution?

ANALYSIS We are given a concentration and a volume, and we need to find the mass of solute by rearranging the equation for (m/v)% concentration.

BALLPARK ESTIMATE The desired (m/v)% value, 1.5%, is between 1 and 2%. For a volume of 250 mL, we would need 2.5 g of solute for a 1% (m/v) solution and 5.0 g of solute for a 2% solution. Thus, for our 1.5% solution, we need a mass midway between 2.5 and 5.0 g, or about 3.8 g.

SOLUTION

$$\text{Since } (\text{m/v})\% = \frac{\text{Mass of solute in g}}{\text{Volume of solution in mL}} \times 100$$

$$\text{then } \quad \text{Mass of solute in grams} = \frac{(\text{Volume of solution in mL})[(\text{m/v})]\%}{100}$$

$$= \frac{(250)(1.5\%)}{100} = 3.75 \text{ g} = 3.8 \text{ g NaCl}$$

(2 significant figures)

BALLPARK CHECK The calculated answer matches our estimate.

PROBLEM 9.6

A metal alloy contains 15.8% nickel (m/m)%. What mass of the metal alloy would contain 36.5 g of nickel?

PROBLEM 9.7

How would you use a 500.0 mL volumetric flask to prepare a 7.5% (v/v) solution of acetic acid in water?

PROBLEM 9.8

In clinical lab reports, some concentrations are given in mg/dL. Convert a Ca^{2+} concentration of 8.6 mg/dL to mass/volume percent.

PROBLEM 9.9

What amounts of solute or solvent are needed to prepare the following solutions?

(a) Mass of glucose needed to prepare 125.0 mL of 16% (m/v) glucose ($C_6H_{12}O_6$).

(b) Volume of water needed to prepare a 2.0% (m/v) KCl solution using 1.20 g KCl.

Parts per Million (ppm) or Parts per Billion (ppb)

The concentration units mass/mass percent (m/m)%, volume/volume percent (v/v)%, and mass/volume percent (w/v)% can also be defined as *parts per hundred* (pph) since 1% means one item per 100 items. When concentrations are very small, as often occurs in dealing with trace amounts of pollutants or contaminants, it is more convenient to use **parts per million (ppm)** or **parts per billion (ppb).** The "parts" can be in any unit of either mass or volume as long as the units of both solute and solvent are the same.

Parts per million (ppm) Number of parts per one million (10^6) parts.

Parts per billion (ppb) Number of parts per one billion (10^9) parts.

$$\text{ppm} = \frac{\text{Mass of solute (g)}}{\text{Mass of solution (g)}} \times 10^6 \quad \text{or} \quad \frac{\text{Volume of solute (mL)}}{\text{Volume of solution (mL)}} \times 10^6$$

$$\text{ppb} = \frac{\text{Mass of solute (g)}}{\text{Mass of solution (g)}} \times 10^9 \quad \text{or} \quad \frac{\text{Volume of solute (mL)}}{\text{Volume of solution (mL)}} \times 10^9$$

To take an example, the maximum allowable concentration in air of the organic solvent benzene (C_6H_6) is currently set by government regulation at 1 ppm. A concentration of 1 ppm means that if you take a million "parts" of air in any unit—say, mL—then one of those parts is benzene vapor and the other 999,999 parts are other gases.

$$1 \text{ ppm} = \frac{1 \text{ mL}}{1{,}000{,}000 \text{ mL}} \times 10^6$$

Because the density of water is approximately 1.0 g/mL at room temperature, 1.0 L (or 1000 mL) of an aqueous solution weighs 1000 g. Therefore, when dealing with very dilute concentrations of solutes dissolved in water, ppm is equivalent to mg solute/L solution, and ppb is equivalent to μg solute/L solution. To demonstrate that these units are equivalent, the conversion from ppm to mg/L is as follows:

$$1 \text{ ppm} = \left(\frac{1 \text{ g solute}}{10^6 \text{ g solution}}\right)\left(\frac{1 \text{ mg solute}}{10^{-3} \text{ g solute}}\right)\left(\frac{10^3 \text{ g solution}}{1 \text{ L solution}}\right) = \frac{1 \text{ mg solute}}{1 \text{ L solution}}$$

Worked Example 9.8 ppm as Conversion Factor: Mass of Solution to Mass of Solute

The maximum allowable concentration of chloroform, $CHCl_3$, in drinking water is 100 ppb. What is the maximum amount (in grams) of chloroform allowed in a glass containing 400 g (400 mL) of water?

ANALYSIS We are given a solution amount (400 g) and a concentration (100 ppb). This concentration of 100 ppb means

$$100 \text{ ppb} = \frac{\text{Mass of solute (g)}}{\text{Mass of solution (g)}} \times 10^9$$

This equation can be rearranged to find the mass of solute.

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BALLPARK ESTIMATE A concentration of 100 ppb means there are 100×10^{-9} g $(1 \times 10^{-7}$ g$)$ of solute in 1 g of solution. In 400 g of solution, we should have 400 times this amount, or $400 \times 10^{-7} = 4 \times 10^{-5}$ g.

SOLUTION

$$\text{Mass of solute (g)} = \frac{\text{Mass of solution (g)}}{10^9} \times 100 \text{ ppb}$$

$$= \frac{400 \text{ g}}{10^9} \times 100 \text{ ppb} = 4 \times 10^{-5} \text{ g (or 0.04 mg)}$$

BALLPARK CHECK The calculated answer matches our estimate.

PROBLEM 9.10

What is the concentration in ppm of sodium fluoride in tap water that has been fluoridated by the addition of 32 mg of NaF for every 20 kg of solution?

PROBLEM 9.11

The maximum amounts of lead and copper allowed in drinking water are 0.015 mg/kg for lead and 1.3 mg/kg for copper. Express these values in parts per million, and tell the maximum amount of each (in grams) allowed in 100 g of water.

Mole/Volume Concentration: Molarity

We saw in Chapter 6 that the various relationships between amounts of reactants and products in chemical reactions are calculated in *moles* (Sections 6.1–6.3). Thus, the most generally useful means of expressing concentration in the laboratory is **molarity *(M)***, the number of moles of solute dissolved per liter of solution. For example, a solution made by dissolving 1.00 mol (58.5 g) of NaCl in enough water to give 1.00 L of solution has a concentration of 1.00 mol/L, or 1.00 *M*. The molarity of any solution is found by dividing the number of moles of solute by the number of liters of solution (solute + solvent).

Molarity *(M)* Concentration expressed as the number of moles of solute per liter of solution.

$$\textbf{Molarity } (M) = \frac{\text{Moles of solute}}{\text{Liters of solution}}$$

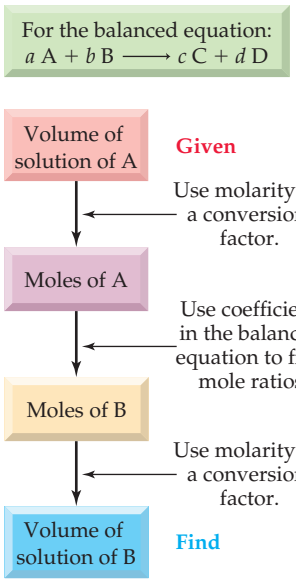
Note that a solution of a given molarity is prepared by dissolving the solute in enough solvent to give a *final* solution volume of 1.00 L, not by dissolving it in an *initial* volume of 1.00 L. If an initial volume of 1.00 L was used, the final solution volume might be a bit larger than 1.00 L because of the additional volume of the solute. In practice, solutions are prepared using a volumetric flask, as shown previously in Figure 9.6.

Molarity can be used as a conversion factor to relate the volume of a solution to the number of moles of solute it contains. If we know the molarity and volume of a solution, we can calculate the number of moles of solute. If we know the number of moles of solute and the molarity of the solution, we can find the solution's volume.

$$\text{Molarity} = \frac{\text{Moles of solute}}{\text{Volume of solution (L)}}$$

$$\text{Moles of solute} = \text{Molarity} \times \text{Volume of solution}$$

$$\text{Volume of solution} = \frac{\text{Moles of solute}}{\text{Molarity}}$$



▲ Figure 9.7
Molarity and conversions. A flow diagram summarizing the use of molarity for conversions between solution volume and moles to find quantities of reactants and products for chemical reactions in solution.

The flow diagram in Figure 9.7 shows how molarity is used in calculating the quantities of reactants or products in a chemical reaction, and Worked Examples 9.10 and 9.11 show how the calculations are done. Note that Problem 9.14 employs *millimolar* (mM) concentrations, which are useful in health-care fields for expressing low concentrations such as are often found in body fluids $(1 \text{ mM} = 0.00\,1M)$.

Worked Example 9.9 Solution Concentration: Molarity

What is the molarity of a solution made by dissolving 2.355 g of sulfuric acid (H_2SO_4) in water and diluting to a final volume of 50.0 mL? The molar mass of H_2SO_4 is 98.1 g/mol.

ANALYSIS Molarity is defined as moles of solute per liter of solution: M = mol/L. Thus, we must first find the number of moles of sulfuric acid by doing a mass to mole conversion and then divide the number of moles by the volume of the solution.

BALLPARK ESTIMATE The molar mass of sulfuric acid is about 100 g/mol, so 2.355 g is roughly 0.025 mol. The volume of the solution is 50.0 mL, or 0.05 L, so we have about 0.025 mol of acid in 0.05 L of solution, which is a concentration of about 0.5 M.

SOLUTION

STEP 1: Identify known information. We know the mass of sulfuric acid and the final volume of solution.

Mass of H_2SO_4 = 2.355 g
Volume of solution = 50.0 mL

STEP 2: Identify answer including units. We need to find the molarity *(M)* in units of moles per liter.

$$\text{Molarity} = \frac{\text{Moles } H_2SO_4}{\text{Liters of solution}}$$

STEP 3: Identify conversion factors and equations. We know both the amount of solute and the volume of solution, but first we must make two conversions: convert mass of H_2SO_4 to moles of H_2SO_4, using molar mass as a conversion factor, and convert volume from milliliters to liters.

$$(2.355 \text{ g } \cancel{H_2SO_4})\left(\frac{1 \text{ mol } H_2SO_4}{98.1 \text{ g } \cancel{H_2SO_4}}\right) = 0.0240 \text{ mol } H_2SO_4$$

$$(50.0 \text{ } \cancel{\text{mL}})\left(\frac{1 \text{ L}}{1000 \text{ } \cancel{\text{mL}}}\right) = 0.0500 \text{ L}$$

STEP 4: Solve. Substitute the moles of solute and volume of solution into the molarity expression.

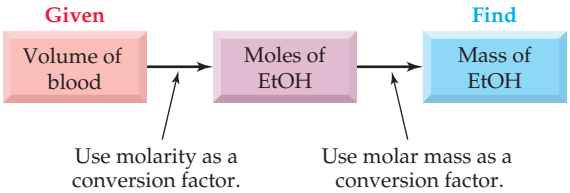
$$\text{Molarity} = \frac{0.0240 \text{ mol } H_2SO_4}{0.0500 \text{ L}} = 0.480 \text{ } M$$

BALLPARK CHECK The calculated answer is close to our estimate, which was 0.5 M.

Worked Example 9.10 Molarity as Conversion Factor: Molarity to Mass

A blood concentration of 0.065 M ethanol (EtOH) is sufficient to induce a coma. At this concentration, what is the total mass of alcohol (in grams) in an adult male whose total blood volume is 5.6 L? The molar mass of ethanol is 46.0 g/mol. (Refer to the flow diagram in Figure 9.7 to identify which conversions are needed.)

ANALYSIS We are given a molarity (0.065 M) and a volume (5.6 L), which allows us to calculate the number of moles of alcohol in the blood. A mole to mass conversion then gives the mass of alcohol.



SOLUTION

$$(5.6 \text{ L } \cancel{\text{blood}})\left(\frac{0.065 \text{ mol EtOH}}{1 \text{ L } \cancel{\text{blood}}}\right) = 0.36 \text{ mol EtOH}$$

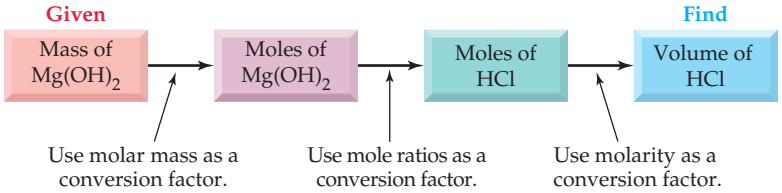
$$(0.36 \text{ } \cancel{\text{mol EtOH}})\left(\frac{46.0 \text{ g EtOH}}{1 \text{ } \cancel{\text{mol EtOH}}}\right) = 17 \text{ g EtOH}$$

Worked Example 9.11 Molarity as Conversion Factor: Molarity to Volume

In our stomachs, gastric juice that is about 0.1 *M* in HCl aids in digestion. How many milliliters of gastric juice will react completely with an antacid tablet that contains 500 mg of magnesium hydroxide? The molar mass of $Mg(OH)_2$ is 58.3 g/mol, and the balanced equation is

$$2\,HCl(aq) + Mg(OH)_2(aq) \longrightarrow MgCl_2(aq) + 2\,H_2O(l)$$

ANALYSIS We are given the molarity of HCl and need to find the volume. We first convert the mass of $Mg(OH)_2$ to moles and then use the coefficients in the balanced equation to find the moles of HCl that will react. Once we have the moles of HCl and the molarity in moles per liter, we can find the volume.



SOLUTION

$$[500\ \text{mg}\ Mg(OH)_2]\left(\frac{1\ \text{g}}{1000\ \text{mg}}\right)\left[\frac{1\ \text{mol}\ Mg(OH)_2}{58.3\ \text{g}\ Mg(OH)_2}\right] = 0.008\,58\ \text{mol}\ Mg(OH)_2$$

$$[0.00858\ \text{mol}\ Mg(OH)_2]\left[\frac{2\ \text{mol HCl}}{1\ \text{mol}\ Mg(OH)_2}\right]\left(\frac{1\ \text{L HCl}}{0.1\ \text{mol HCl}}\right) = 0.2\ \text{L}\ (200\ \text{mL})$$

PROBLEM 9.12

What is the molarity of a solution that contains 50.0 g of vitamin B_1 hydrochloride (molar mass = 337 g/mol) in 160 mL of solution?

PROBLEM 9.13

How many moles of solute are present in the following solutions?

(a) 175 mL of 0.35 *M* $NaNO_3$

(b) 480 mL of 1.4 *M* HNO_3

PROBLEM 9.14

The concentration of cholesterol ($C_{27}H_{46}O$) in blood is approximately 5.0 mM. How many grams of cholesterol are in 250 mL of blood?

PROBLEM 9.15

Calcium carbonate reacts with HCl according to the following equation:

$$2\,HCl(aq) + CaCO_3(aq) \longrightarrow CaCl_2(aq) + H_2O(l) + CO_2(g)$$

(a) How many moles of HCl are in 65 mL of 0.12 *M* HCl?

(b) What mass of calcium carbonate (in grams) is needed for complete reaction with the HCl in (a)?

9.7 Dilution

Learning Objective:

- Use dilution factors to calculate molarities or volumes of dilute solutions prepared from concentrated solutions.

Many solutions, from orange juice to chemical reagents, are stored in high concentrations and then prepared for use by *dilution*—that is, by adding additional solvent to lower the concentration. For example, you might make up 2 L of orange juice by

adding water to a canned concentrate. In the same way, you might buy a medicine or chemical reagent as a concentrated solution and dilute it before use.

The key fact to remember about dilution is that the amount of *solute* remains constant; only the *volume* is changed by adding more solvent. If, for example, the initial and final concentrations are given in molarity, then we know that the number of moles of solute is the same both before and after dilution and can be determined by multiplying molarity times volume.

$$\text{Number of moles} = \text{Molarity (mol/L)} \times \text{Volume (L)}$$
$$M = \text{moles/volume}$$

Because the number of moles remains constant, we can set up the following equation, where M_c and V_c refer to the concentrated solution (before dilution), and M_d and V_d refer to the solution after dilution.

$$\text{Moles of solute} = M_c V_c = M_d V_d$$

This equation can be rewritten to solve for M_d, the concentration of the solution after dilution.

$$M_d = M_c \times \frac{V_c}{V_d}, \qquad \text{where} \qquad \frac{V_c}{V_d} \qquad \text{is a } \textit{dilution factor.}$$

The equation shows that the concentration after dilution (M_d) can be found by multiplying the initial concentration (M_c) by a **dilution factor,** which is simply the ratio of the initial and final solution volumes (V_c/V_d). If, for example, the solution volume *increases* by a factor of 5, from 10 mL to 50 mL, then the concentration must *decrease* to one-fifth of its initial value because the dilution factor is 10 mL/50 mL, or 1/5. Worked Example 9.12 shows how to use this relationship for calculating dilutions.

Dilution factor The ratio of the initial and final solution volumes (V_c/V_d).

The relationship between concentration and volume can also be used to find what volume of initial solution to start with to achieve a given dilution.

$$\text{Since} \quad M_c V_c = M_d V_d,$$
$$\text{then} \quad V_c = V_d \times \frac{M_d}{M_c}.$$

In this case, V_c is the initial volume that must be diluted to prepare a less concentrated solution with volume V_d. The initial volume is found by multiplying the final volume (V_d) by the ratio of the final and initial concentrations (M_d/M_c). For example, to decrease the concentration of a solution to one-fifth its initial value, the initial volume must be one-fifth the desired final volume. Worked Example 9.13 gives a sample calculation.

Although the preceding discussion and the following Worked Examples use concentration units of molarity, the dilution equation can be generalized to allow for the use of other concentration units. A more general equation would be $C_c V_c = C_d V_d$, where C refers to other concentration units, such as ppm, or m/v%.

Worked Example 9.12 Dilution of Solutions: Concentration

What is the final concentration if 75 mL of a 3.5 *M* glucose solution is diluted to a volume of 450 mL?

ANALYSIS The number of moles of solute is constant, so

$$M_c V_c = M_d V_d$$

Of the four variables in this equation, we know the initial concentration M_c (3.5 *M*), the initial volume V_c (75 mL), and the final volume V_d (450 mL), and we need to find the final concentration M_d.

BALLPARK ESTIMATE The volume increases by a factor of 6, from 75 mL to 450 mL, so the concentration must decrease by a factor of 6, from 3.5 *M* to about 0.6 *M*.

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SOLUTION

Solving the above equation for M_d and substituting in the known values gives

$$M_d = \frac{M_c V_c}{V_d} = \frac{(3.5\ M\ \text{glucose})(75\ \cancel{mL})}{450\ \cancel{mL}} = 0.58\ M\ \text{glucose}$$

BALLPARK CHECK The calculated answer is close to our estimate of 0.6 *M*.

Worked Example 9.13 Dilution of Solutions: Volume

Aqueous NaOH can be purchased at a concentration of 1.0 *M*. How would you use this concentrated solution to prepare 750 mL of 0.32 *M* NaOH?

ANALYSIS The number of moles of solute is constant, so

$$M_c V_c = M_d V_d$$

Of the four variables in this equation, we know the initial concentration M_c (1.0 *M*), the final volume V_d (750 mL), and the final concentration M_d (0.32 *M*), and we need to find the initial volume V_c.

BALLPARK ESTIMATE We want the solution concentration to decrease by a factor of about 3, from 1.0 *M* to 0.32 *M*, which means we need to dilute the 1.0 *M* solution by a factor of 3. This means the final volume must be about three times greater than the initial volume. Because our final volume is to be 750 mL, we must start with an initial volume of about 250 mL.

SOLUTION

Solving the above equation for V_1 and substituting in the known values gives

$$V_c = \frac{V_d M_d}{M_c} = \frac{(750\ \text{mL})(0.32\ \cancel{M})}{1.0\ \cancel{M}} = 240\ \text{mL}$$

To prepare the desired solution, dilute 240 mL of 1.0 *M* NaOH with water to make a final volume of 750 mL.

BALLPARK CHECK The calculated answer (240 mL) is reasonably close to our estimate of 250 mL.

PROBLEM 9.16

Aqueous ammonia is commercially available at a concentration of 16.0 *M*. How much of the concentrated solution would you use to prepare 500.0 mL of a 1.25 *M* solution?

PROBLEM 9.17

The Environmental Protection Agency has set the limit for arsenic in drinking water at 0.010 ppm. To what volume would you need to dilute 1.5 L of water containing 5.0 ppm arsenic to reach the acceptable limit?

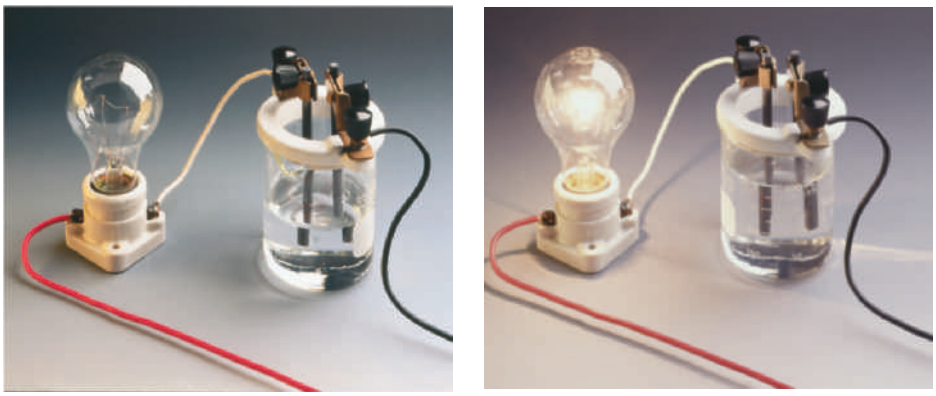
9.8 Ions in Solution: Electrolytes

Learning Objectives:

- Identify solutes as strong electrolytes, weak electrolytes, or nonelectrolytes.
- Calculate equivalents for an ionic solute in solution.

Look at Figure 9.8, which shows a light bulb connected to a power source through a circuit that is interrupted by two metal strips dipped into a beaker of liquid. When the strips are dipped into pure water, the bulb remains dark, but when they are dipped into an aqueous NaCl solution, the circuit is closed and the bulb lights. This simple demonstration shows that ionic compounds in aqueous solution can conduct electricity.

◀◀ As we learned in Section 3.1, electricity can only flow through a medium containing charged particles that are free to move.



(a) (b)

◄ Figure 9.8
A simple demonstration shows that electricity can flow through a solution of ions.
(a) With pure water in the beaker, the circuit is incomplete, no electricity flows, and the bulb does not light. (b) With a concentrated NaCl solution in the beaker, the circuit is complete, electricity flows, and the light bulb glows.

Substances like NaCl that conduct an electric current when dissolved in water are called **electrolytes.** Conduction occurs because negatively charged Cl^- anions migrate through the solution toward the metal strip connected to the positive terminal of the power source, whereas positively charged Na^+ cations migrate toward the strip connected to the negative terminal. As you might expect, the ability of a solution to conduct electricity depends on the concentration of ions in solution. Distilled water contains virtually no ions and is nonconducting, ordinary tap water contains low concentrations of dissolved ions (mostly Na^+, K^+, Mg^{2+}, Ca^{2+}, and Cl^-) and is weakly conducting, and a concentrated solution of NaCl is strongly conducting.

Electrolyte A substance that produces ions and therefore conducts electricity when dissolved in water.

Ionic substances like NaCl that ionize completely when dissolved in water are called **strong electrolytes,** and molecular substances like acetic acid (CH_3CO_2H) that are only partially ionized are **weak electrolytes.** Molecular substances like glucose that do not produce ions when dissolved in water are **nonelectrolytes.**

Strong electrolyte A substance that ionizes completely when dissolved in water.

Weak electrolyte A substance that is only partly ionized in water.

Nonelectrolyte A substance that does not produce ions when dissolved in water.

Strong electrolyte; completely ionized
$$NaCl(s) \xrightarrow[\text{in water}]{\text{Dissolve}} Na^+(aq) + Cl^-(aq)$$

Weak electrolyte; partly ionized
$$CH_3CO_2H(l) \underset{\text{in water}}{\overset{\text{Dissolve}}{\rightleftharpoons}} CH_3CO_2^-(aq) + H^+(aq)$$

Nonelectrolyte; not ionized
$$\text{Glucose}(s) \underset{\text{in water}}{\overset{\text{Dissolve}}{\rightleftharpoons}} \text{Glucose}(aq)$$

But what happens if strong electrolytes, such as NaCl and KBr, are dissolved in the same solution? Because the cations (K^+ and Na^+) and anions (Cl^- and Br^-) are all mixed together and no reactions occur between them, an identical solution could just as well be made from KCl and NaBr. Thus, we can no longer speak of having a NaCl + KBr solution; we can only speak of having a solution with four different ions in it.

A similar situation exists for blood and other body fluids, which contain many different anions and cations. Since they are all mixed together, it is difficult to "assign" specific cations to specific anions or to talk about specific ionic compounds. Instead, we are interested only in individual ions and in the total numbers of positive and negative charges. To discuss such mixtures, we use a new term—*equivalents* of ions. For ions, one **equivalent (Eq)** is equal to the number of ions that carry 1 mol of charge.

Equivalent (Eq) For ions, the amount equal to 1 mol of charge.

The number of equivalents of a given ion per liter of solution can be found by multiplying the molarity of the ion (moles per liter) by the charge on the ion. Because ion concentrations in body fluids are often low, clinical chemists find it more convenient to talk about *milliequivalents* of ions rather than equivalents. One milliequivalent (mEq) of an ion is one-thousandth of an equivalent. For example, the normal concentration of Na^+ in blood is 0.14 Eq/L, or 140 mEq/L.

$$1 \text{ mEq} = 0.001 \text{ Eq} \qquad 1 \text{ Eq} = 1000 \text{ mEq}$$

CHEMISTRY IN ACTION

Electrolytes, Fluid Replacement, and Sports Drinks

Electrolytes are essential in many physiological processes, and significant deviations from the blood electrolyte levels listed in the following table can be potentially life-threatening if not addressed quickly. Heavy and continuous diarrhea from conditions such as cholera can result in dehydration and very low sodium levels in the body (hyponatremia). Restoration of electrolytes can be accomplished by oral rehydration therapy (ORT). The introduction of ORT in developing countries decreased infant mortality from diarrhea, which had previously been the leading cause of death in children under 5 years of age. A typical ORT solution contains sodium (75 mEq/L), potassium (75 mEq/L), chloride (65 mEq/L), citrate (10 mEq/L), and glucose (75 mmol/L). Heavy sweating during strenuous exercise can also lead to dehydration and loss of electrolytes.

Concentrations of Major Electrolytes in Blood Plasma

Cation	Concentration (mEq/L)
Na^+	136–145
Ca^{2+}	4.5–6.0
K^+	3.6–5.0
Mg^{2+}	3
Anion	**Concentration (mEq/L)**
Cl^-	98–106
HCO_3^-	25–29
SO_4^{2-} and HPO_4^{2-}	2

If water and electrolytes are not replaced, dehydration, hyperthermia and heat stroke, dizziness, nausea, muscle cramps, impaired kidney function, and other difficulties ensue. As a rule of thumb, a sweat loss equal to 5% of body weight—about 3.5 L for a 68 kg person—is the maximum amount that can be safely allowed for a well-conditioned athlete.

Plain water works perfectly well to replace sweat during short bouts of activity, but a carbohydrate–electrolyte beverage, or "sports drink," is much superior for rehydrating during and after longer activity in which substantial amounts of electrolytes have been lost. While some sports drinks are little more than overpriced sugar–water solutions, others are carefully formulated and highly effective for fluid replacement. Nutritional research has shown that a serious sports drink should meet the following criteria.

- The drink should contain 6–8% of soluble complex carbohydrates (about 15 g per 236 mL serving) and only a small amount of simple sugar for taste. The complex carbohydrates, which usually go by the name "maltodextrin," provide a slow release of glucose into the bloodstream to provide a steady source of energy and enhance the absorption of water from the stomach.
- The drink should contain electrolytes to replenish those lost in sweat, about 100 mg sodium, 100 mg potassium, and 25 mg magnesium per 236 mL serving.
- The drink should be noncarbonated because carbonation can cause gastrointestinal upset during exercise, and it should not contain caffeine, which acts as a diuretic.
- The drink should taste good so the athlete will want to drink it. Thirst is a poor indicator of fluid requirements, and most people will drink less than needed unless a beverage is flavored.

▲ An athlete places labels on electrolyte solutions for easy identification. These solutions will be distributed at hydration stations for his use during a long-distance competition.

In addition to complex carbohydrates, electrolytes, and flavorings, some sports drinks also contain vitamin A (as beta-carotene), vitamin C (ascorbic acid), and selenium, which act as antioxidants to protect cells from damage. Some drinks also contain the amino acid glutamine, which appears to lessen lactic acid buildup in muscles and thus helps muscles bounce back more quickly after an intense workout.

CIA Problem 9.5 What are the major electrolytes in sweat, and what are their approximate concentrations in mEq/L?

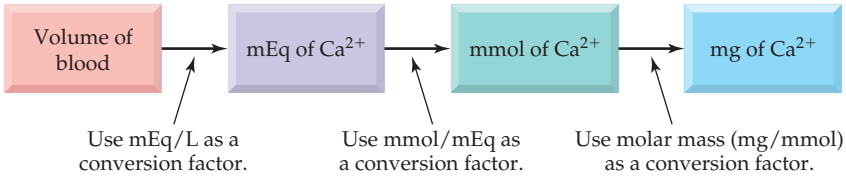
CIA Problem 9.6 Why is a sport drink more effective than plain water for rehydration after extended exercise?

CIA Problem 9.7 A typical sport drink for electrolyte replacement contains 20 mEq/L of Na^+ and 10 mEq/L of K^+ ions. Convert these concentrations to m/v%.

Worked Example 9.14 Equivalents as Conversion Factors: Volume to Mass

The normal concentration of Ca^{2+} in blood is 5.0 mEq/L. How many milligrams of Ca^{2+} are in 1.00 L of blood?

ANALYSIS We are given a volume and a concentration in milliequivalents per liter, and we need to find an amount in milligrams. Thus, we need to calculate the equivalents/mol (or mEq/mmol) for Ca^{2+} and then use concentration and molar mass (g/mol or mg/mmol) as conversion factors between volume and mass, as indicated in the following flow diagram:



BALLPARK ESTIMATE The molar mass of calcium is 40.08 g/mol, and the calcium ion carries a charge of 2+. Thus, 1 millimole of Ca^{2+} (40 mg) equals about 2 mEq, and 1.0 mEq would correspond to about 0.50 mmol, or 20 mg. This means that the 5.0 mEq of Ca^{2+} ions in 1.00 L of blood corresponds to a mass of 5.0 mEq Ca^{2+} × 20 mg/mEq = 100 mg Ca^{2+}.

SOLUTION

$$(1.00\ \cancel{\text{L blood}})\left(\frac{5.0\ \cancel{\text{mEq Ca}^{2+}}}{1.0\ \cancel{\text{L blood}}}\right)\left(\frac{40.08\ \text{mg Ca}^{2+}}{2\ \cancel{\text{mEq Ca}^{2+}}}\right) = 100\ \text{mg Ca}^{2+}$$

BALLPARK CHECK The calculated answer (100 mg of Ca^{2+} in 1.00 L of blood) matches our estimate.

PROBLEM 9.18

How many grams are in 1 Eq of the following ions? How many grams in 1 mEq?

(a) K^+ **(b)** Br^- **(c)** Mg^{2+} **(d)** SO_4^{2-} **(e)** Al^{3+} **(f)** PO_4^{3-}

PROBLEM 9.19

The typical concentration of Mg^{2+} in blood is 3 mEq/L. How many milligrams of Mg^{2+} are in 250 mL of blood?

9.9 Properties of Solutions

Learning Objective:

- Calculate the colligative properties of boiling-point elevation and freezing-point depression for a solution.

The properties of solutions are similar in many respects to those of pure solvents, but there are also some interesting and important differences. One such difference is that solutions have higher boiling points than the pure solvents; another is that solutions have lower freezing points. Pure water boils at 100.0 °C (373 K) and freezes at 0.0 °C (273 K), for example, but a 1.0 *M* solution of NaCl in water boils at 101.0 °C (374.2 K) and freezes at −3.7 °C (269.5 K).

The elevation of boiling point and the lowering of freezing point for a solution as compared with a pure solvent are examples of **colligative properties**—properties that depend on the *concentration* of a dissolved solute but not on its chemical identity. Other colligative properties are a lower vapor pressure for a solution compared with the pure solvent and *osmosis,* the migration of solvent molecules through a semipermeable membrane.

Colligative property A property of a solution that depends only on the number of dissolved particles not on their chemical identity.

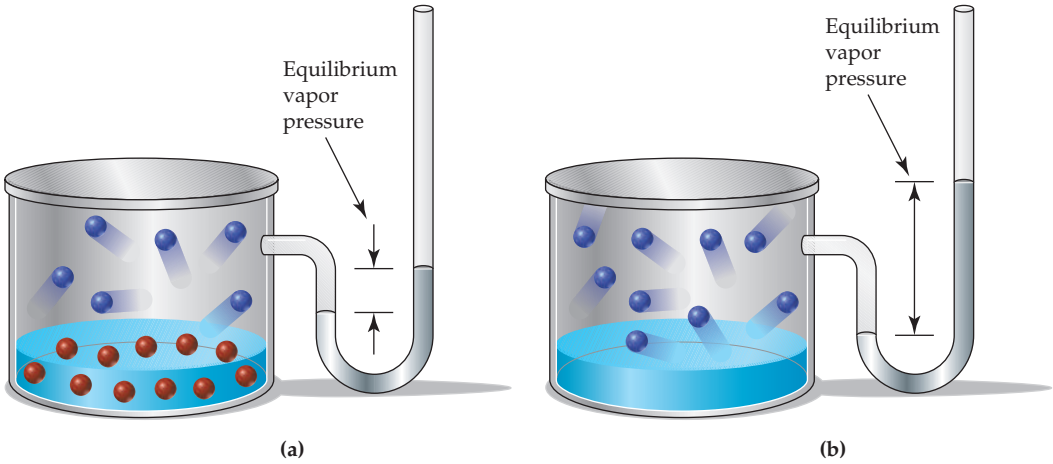
Colligative Properties

- Vapor pressure is lower for a solution than for a pure solvent.
- Boiling point is higher for a solution than for a pure solvent.

- Freezing point is lower for a solution than for a pure solvent.
- Osmosis occurs when a solution is separated from a pure solvent by a semipermeable membrane.

Vapor-Pressure Lowering in Solutions

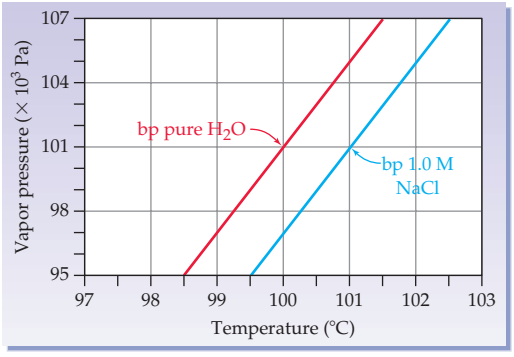
We learned in Section 8.12 that the vapor pressure of a liquid depends on the equilibrium between molecules entering and leaving the liquid surface. Only those molecules at the surface of the liquid that are sufficiently energetic will evaporate. If, however, some of the liquid (solvent) molecules at the surface are replaced by other (solute) particles that do not evaporate, then the rate of evaporation of solvent molecules decreases and the vapor pressure of a solution is lower than that of the pure solvent (Figure 9.9). Note that the *identity* of the solute particles is irrelevant—only their concentration matters.



▶ **Figure 9.9**
Vapor-pressure lowering of solution. (a) The vapor pressure of a solution is lower than (b) the vapor pressure of the pure solvent because fewer solvent molecules are able to escape from the surface of the solution.

Boiling-Point Elevation of Solutions

One consequence of the vapor-pressure lowering for a solution is that the boiling point of the solution is higher than that of the pure solvent. Recall from Section 8.12 that boiling occurs when the vapor pressure of a liquid reaches atmospheric pressure. But because the vapor pressure of a solution is lower than that of the pure solvent at a given temperature, the solution must be heated to a higher temperature for its vapor pressure to reach atmospheric pressure. Figure 9.10 shows a close-up plot of vapor pressure versus temperature for pure water and for a 1.0 *M* NaCl solution. The vapor pressure of pure water reaches atmospheric pressure (1 atm = 101,325 Pa) at 100.0 °C (373.2 K), but the vapor pressure of the NaCl solution does not reach the same point until 101.0 °C (374.2 K).



▲ **Figure 9.10**
Vapor pressure and temperature. A close-up plot of vapor pressure versus temperature for pure water (red curve) and for a 1.0 *M* NaCl solution (blue curve). Pure water boils at 100.0 °C (373.2 K), but the solution does not boil until 101.0 °C (374.2 K).

For each mole of solute particles added, regardless of chemical identity, the boiling point of 1 kg of water is raised by 0.51 °C (0.51 K), or

$$\Delta T_{\text{boiling}} = \left(0.51\ ^\circ\text{C}\ \frac{\text{kg water}}{\text{mol particles}}\right)\left(\frac{\text{mol particles}}{\text{kg water}}\right)$$

The addition of 1 mol of a molecular substance like glucose to 1 kg of water therefore raises the boiling point from 100.0 °C (373.2 K) to 100.51 °C (373.7 K). The addition of 1 mol of NaCl per kilogram of water, however, raises the boiling point by 2 × 0.51 °C = 1.02 °C (1.02 K) because the solution contains 2 mol of solute particles—Na^+ and Cl^- ions.

Worked Example 9.15 Properties of Solutions: Boiling-Point Elevation

What is the boiling point (in °C and K) of a solution of 0.75 mol of KBr in 1.0 kg of water?

ANALYSIS The boiling point increases 0.51 °C (0.51 K) for each mole of solute per kilogram of water. Since KBr is a strong electrolyte, there are 2 moles of ions (K^+ and Br^-) for every 1 mole of KBr that dissolves.

BALLPARK ESTIMATE The boiling point will increase about 0.5 °C (0.5 K) for every 1 mol of ions in 1 kg of water. Since 0.75 mol of KBr produce 1.5 mol of ions, the boiling point should increase by $(1.5 \text{ mol ions}) \times (0.5\,^\circ\text{C/mol ions}) = 0.75\,^\circ\text{C}$ or, $(1.5 \text{ mol ions}) \times (0.5 \text{ K/mol ions}) = 0.75 \text{ K}$.

SOLUTION

$$\Delta T_{\text{boiling}} = \left(0.51\,^\circ\text{C}\,\frac{\cancel{\text{kg water}}}{\cancel{\text{mol ions}}}\right)\left(\frac{2\ \cancel{\text{mol ions}}}{1\ \cancel{\text{mol KBr}}}\right)\left(\frac{0.75\ \cancel{\text{mol KBr}}}{1.0\ \cancel{\text{kg water}}}\right) = 0.77\,^\circ\text{C/K}$$

The normal boiling point of pure water is 100 °C or 373 K so the boiling point of the solution increases to 100.77 °C or 373.77 K.

BALLPARK CHECK The 0.77 °C/K increase is consistent with our estimate of 0.75 °C/K.

PROBLEM 9.20

A solution is prepared by dissolving 0.67 mol of $MgCl_2$ in 0.50 kg of water.

(a) How many moles of ions are present in solution?

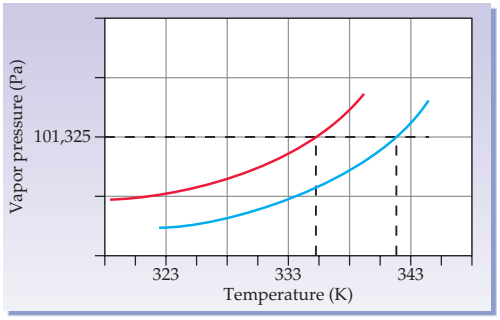
(b) What is the change in the boiling point of the aqueous solution?

PROBLEM 9.21

When 1.0 mol of HF is dissolved in 1.0 kg of water, the boiling point of the resulting solution is 373.7 K (100.5 °C). Is HF a strong or weak electrolyte? Explain.

KEY CONCEPT PROBLEM 9.22

The diagram to the right shows plots of vapor pressure versus temperature for a solvent and a solution.



(a) Which curve represents the pure solvent and which the solution?

(b) What is the approximate boiling-point elevation for the solution?

(c) What is the approximate concentration of the solution in mol/kg, if 1 mol of solute particles raises the boiling point of 1 kg of solvent by 3.63 °C (3.63 K)?

Freezing-Point Depression of Solutions

Just as solutions have lower vapor pressure and consequently higher boiling points than pure solvents, they also have lower freezing points. Motorists in cold climates take advantage of this effect when they add "antifreeze" to the water in automobile cooling systems. Antifreeze is a nonvolatile solute, usually ethane-1,2-diol ($HOCH_2CH_2OH$), that is added in sufficient concentration to lower the freezing point below the lowest expected outdoor temperature. In the same way, salt sprinkled on icy roads lowers the freezing point of ice below the road temperature and thus causes ice to melt.

Freezing-point depression has much the same cause as vapor-pressure lowering and boiling-point elevation. Solute molecules are dispersed between solvent molecules throughout the solution, thereby making it more difficult for solvent molecules to come together and organize into ordered crystals.

For each mole of nonvolatile solute particles, the freezing point of 1 kg of water is lowered by 1.86 °C, or

$$\Delta T_{\text{freezing}} = \left(-1.86\,^\circ\text{C}\,\frac{\text{kg water}}{\text{mol particles}}\right)\left(\frac{\text{mol particles}}{\text{kg water}}\right)$$

Thus, addition of 1 mol of antifreeze to 1 kg of water lowers the freezing point from 0.00 °C to −1.86 °C or 273.15 K to 271.29 K, and addition of 1 mol of NaCl (2 mol of particles) to 1 kg of water lowers the freezing point from 0.00 °C to −3.72 °C or 273.15 K to 269.43.

Worked Example 9.16 Properties of Solutions: Freezing-Point Depression

The cells of a tomato contain mostly an aqueous solution of sugar and other substances. If a typical tomato freezes at −2.5 °C (270.65 K), what is the concentration of dissolved particles in the tomato cells (in moles of particles per kg of water)?

ANALYSIS The freezing point decreases by 1.86 °C for each mole of solute dissolved in 1 kg of water. We can use the decrease in freezing point (2.5 °C) to find the amount of solute per kg of water.

BALLPARK ESTIMATE The freezing point will decrease by about 1.9 °C for every 1 mol of solute particles in 1 kg of water. To lower the freezing point by 2.5 °C (about 30% more) will require about 30% more solute, or 1.3 mol.

SOLUTION

$$\Delta T_{\text{freezing}} = -2.5\ ^\circ\text{C}$$

$$= \left(-1.86\ ^\circ\text{C}\ \frac{\cancel{\text{kg water}}}{\cancel{\text{mol solute particles}}}\right)\left(\frac{??\ \cancel{\text{mol solute particles}}}{1.0\ \cancel{\text{kg water}}}\right)$$

We can rearrange this expression to

$$(-2.5\ \cancel{^\circ\text{C}})\left(\frac{1}{-1.86\ \cancel{^\circ\text{C}}}\ \frac{\text{mol solute particles}}{\text{kg water}}\right) = 1.3\ \frac{\text{mol solute particles}}{\text{kg water}}$$

BALLPARK CHECK The calculated answer agrees with our estimate of 1.3 mol/kg.

PROBLEM 9.23

What is the freezing point of a solution of 1.0 mol of glucose in 1.0 kg of water?

PROBLEM 9.24

When 0.5 mol of a certain ionic substance is dissolved in 1.0 kg of water, the freezing point of the resulting solution is −2.8 °C (270.35 K), How many ions does the substance give when it dissolves?

HANDS-ON CHEMISTRY 9.1

Place about 4–5 cups of cold water in a small pot and set in on the stove. Turn on the heat and monitor the temperature of the water every few minutes with a thermometer that can be read to the nearest 1 °C.

a. Note the temperature when you see bubbles start to form—are you at the boiling point? What is responsible for the formation of bubbles? (see Section 9.4 and Figure 9.3b)

b. As the water temperature approaches 100 °C, what happens to the bubbles? When boiling occurs, record the temperature of the water.

c. Remove the pot from the stove and carefully add half a cup of salt to the water, and stir until it is completely dissolved. Return the pot to the stove and reheat until the water again begins to boil. How does the boiling point temperature of the salt solution compare to the boiling point of pure water? Is this consistent with Figure 9.10?

9.10 Osmosis and Osmotic Pressure

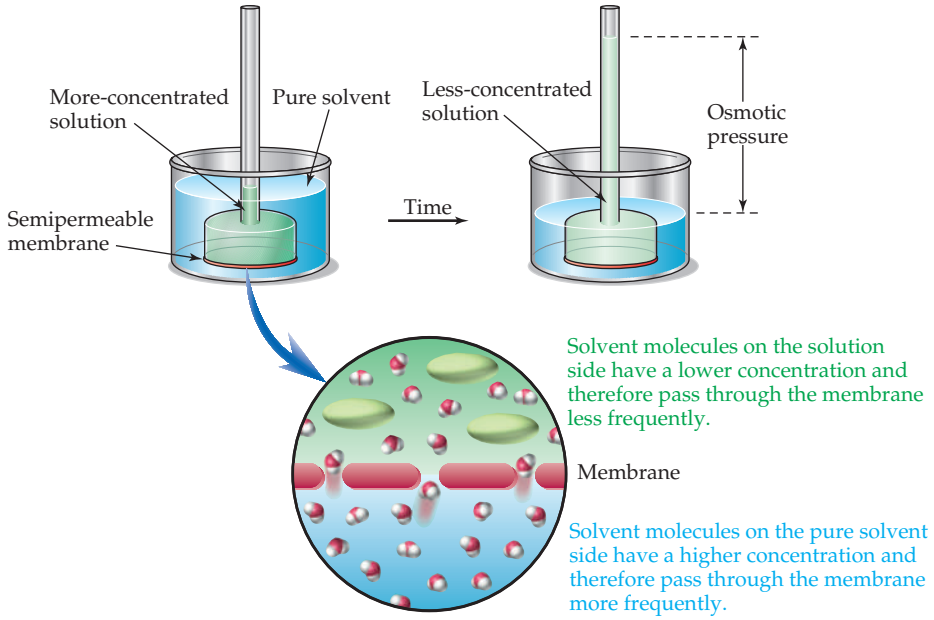
Learning Objective:

- Calculate the osmotic pressure of a solution and predict the direction of solvent flow across a semipermeable membrane due to osmosis.

Certain materials, including those that make up the membranes around living cells, are *semipermeable*. They allow water and other small molecules to pass through, but they block the passage of large solute molecules or ions. When a solution and a pure solvent, or two solutions of different concentration, are separated by a semipermeable membrane, solvent molecules pass through the membrane in a process called **osmosis.** Although the passage of solvent through the membrane takes place in both directions, passage from the pure solvent side to the solution side is favored and occurs more often. As a result, the amount of liquid on the pure solvent side decreases, the amount of liquid on the solution side increases, and the concentration of the solution decreases.

Osmosis The passage of solvent through a semipermeable membrane separating two solutions of different concentration.

For the simplest explanation of osmosis, let us look at what happens on the molecular level. As shown in Figure 9.11, a solution inside a bulb is separated by a semipermeable membrane from pure solvent in the outer container. Solvent molecules in the outer container, because of their somewhat higher concentration, approach the membrane more frequently than do molecules in the bulb, thereby passing through more often and causing the liquid level in the attached tube to rise.



◀ **Figure 9.11**
The phenomenon of osmosis. A solution inside the bulb is separated from pure solvent in the outer container by a semipermeable membrane. Solvent molecules in the outer container have a higher concentration than molecules in the bulb and therefore pass through the membrane more frequently. The liquid in the tube therefore rises until an equilibrium is reached. At equilibrium, the osmotic pressure exerted by the column of liquid in the tube is sufficient to prevent further net passage of solvent.

As the liquid in the tube rises, its increased weight creates an increased pressure that pushes solvent back through the membrane until the rates of forward and reverse passage become equal and the liquid level stops rising. The amount of pressure necessary to achieve this equilibrium is called the **osmotic pressure** (π) of the solution and can be determined from the following expression:

$$\pi = \left(\frac{n}{V}\right)RT$$

Osmotic pressure The amount of external pressure that must be applied to a solution to prevent the net movement of solvent molecules across a semipermeable membrane.

where n is the number of moles of particles in the solution, V is the solution volume, R is the gas constant (Section 8.10), and T is the absolute temperature of the solution. Note the similarity between this equation for the osmotic pressure of a solution and the equation for the pressure of an ideal gas, $P = (n/V)RT$. In both cases, the pressure has units of atmospheres.

Osmotic pressures can be extremely high, even for relatively dilute solutions. The osmotic pressure of a 0.15 M NaCl solution at 25 °C (298 K), for example, is 7.4×10^5 Pa, a value that supports a difference in water level of approximately 76 m!

Osmolarity (osmol/L) The sum of the molarities of all dissolved particles (osmol) in 1.0 liter of solution.

As with other colligative properties, the amount of osmotic pressure depends only on the concentration of solute particles, not on their identity. Thus, it is convenient to use a new unit, *osmolarity,* to describe the concentration of particles in solution. The **osmolarity (osmol/L)** of a solution is equal to the number of moles of dissolved particles (ions or molecules) per liter of solution. A 0.2 *M* glucose solution, for instance, has an osmolarity of 0.2 osmol/L, but a 0.2 *M* solution of NaCl has an osmolarity of 0.4 osmol/L because it contains 0.2 mol of Na^+ ions and 0.2 mol of Cl^- ions.

Osmosis is particularly important in living organisms because the membranes around cells are semipermeable. The fluids both inside and outside cells must therefore have the same osmolarity to prevent buildup of osmotic pressure and consequent rupture of the cell membrane.

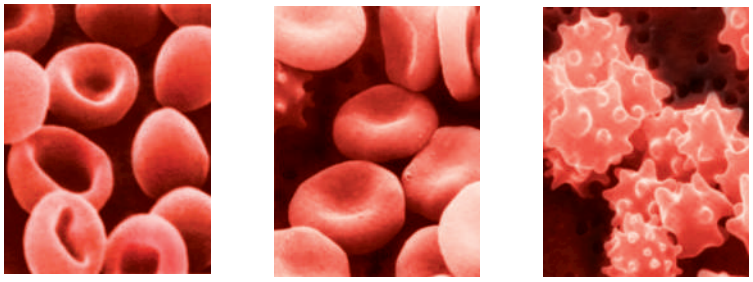
Isotonic Having the same osmolarity.

In blood, the plasma surrounding red blood cells has an osmolarity of approximately 0.30 osmol/L and is said to be **isotonic** with (i.e., has the same osmolarity as) the cell contents. If the cells are removed from plasma and placed in 0.15 *M* NaCl (called *physiological saline solution*), they are unharmed because the osmolarity of the saline solution (0.30 osmol/L) is the same as that of plasma. If, however, red blood cells are placed in pure water or in any solution with an osmolarity much lower than 0.30 osmol/L (a **hypotonic** solution), water passes through the membrane into the cell, causing the cell to swell up and burst, a process called *hemolysis.*

Hypotonic Having an osmolarity *less than* the surrounding blood plasma or cells.

Hypertonic Having an osmolarity *greater than* the surrounding blood plasma or cells.

Finally, if red blood cells are placed in a solution having an osmolarity greater than the cell contents (a **hypertonic** solution), water passes out of the cells into the surrounding solution, causing the cells to shrivel, a process called *crenation.* Figure 9.12 shows red blood cells under all three conditions: isotonic, hypotonic, and hypertonic. Therefore, it is critical that any solution used intravenously be isotonic to prevent red blood cells from being destroyed.



▶ **Figure 9.12**
Red blood cells.
In an isotonic solution the blood cells are normal in appearance (a), but the cells in a hypotonic solution (b) are swollen because of water gain, and those in a hypertonic solution (c) are shriveled because of water loss.

Worked Example 9.17 Properties of Solutions: Osmolarity

The solution of glucose commonly used intravenously has a concentration of 5.0% (m/v) glucose. What is the osmolarity of this solution? The molar mass of glucose is 180 g/mol.

ANALYSIS Since glucose is a molecular substance that does not give ions in solution, the osmolarity of the solution is the same as the molarity. Recall from Section 9.7 that a solution of 5.0% (m/v) glucose has a concentration of 5.0 g glucose per 100 mL of solution, which is equivalent to 50 g per liter of solution. Thus, finding the molar concentration of glucose requires a mass to mole conversion.

BALLPARK ESTIMATE One liter of solution contains 50 g of glucose (Molar mass = 180 g/mol). Thus, 50 g of glucose is equal to a little more than 0.25 mol, so a solution concentration of 50 g/L is equal to about 0.25 osmol/L, or 0.25 *M*.

SOLUTION

STEP 1: Identify known information. We know the (m/v)% concentration of the glucose solution.

$$5.0\%(\text{m/v}) = \frac{5.0\text{ g glucose}}{100\text{ mL solution}} \times 100\%$$

STEP 2: Identify answer and units. We are looking for osmolarity, which in this case is equal to the molarity of the solution because glucose is a molecular substance and does not dissociate into ions.

$$\text{Osmolarity} = \text{Molarity} = ??\text{ mol/liter}$$

STEP 3: Identify conversion factors. The (m/v)% concentration is defined as grams of solute per 100 mL of solution, and molarity is defined as moles of solute per liter of solution. We will need to convert from milliliters to liters and then use molar mass to convert grams of glucose to moles of glucose.

$$\frac{\text{g glucose}}{100\ \cancel{\text{mL}}} \times \frac{1000\ \cancel{\text{mL}}}{\text{L}} \longrightarrow \frac{\text{g glucose}}{\text{L}}$$

$$\frac{\cancel{\text{g glucose}}}{\text{L}} \times \frac{1\ \text{mol glucose}}{180\ \cancel{\text{g glucose}}} \longrightarrow \frac{\text{moles glucose}}{\text{L}}$$

STEP 4: Solve. Starting with the (m/v)% glucose concentration, we first find the number of grams of glucose in 1 L of solution and then convert to moles of glucose per liter.

$$\left(\frac{5.0\ \text{g glucose}}{100\ \cancel{\text{mL}}\ \text{solution}}\right)\left(\frac{1000\ \cancel{\text{mL}}}{1\ \text{L}}\right) = \frac{50\ \text{g glucose}}{\text{L solution}}$$

$$\left(\frac{50\ \cancel{\text{g}}\ \text{glucose}}{1\ \text{L}}\right)\left(\frac{1\ \text{mol}}{180\ \cancel{\text{g}}}\right) = 0.28\ M\ \text{glucose} = 0.28\ \text{osmol}$$

BALLPARK CHECK The calculated osmolarity is reasonably close to our estimate of 0.25 osmol/L.

Worked Example 9.18 Properties of Solutions: Osmolarity

What mass of NaCl is needed to make 1.50 L of a 0.300 osmol/L solution? The molar mass of NaCl is 58.44 g/mol.

ANALYSIS Since NaCl is an ionic substance that produces 2 mol of ions (Na^+, Cl^-) when it dissociates, the osmolarity of the solution is twice the molarity. From the volume and the osmolarity we can determine the moles of NaCl needed and then perform a mole to mass conversion.

SOLUTION

STEP 1: Identify known information. We know the volume and the osmolarity of the final NaCl solution.

$$V = 1.50\ \text{L}$$

$$0.300\ \text{osmol/L} = \left(\frac{0.300\ \text{mol ions}}{\text{L}}\right)$$

$$\text{Mass of NaCl} = ??\ \text{g}$$

STEP 2: Identify answer and units. We are looking for the mass of NaCl.

STEP 3: Identify conversion factors. Starting with osmolarity in the form (moles NaCl/L), we can use volume to determine the number of moles of solute. We can then use molar mass for the mole to mass conversion.

$$\left(\frac{\text{moles NaCl}}{\cancel{\text{L}}}\right) \times (\cancel{\text{L}}) = \text{moles NaCl}$$

$$(\cancel{\text{moles NaCl}}) \times \left(\frac{\text{g NaCl}}{\cancel{\text{moles NaCl}}}\right) = \text{g NaCl}$$

STEP 4: Solve. Use the appropriate conversions, remembering that NaCl produces two ions per formula unit, to find the mass of NaCl.

$$\left(\frac{0.300\ \cancel{\text{mol ions}}}{\cancel{\text{L}}}\right)\left(\frac{1\ \text{mol NaCl}}{2\ \cancel{\text{mol ions}}}\right)(1.50\ \cancel{\text{L}}) = 0.225\ \text{mol NaCl}$$

$$(0.225\ \cancel{\text{mol NaCl}})\left(\frac{58.44\ \text{g NaCl}}{\cancel{\text{mol NaCl}}}\right) = 13.1\ \text{g NaCl}$$

PROBLEM 9.25

What is the osmolarity of the following solutions?

(a) 0.35 *M* KBr
(b) 0.15 *M* glucose + 0.05 *M* K_2SO_4

PROBLEM 9.26

A typical oral rehydration solution (ORS) for infants contains 90 mEq/L Na^+, 20 mEq/L K^+, 110 mEq/L Cl^-, and 2.0% (m/v) glucose (Molar mass = 180 g/mol).

(a) Calculate the concentration of each ORS component in units of molarity.
(b) What is the osmolarity of the solution, and how does it compare with the osmolarity of blood plasma?

HANDS-ON CHEMISTRY 9.2

Obtain two clear glasses and two stalks of celery. If you do not have celery, some lettuce leaves will do. Fill both glasses about three quarters full with fresh water. Add about 2 teaspoons of salt to one glass and stir until it is dissolved. Place one celery stalk (or a large piece of lettuce) in each glass.

a. After about 15–30 minutes, check on the celery/lettuce in each glass. Do they appear different? In what ways?

b. Based on your observations, explain what has occurred based on osmotic flow.

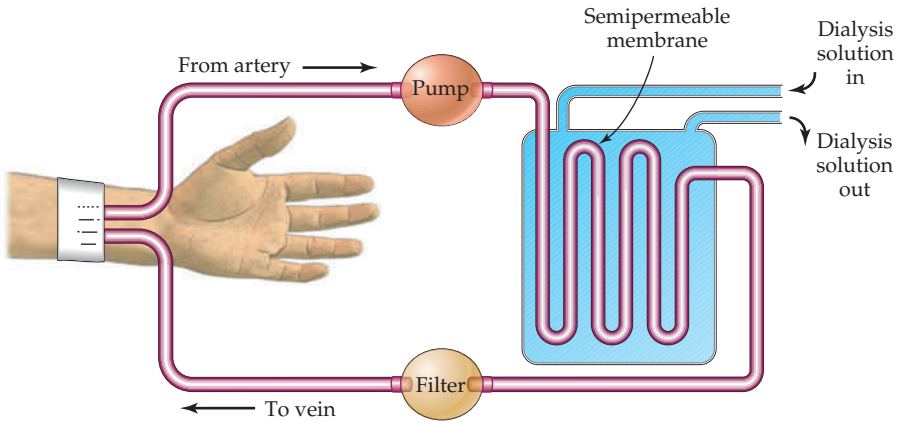
9.11 Dialysis

Learning Objective:

- Distinguish between osmosis and dialysis, and discuss dialysis applications.

Dialysis is similar to osmosis, except that the pores in a dialysis membrane are larger than those in an osmotic membrane so that both solvent molecules and small solute particles can pass through, but large colloidal particles such as proteins cannot pass. (The exact dividing line between a "small" molecule and a "large" one is imprecise, and dialysis membranes with a variety of pore sizes are available.) Dialysis membranes include animal bladders, parchment, and cellophane.

Perhaps the most important medical use of dialysis is in artificial kidney machines, where *hemodialysis* is used to cleanse the blood of patients whose kidneys malfunction (Figure 9.13). Blood is diverted from the body and pumped through a long cellophane dialysis tube suspended in an isotonic solution formulated to contain many of the same components as blood plasma. These substances—glucose, NaCl, $NaHCO_3$, and KCl—have the same concentrations in the dialysis solution as they do in blood so that they have no net passage through the membrane.



▶ **Figure 9.13**
Operation of a hemodialysis unit used for purifying blood. Blood is pumped from an artery through a coiled semipermeable membrane of cellophane. Small waste products pass through the membrane and are washed away by an isotonic dialysis solution.

Small waste materials such as urea pass through the dialysis membrane from the blood to the solution side where they are washed away, but cells, proteins, and other important blood components are prevented from passing through the membrane because of their larger size. In addition, the dialysis fluid concentration can be controlled so that imbalances in electrolytes are corrected. The wash solution is changed every two hours, and a typical hemodialysis procedure lasts for four to seven hours.

As previously noted, colloidal particles are too large to pass through a semipermeable membrane. Protein molecules, in particular, do not cross semipermeable membranes and thus play an essential role in determining the osmolarity of body fluids. The distribution of water and solutes across the capillary walls that separate blood plasma from the fluid surrounding cells is controlled by the balance between blood pressure and osmotic pressure. The pressure of blood inside the capillary tends to push water out of the plasma (filtration), but the osmotic pressure of colloidal protein molecules tends to draw water into the plasma (reabsorption). The balance between the two processes

CHEMISTRY IN ACTION

Timed-Release Drug Delivery Systems

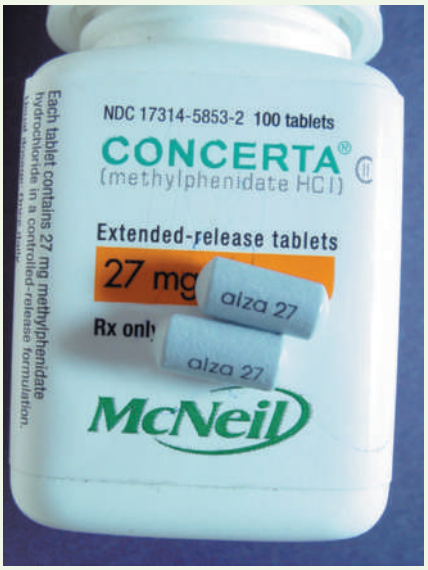
There is much more in most medications than medicine. Even something as simple as a generic aspirin tablet contains a binder to keep it from crumbling, a filler to bring it to the right size and help it disintegrate in the stomach, and a lubricant to keep it from sticking to the manufacturing equipment. Timed-release medications are even more complex.

The widespread use of timed-release medication dates from the introduction of Contac decongestant in 1961. The original idea was simple: tiny beads of medicine were encapsulated by coating them with varying thicknesses of a slow-dissolving polymer. Those beads with a thinner coat dissolve and release their medicine more rapidly; those with a thicker coat dissolve more slowly. Combining the right number of beads with the right thicknesses into a single capsule makes possible the gradual release of medication over a predictable time.

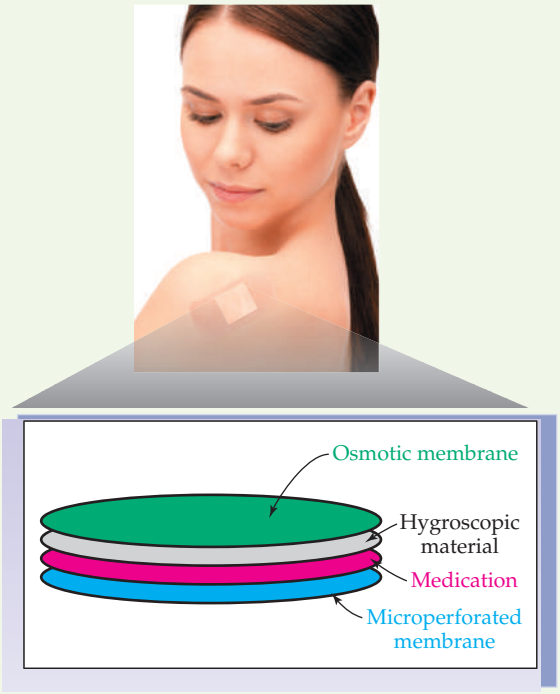
The technology of timed-release medications has become much more sophisticated in recent years, and the kinds of medications that can be delivered have become more numerous, as mentioned in the opening paragraph to this chapter. Slow-dissolving polymer coatings have been replaced by an insoluble porous polymer matrix; the drug is embedded in the matrix and slowly dissolves and diffused out of the holes. The release rate can be controlled by modifying the size of the pores in the matrix. Other delivery systems utilize polymer tablets with a porous membrane on one side and a laser-drilled hole on the other. As stomach fluids diffuse through the porous membrane, the drug is forced out the laser-drilled hole on the other side. After the entire drug dose has been delivered over a period of several hours, the insoluble matrix or tablet passes through the digestive system and is excreted.

Similar technology has been incorporated into transdermal patches to deliver drugs directly by diffusion through the skin. These patches use the osmotic effect to force a drug from its reservoir. Useful only for drugs that do not dissolve in water, the device is divided into two compartments, one containing medication covered by a perforated membrane and the other containing a hygroscopic material (p. 292) covered by a semipermeable membrane. As moisture from the air diffuses through the membrane into the compartment with the hygroscopic material, the buildup of pressure squeezes the medication out of the other compartment through tiny holes. Popular uses of transdermal patches include nicotine patches to reduce cigarette cravings, hormonal patches to treat menopausal symptoms or for contraception, opioid medications to provide long-term pain relief, and patches to treat motion sickness.

CIA Problem 9.8 What is the purpose of the hygroscopic material in the transdermal patch illustrated in the figure to the right?



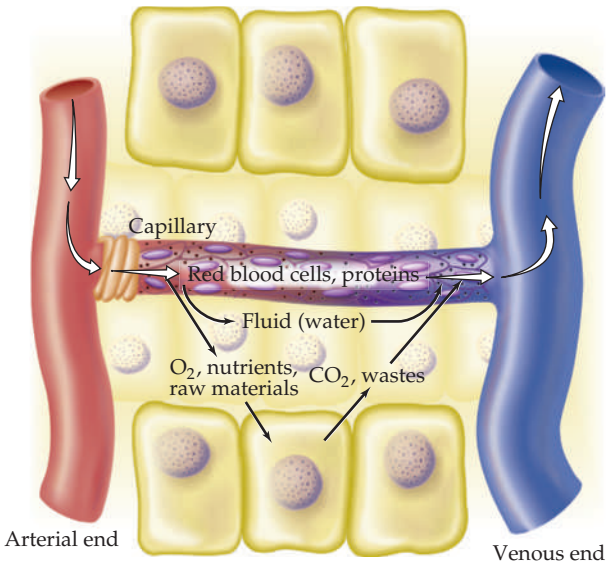
▲ This time-release medication uses a semipermeable membrane and osmotic pressure to deliver controlled amounts of a drug to treat ADHD.



CIA Problem 9.9 Which of the following polymers would be more appropriate for use as a hygroscopic material? Explain your choice.

Polyethene ($-[CH_2-CH_2]_n-$) or
nylon ($-[CO(CH_2)_4CONH(CH_2)_6NH]_n-$)

▶ **Figure 9.14**
The delivery of oxygen and nutrients to the cells and the removal of waste products are regulated by osmosis.



varies with location in the body (see Figure 9.14). At the arterial end of a capillary, where blood pumped from the heart has a higher pressure, filtration is favored. At the venous end, where blood pressure is lower, reabsorption is favored, causing waste products from metabolism to enter the bloodstream, to be removed by the kidneys.

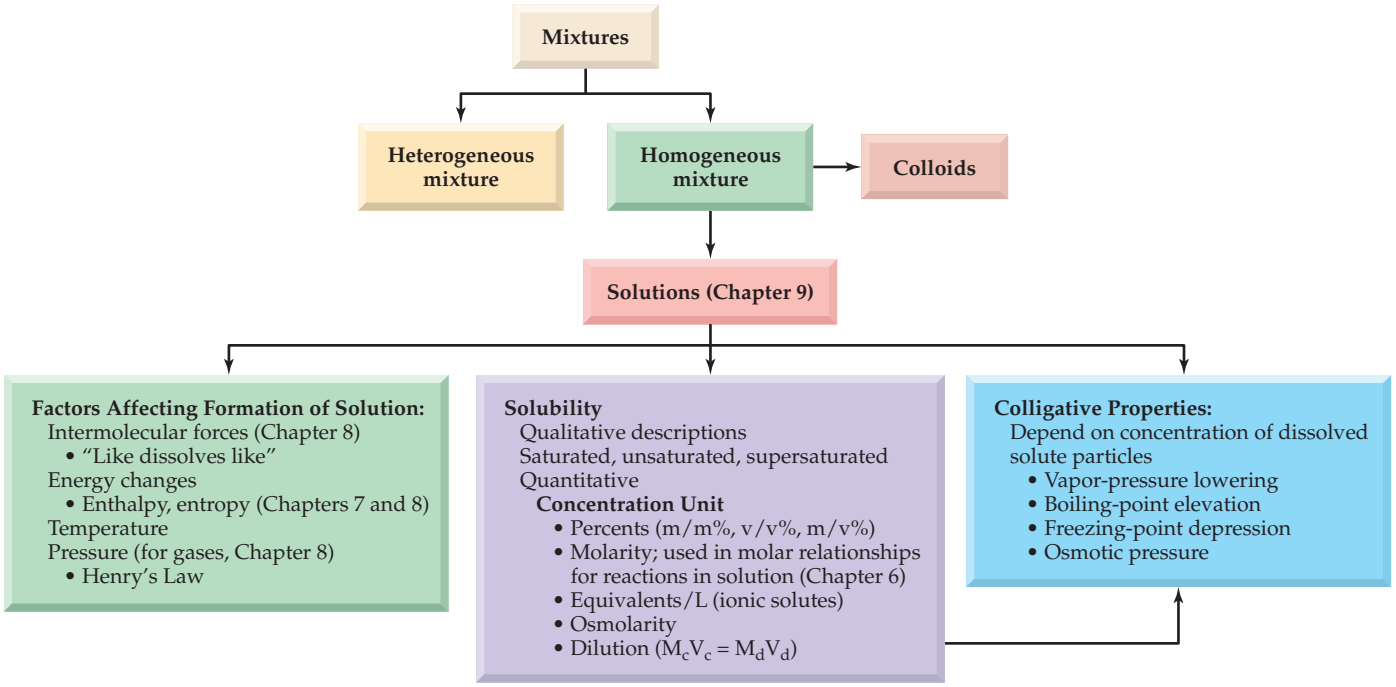
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Distinguish between heterogeneous and homogeneous mixtures and between solutions and colloids.** Mixtures are classified as either *heterogeneous,* if the mixing is nonuniform, or *homogeneous,* if the mixing is uniform. *Solutions* are homogeneous mixtures that contain particles the size of ions and molecules (<2.0 nm diameter), whereas larger particles (2.0–500 nm diameter) are present in *colloids (see Problems 32, 33, and 36).*
- **Predict whether a solution is likely to form based on the relative polarity and intermolecular forces between solute and solvent.** The general rule for solution formation is "like dissolves like"; polar solutes will tend to be soluble in polar solvents, whereas nonpolar solutes will be soluble in nonpolar solvents. In other words, substances tend to be mutually soluble when their intermolecular forces are similar *(see Problems 34, 35, 37, and 92).*
- **Define the properties of a solution, including miscibility, saturation, and solubility.** *Miscibility* refers to the tendency of two substances to be completely soluble in any proportions. The maximum amount of one substance (the *solute*) that can be dissolved in another (the *solvent*) is called the substance's *solubility. Saturation* is determined by the amount of solute dissolved compared to the substances maximum solubility. When the maximum amount of a given solute is dissolved, the solution is *saturated (see Problems 34, 35, 37–40, 92, and 96).*
- **Determine the effect of temperature changes on the solubility of a solute in a solution.** The solubility in water of a solid often increases with temperature, but the solubility of a gas decreases with temperature *(see Problems 38, 39, and 100).*
- **Determine the effect of a change in pressure on the solubility of a gas in solution.** Pressure significantly affects gas solubilities, which are directly proportional to their partial pressure over the solution *(Henry's law) (see Problems 42, 43, and 100).*
- **Define units of concentration, and calculate the concentration of a solute in solution.** The concentration of a solution can be expressed in several ways, including molarity, weight/weight percent composition, weight/volume percent composition, and parts per million (or billion). Osmolarity is used to express the total concentration of dissolved particles (ions and molecules). Molarity, which expresses concentration as the number of moles of solute per liter of solution, is the most useful method when calculating quantities of reactants or products for reactions in aqueous solution *(see Problems 40–43, 49–60, 83–92, 94, 95, 97, and 98).*
- **Use dilution factors to calculated molarities or volumes of dilute solutions prepared from concentrated solutions.** A dilution is carried out by adding more solvent to an existing solution. Only the amount of solvent changes; the amount of solute remains the same. Thus, the molarity times the volume of the dilute solution is equal to the molarity times the volume of the concentrated solution: $M_cV_c = M_dV_d$ *(see Problems 31, 44–48, 61–66, and 87).*
- **Identify solutes as strong electrolytes, weak electrolytes, or nonelectrolytes.** Substances that form ions when dissolved in water and whose water solutions therefore conduct an electric current are called *electrolytes.* Substances that ionize completely in water are *strong electrolytes,* those that ionize partially are *weak electrolytes,* and those that do not ionize are *nonelectrolytes (see Problems 28, 29, 67, 68, 82, and 95).*
- **Calculate equivalents for ionic solutes in solution.** Body fluids contain small amounts of many different electrolytes, whose concentrations are expressed as moles of ionic charge, or *equivalents*, per liter *(see Problems 67–74, 86, and 98).*
- **Calculate the colligative properties of boiling-point elevation and freezing-point depression for a solution.** In comparing a solution to a pure solvent, the solution has a lower vapor pressure at a given temperature, a higher boiling point, and a lower melting point. Called *colligative properties,* these effects depend only on the number of dissolved particles, not on their chemical identity. The colligative properties of aqueous solutions can be calculated as described in Section 9.9 *(see Problems 28–30, 75–78, 95, and 99).*
- **Calculate the osmotic pressure of a solution and predict the direction of solvent flow across a semipermeable membrane due to osmosis.** *Osmosis* occurs when solutions of different

concentration are separated by a semipermeable membrane that allows solvent molecules to pass but blocks the passage of solute ions and molecules. Solvent flows from the more dilute side to the more concentrated side until sufficient *osmotic pressure* builds up and stops the flow. An effect similar to osmosis occurs when membranes of larger pore size are used. *Osmotic pressure* (π) can be calculated as $\pi = (n/V)RT$ *(see Problems 27, 79–84, and 98).*

- **Distinguish between osmosis and dialysis, and discuss dialysis applications.** An effect similar to osmosis occurs when membranes of larger pore size are used. In *dialysis*, the membrane allows the passage of solvent and small dissolved molecules but prevents passage of proteins and larger particles. Dialysis is commonly used to remove metabolic waste products from blood *(see Problem 101).*

CONCEPT MAP: SOLUTIONS



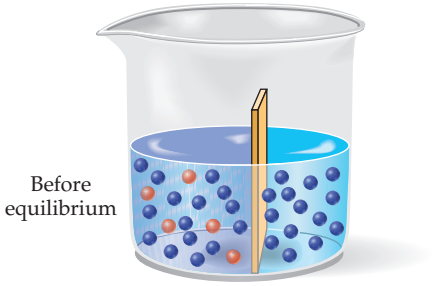
▲ **Figure 9.15 Concept Map.** Formation of a solution depends on many factors, including the attractive forces between solute and solvent particles, temperature, and pressure (gases). The extent to which a solute dissolves in solution can be expressed either qualitatively or using quantitative concentration units. The most common concentration unit in chemical applications is molarity (moles of solute/L solution), which is also useful in quantitative relationships involving reactions that take place in solution. Colligative properties of solution, including boiling and freezing points, will vary with the amount of solute dissolved in solution. These relationships are illustrated in this concept map.

KEY WORDS

Colligative property, *p. 309*
Colloid, *p. 289*
Dilution factor, *p. 305*
Electrolyte, *p. 307*
Equivalent (Eq), *p. 307*
Henry's law, *p. 295*
Hypertonic, *p. 314*
Hypotonic, *p. 314*
Isotonic, *p. 314*
Mass/mass percent concentration, (m/m)%, *p. 297*
Mass/volume percent concentration, (m/v)%, *p. 297*
Miscible, *p. 293*
Molarity (*M*), *p. 302*
Nonelectrolyte, *p. 307*
Osmolarity (osmol/L), *p. 314*
Osmosis, *p. 313*
Osmotic pressure, *p. 313*
Parts per billion (ppb), *p. 301*
Parts per million (ppm), *p. 301*
Saturated solution, *p. 293*
Solubility, *p. 293*
Solute, *p. 289*
Solution, *p. 289*
Solvation, *p. 291*
Solvent, *p. 289*
Strong electrolyte, *p. 307*
Supersaturated solution, *p. 294*
Volume/volume percent concentration, (v/v)%, *p. 297*
Weak electrolyte, *p. 307*

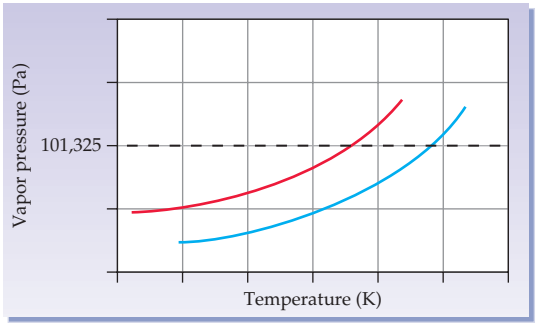
UNDERSTANDING KEY CONCEPTS

9.27 Assume that two liquids are separated by a semipermeable membrane, with pure solvent on the right side and a solution of a solute on the left side. Make a drawing that shows the situation after equilibrium is reached.



9.28 When 1 mol of HCl is added to 1 kg of water, the boiling point increases by 1.0 °C (1.0 K), but when 1 mol of acetic acid, CH_3CO_2H, is added to 1 kg of water, the boiling point increases by only 0.5 °C (0.5 K). Explain.

9.29 HF is a weak electrolyte and HBr is a strong electrolyte. Which of the curves in the figure represents the change in the boiling point of an aqueous solution when 1 mole of HF is added to 1 kg of water, and which represents the change when 1 mol of HBr is added?



9.30 Assume that you have two full beakers, one containing pure water (blue) and the other containing an equal volume of a 10% (w/v) solution of glucose (green). Which of the drawings (a)–(c) best represents the two beakers after they have stood uncovered for several days and partial evaporation has occurred? Explain.

9.31 A beaker containing 150.0 mL of 0.1 *M* glucose is represented by (a). Which of the drawings (b)–(d) represents the solution that results when 50.0 mL is withdrawn from (a) and then diluted by a factor of 4?

ADDITIONAL PROBLEMS

SOLUTIONS AND SOLUBILITY (SECTIONS 9.1–9.5)

9.32 What is the difference between a homogeneous mixture and a heterogeneous one?

9.33 How can you tell a solution from a colloid?

9.34 What characteristic of water allows it to dissolve ionic solids?

9.35 Why does water not dissolve motor oil?

9.36 Which of the following are solutions?

(a) Italian salad dressing

(b) Rubbing alcohol

(c) Algae in pond water

(d) Mouthwash

9.37 Based on the predominant intermolecular forces, which of the following pairs of liquids are likely to be miscible?

(a) H_2SO_4 and H_2O **(b)** C_8H_{18} and C_6H_6

(c) CH_2Cl_2 and H_2O **(d)** CS_2 and CCl_4

9.38 The solubility of NH_3 gas in water at an NH_3 pressure of 101,325 Pa and 25 °C (298 K) is 51.8 g/100 mL and 27.0 g/100 mL at 50 °C (323 K).

(a) What is the solubility of NH_3 if its partial pressure is reduced to 30,000 Pa?

(b) How many moles of NH_3 would be released from 1.0 L of a saturated NH_3 solution if the temperature was increased from 25 to 50 °C (298 K to 323 K)?

9.39 The solubility of CO_2 gas in water is 0.15 g/100 mL at a CO_2 pressure of 101,325 Pa.

(a) What is the solubility of CO_2 in a soft drink (which is mainly water) that was bottled under a CO_2 pressure of 4.6×10^5 Pa?

(b) An atmospheric concentration of 380 ppm, CO_2 corresponds to a partial pressure of 38.5 Pa. What percentage of the CO_2 originally dissolved in the solution in part (a) remains in solution after the soft drink reaches equilibrium with the ambient atmosphere?

(c) One bottle of soda is stored in a refrigerator at 3 °C (276 K), and another is stored at room temperature (25 °C or 298 K). If both bottles are opened simultaneously, which one would exhibit greater carbonation (i.e., bubbles)? Explain.

CONCENTRATION AND DILUTION OF SOLUTIONS (SECTIONS 9.6 AND 9.7)

9.40 Is a solution highly concentrated if it is saturated? Is a solution saturated if it is highly concentrated?

9.41 How is mass/volume percent concentration defined and for what types of solutions is it typically used?

9.42 How is molarity defined?

9.43 How is volume/volume percent concentration defined and for what types of solutions is it typically used?

9.44 A 750.0 mL bottle of Listerine is of a 21% (v/v) ethanol.

(a) What is the volume (in mL) of ethanol in the bottle?

(b) If the density of ethanol is 0.789 g/mL and the molar mass is 46.07 g/mol, calculate the molarity of ethanol in Listerine.

9.45 A dilute aqueous solution of boric acid, H_3BO_3, is often used as an eyewash. How would you prepare 500.0 mL of a 0.50% (m/v) boric acid solution?

9.46 Describe how you would prepare 250 mL of a 0.10 *M* NaCl solution.

9.47 Describe how you would prepare 1.50 L of a 7.50% (m/v) $Mg(NO_3)_2$ solution.

9.48 What is the mass/volume percent concentration of the following solutions?

(a) 0.078 mol KCl in 75 mL of solution

(b) 0.044 mol sucrose ($C_{12}H_{22}O_{11}$) in 380 mL of solution

9.49 The concentration of glucose in blood is approximately 90 mg/100 mL. What is the mass/volume percent concentration of glucose? What is the molarity of glucose?

9.50 How many moles of each substance are needed to prepare the following solutions?

(a) 50.0 mL of 8.0% (m/v) KCl (Molar mass = 74.55 g/mol)

(b) 200.0 mL of 7.5% (m/v) acetic acid (Molar mass = 60.05 g/mol)

9.51 Which of the following solutions is more concentrated?

(a) 0.50 *M* KCl or 5.0% (m/v) KCl

(b) 2.5% (m/v) $NaHSO_4$ or 0.025 *M* $NaHSO_4$

9.52 If you had only 23 g of KOH remaining in a bottle, how many milliliters of 10.0% (m/v) solution could you prepare? How many milliliters of 0.25 *M* solution?

9.53 Over-the-counter hydrogen peroxide (H_2O_2) solutions are 3% (m/v). What is this concentration in moles per liter?

9.54 The lethal dosage of potassium cyanide (KCN) in rats is 10 mg KCN per kilogram of body weight. What is this concentration in parts per million?

9.55 What is the molarity of the following solutions?

(a) 12.5 g $NaHCO_3$ in 350.0 mL solution

(b) 45.0 g H_2SO_4 in 300.0 mL solution

(c) 30.0 g NaCl dissolved to make 500.0 mL solution

9.56 How many grams of solute are in the following solutions?

(a) 200 mL of 0.30 *M* acetic acid, CH_3CO_2H

(b) 1.50 L of 0.25 *M* NaOH

(c) 750 mL of 2.5 *M* nitric acid, HNO_3

9.57 How many milliliters of a 0.75 *M* HCl solution do you need to obtain 0.0040 mol of HCl?

9.58 Nalorphine, a relative of morphine, is used to combat withdrawal symptoms in heroin users. How many milliliters of a 0.40% (m/v) solution of nalorphine must be injected to obtain a dose of 1.5 mg?

9.59 A flask containing 450 mL of 0.50 *M* H_2SO_4 was accidentally knocked to the floor. How many grams of $NaHCO_3$ do you need to put on the spill to neutralize the acid according to the following equation?

$$H_2SO_4(aq) + 2\,NaHCO_3(aq) \longrightarrow Na_2SO_4(aq) + 2\,H_2O(l) + 2\,CO_2(g)$$

9.60 Sodium thiosulfate ($Na_2S_2O_3$), the major component in photographic fixer solution, reacts with silver bromide to dissolve it according to the following reaction:

$$AgBr(s) + 2\,Na_2S_2O_3(aq) \longrightarrow Na_3Ag(S_2O_3)_2(aq) + NaBr(aq)$$

(a) How many moles of $Na_2S_2O_3$ would be required to react completely with 0.450 g of AgBr?

(b) How many mL of 0.02 *M* $Na_2S_2O_3$ contain this number of moles?

9.61 What is the final volume of an orange juice prepared from 100.0 mL of orange juice concentrate if the final juice is to be 20.0% of the strength of the original?

9.62 What is the final volume of NaOH solution prepared from 100.0 mL of 0.500 *M* NaOH if you wanted the final concentration to be 0.150 *M*?

9.63 An aqueous solution that contains 285 ppm of potassium nitrate (KNO_3) is being used to feed plants in a garden. What volume of this solution is needed to prepare 2.0 L of a solution that is 75 ppm in KNO_3?

9.64 What is the concentration of a NaCl solution, in (m/v)%, prepared by diluting 65 mL of a saturated solution, which has a concentration of 37 (m/v)%, to 480 mL?

9.65 Concentrated (12.0 *M*) hydrochloric acid is sold for household and industrial purposes under the name "muriatic acid." How many milliliters of 0.500 *M* HCl solution can be made from 25.0 mL of 12.0 *M* HCl solution?

9.66 Dilute solutions of $NaHCO_3$ are sometimes used in treating acid burns. How many milliliters of 0.100 *M* $NaHCO_3$ solution are needed to prepare 750.0 mL of 0.0500 *M* $NaHCO_3$ solution?

ELECTROLYTES (SECTION 9.8)

9.67 What is an electrolyte?

9.68 Give an example of a strong electrolyte and a nonelectrolyte.

9.69 What does it mean when we say that the concentration of Ca^{2+} in blood is 3.0 mEq/L?

9.70 What is the total anion concentration (in mEq/L) of a solution that contains 5.0 mEq/L Na^+, 12.0 mEq/L Ca^{2+}, and 2.0 mEq/L Li^+?

9.71 Kaochlor, a 10% (m/v) KCl solution, is an oral electrolyte supplement administered for potassium deficiency. How many milliequivalents of K^+ are in a 30 mL dose?

9.72 Calculate the mass needed for each of the following ion equivalents:

(a) 0.25 Eq Ca^{2+} **(b)** 75 mEq K^+

(c) 199 mEg SO_4^{2-} **(d)** 0.65 Eq PO_4^{3-}

9.73 The concentration of Cl^- ion in blood is approximately 100 mEq/L. How many milliliters of blood would be needed to obtain 1.0 g of Cl^- ions?

9.74 Normal blood contains 3 mEq/L of Mg^{2+}. How many milligrams of Mg^{2+} are present in 150.0 mL of blood?

PROPERTIES OF SOLUTIONS (SECTION 9.9)

9.75 Which lowers the freezing point of 2.0 kg of water more, 0.20 mol NaOH or 0.20 mol $Ba(OH)_2$? Both compounds are strong electrolytes. Explain.

9.76 Which solution has the higher boiling point, 0.500 *M* glucose or 0.300 *M* KCl? Explain.

9.77 Methanol, CH_3OH, is sometimes used as an antifreeze for the water in automobile windshield washer fluids. How many moles of methanol must be added to 5.00 kg of water to lower its freezing point to −10.0 °C (263 K)? (For each mole of solute, the freezing point of 1 kg of water is lowered 1.86 °C/K.)

9.78 Hard candy is prepared by dissolving pure sugar and flavoring in water and heating the solution to boiling. What is the boiling point of a solution produced by adding 650 g of cane sugar (molar mass 342.3 g/mol) to 1.5 kg of water? (For each mole of nonvolatile solute, the boiling point of 1 kg of water is raised 0.51 °C/K.)

OSMOSIS (SECTION 9.10)

9.79 Why do red blood cells swell up and burst when placed in pure water?

9.80 What does it mean when we say that a 0.15 *M* NaCl solution is isotonic with blood, whereas distilled water is hypotonic?

9.81 Which of the following solutions has the higher osmolarity?

(a) 0.25 *M* KBr or 0.20 *M* Na_2SO_4

(b) 0.30 *M* NaOH or 3.0% (m/v) NaOH

9.82 Which of the following solutions will give rise to a greater osmotic pressure at equilibrium: 5.00 g of NaCl in 350.0 mL water or 35.0 g of glucose in 400.0 mL water? For NaCl, molecular mass = 58.5 amu; for glucose, molecular mass = 180 amu.

9.83 A pickling solution for preserving food is prepared by dissolving 270 g of NaCl in 3.8 L of water. Calculate the osmolarity of the solution.

9.84 An isotonic solution must be approximately 0.30 osmol/L. How much KCl is needed to prepare 175 mL of an isotonic solution?

CONCEPTUAL PROBLEMS

9.85 Uric acid, the principal constituent of some kidney stones, has the formula $C_5H_4N_4O_3$. In aqueous solution, the solubility of uric acid is only 0.067 g/L. Express this concentration in (m/v)%, in parts per million, and in molarity.

9.86 Emergency treatment of cardiac arrest victims sometimes involves injection of a calcium chloride solution directly into the heart muscle. How many grams of $CaCl_2$ are administered in an injection of 5.0 mL of a 5.0% (m/v) solution? How many milliequivalents of Ca^{2+}?

9.87 Nitric acid, HNO_3, is available commercially at a concentration of 16 *M*.

(a) What volume would you need to obtain 0.150 mol HNO_3?

(b) To what volume must you dilute this volume of HNO_3 from part (a) to prepare a 0.20 *M* solution?

9.88 One test for vitamin C (ascorbic acid, $C_6H_8O_6$) is based on the reaction of the vitamin with iodine:

$$C_6H_8O_6(aq) + I_2(aq) \longrightarrow C_6H_6O_6(aq) + 2\,HI(aq)$$

(a) A 25.0 mL sample of a fruit juice requires 13.0 mL of 0.0100 *M* I_2 solution for reaction. How many moles of ascorbic acid are in the sample?

(b) What is the molarity of ascorbic acid in the fruit juice?

(c) The Food and Drug Administration recommends that 60 mg of ascorbic acid be consumed per day. How many milliliters of the fruit juice in part (a) must a person drink to obtain the recommended dosage?

9.89 A typical dosage of statin drugs for the treatment of high cholesterol is 10 mg. Assuming a total blood volume of 5.0 L, calculate the (m/v)% concentration of drug in the blood in units of g/100 mL.

9.90 Assuming the density of blood in healthy individuals is approximately 1.05 g/mL, report the concentration of drug in Problem 9.89 in units of ppm.

9.91 In European countries, a person with a blood alcohol concentration of 0.050% (v/v) is considered legally drunk. What volume of total alcohol does this concentration represent, assuming a blood volume of 5.0 L?

9.92 Ammonia, NH_3, is very soluble in water (51.8 g/L at 293 K and 101,325 Pa).

(a) Show how NH_3 can hydrogen bond to water.

(b) What is the solubility of ammonia in water in moles per liter?

9.93 Cobalt(II) chloride, a blue solid, can absorb water from the air to form cobalt(II) chloride hexahydrate, a pink solid. The equilibrium is so sensitive to moisture in the air that $CoCl_2$ is used as a humidity indicator.

(a) Write a balanced equation for the equilibrium. Be sure to include water as a reactant to produce the hexahydrate.

(b) How many grams of water are released by the decomposition of 2.50 g of cobalt(II) chloride hexahydrate?

9.94 How many milliliters of 0.150 *M* $BaCl_2$ are needed to react completely with 35.0 mL of 0.200 *M* Na_2SO_4? How many grams of $BaSO_4$ will be formed?

9.95 Many compounds are only partially dissociated into ions in aqueous solution. Trichloroacetic acid (CCl_3CO_2H), for instance, is partially dissociated in water according to the equation

$$CCl_3CO_2H(aq) \longrightarrow H^+(aq) + CCl_3CO_2^-(aq)$$

For a solution prepared by dissolving 1.00 mol of trichloroacetic acid in 1.00 kg of water, 36.0% of the trichloroacetic acid dissociates to form H^+ and $CCl_3CO_2^-$ ions.

(a) What is the total concentration of dissolved ions and molecules in 1 kg of water?

(b) What is the freezing point of this solution? (The freezing point of 1 kg of water is lowered 1.86 °C/K for each mole of solute particles.)

GROUP PROBLEMS

9.96 Hyperbaric chambers, which provide high pressures (up to 6 atm) of either air or pure oxygen, are used to treat a variety of conditions, ranging from decompression sickness in deep-sea divers to carbon monoxide poisoning. Look up the solubility of O_2, N_2, CO, and CO_2 in water at standard temperature and pressure (101,325 Pa, 298 K).

(a) Explain the trends in relative solubility for these gases. (Refer to Section 8.2 and Section 9.2)

(b) Explain how elevated pressures in a hyperbaric chamber be used to treat decompression sickness (excess N_2 in blood) and carbon monoxide poisoning. (Refer to Section 7.9 and Section 9.5)

9.97 Look up the maximum concentrations set by the U.S. Environmental Protection Agency for lead and cadmium in drinking water.

(a) What are these concentrations in milligrams per liter? In moles/L?

(b) Based on your answers to part (a), which is more toxic? Explain your answer.

(c) How many liters of water contaminated at this maximum level must you drink to consume 1.0 μg of lead? To consume 1.0 μg of cadmium?

9.98 Look up the composition of *Ringer's solution* used in the treatment of burns and wounds.

(a) What is the molarity of each component?

(b) What is the osmolarity of the solution? Is it hypertonic, isotonic, or hypotonic with blood plasma (0.30 osmol)? Discuss possible medicinal reasons for the osmolarity of the solution.

9.99 To prevent accumulation of ice on roads and sidewalks, many municipalities (and home-owners) will apply de-icing compounds to "melt" the ice by lowering the freezing point.

(a) Obtain a package of de-icing compound/mixture and identify the ingredients or look up the composition. Are the compounds ionic or molecular? Discuss possible reasons for the use of these compounds and for the specific compounds used in the formulations.

(b) Some de-icing compositions include dyes or colored compounds called indicators. Why?

9.100 Many carbonate minerals are insoluble in water and appear in water pipes as "scale."

(a) What is "scale"? What are the solubilty equilibria involved in scale formation?

(b) Why is scale formation typically only a problem in hot water pipes?

9.101 Research information related to dialysis and answer the following questions:

(a) What is the difference between hemodialysis and peritoneal dialysis?

(b) In hemodialysis, which substances diffuse out of the blood and into the dialysate (the solution used to remove waste products)? Which substances flow from the dialysate into the blood?

(c) Why is the level of hydrogen carbonate in the dialysate set at a slightly higher level than in normal blood?

10

Acids and Bases

CONTENTS

CONCEPTS TO REVIEW

A. Acids, Bases, and Neutralization Reactions (Sections 3.11 and 5.4)
B. Reversible Reactions and Chemical Equilibrium (Section 7.7)
C. Equilibrium Equations and Equilibrium Constants (Section 7.8)
D. Units of Concentration; Molarity (Section 9.6)
E. Ion Equivalents (Section 9.8)

▲ This young woman is experiencing shortness of breath from respiratory alkalosis, a result of anxiety-related hyperventilation. Breathing into a paper bag restores the balance of blood gases CO_2 and O_2, and returns the blood pH to an appropriate level.

A group of teenagers at a rock concert experiences a collective fainting spell. A woman taking high doses of aspirin for chronic pain appears disoriented and is having trouble breathing. A man with type 1 diabetes complains of tiredness and stomach pains. An athlete who recently completed a highly strenuous workout suffers from muscle cramps and nausea. A patient on an HIV drug regimen experiences increasing weakness and numbness in

the hands and feet. What do all these individuals have in common? Just like the young woman in the opening photograph, they are all experiencing symptoms related to fluctuations in blood pH, conditions referred to as acidosis (low pH) or alkalosis (high pH). The concepts of acids and bases were introduced in previous chapters, but to fully appreciate the significance of blood pH and the means by which it is controlled physiologically, we need to explore further the behavior of acids and bases. Specifically, in this chapter, we will examine the differences between strong and weak acids and bases, the reactions of acids and bases, and the role of acids and bases in solutions called *buffers.*

10.1 Acids and Bases: Definitions

Learning Objective:

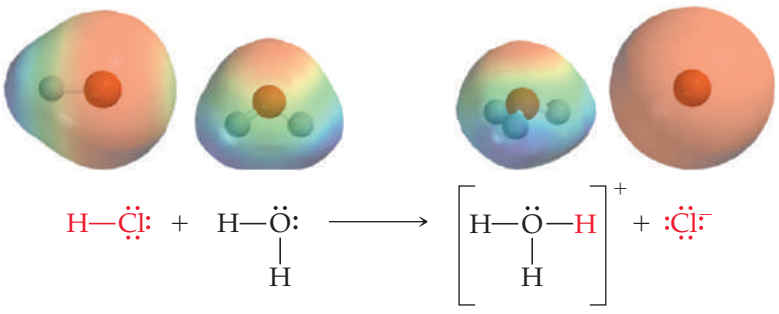
- Define the behavior of acids and bases in solution, and identify conjugate acid-base pairs.

Acids! The word evokes images of dangerous, corrosive liquids that eat away everything they touch. Although a few well-known substances such as sulfuric acid (H_2SO_4) do indeed fit this description, most acids are relatively harmless. In fact, many acids, such as ascorbic acid (vitamin C), are necessary for life. We have already learned a few facts about acids and bases in previous chapters:

- An acid is a substance that produces hydrogen ions, H^+, when dissolved in water. (Section 3.11)
- A base is a substance that produces hydroxide ions, OH^-, when dissolved in water. (Section 3.11)
- The neutralization reaction of an acid with a base yields water plus a *salt,* an ionic compound composed of the cation from the base and the anion from the acid. (Section 5.4)

The above definitions of acids and bases from Section 3.11 were proposed in 1887 by the Swedish chemist Svante Arrhenius and are useful for many purposes. The definitions are limited, however, because they refer only to reactions that take place in aqueous solutions. (We will see shortly how the definitions can be broadened.) Another issue is that the H^+ ion is so reactive it does not exist in water. Instead, H^+ reacts with H_2O to give the **hydronium ion,** H_3O^+, as mentioned in Section 3.11. When gaseous HCl dissolves in water, for instance, H_3O^+ and Cl^- are formed. As described in Section 4.9, electrostatic potential maps show that the hydrogen of HCl is positively polarized and electron-poor (blue), whereas the oxygen of water is negatively polarized and electron-rich (red):

Hydronium ion The H_3O^+ ion, formed when an acid reacts with water.



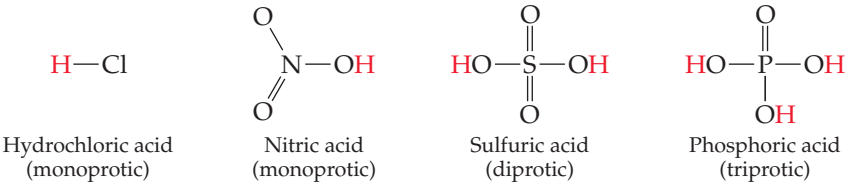
Thus, the Arrhenius definition was updated to acknowledge that an acid yields H_3O^+ in water rather than H^+; however, the notations H_3O^+ and $H^+(aq)$ are often used interchangeably.

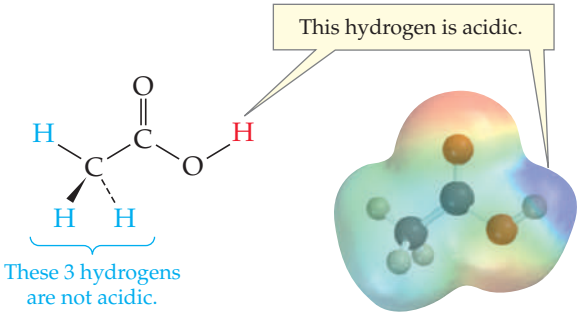
The Arrhenius definition of a base is obvious in some cases, but what about substances in which the hydroxide ions are not obvious? It is important to realize that the OH^- ions "produced" by the base can come from either of two sources. Metal hydroxides, such as NaOH, KOH, and $Ba(OH)_2$, are ionic compounds that already contain OH^- ions and merely release those ions when they dissolve in water. But, metal oxides can also react with water to generate OH^- ions. In addition, some molecular compounds, such as ammonia, are not ionic and contain no OH^- ions in their structure. Nonetheless, they can act as bases to produce OH^- ions in reactions with water.

The Arrhenius definition of acids and bases applies only to processes that take place in an aqueous solution. A far more general definition was proposed in 1923 by the Danish chemist Johannes Brønsted and the English chemist Thomas Lowry. A **Brønsted–Lowry acid** is any substance that is able to give a hydrogen ion, H^+, to another molecule or ion. A hydrogen *atom* consists of a proton and an electron, so a hydrogen *ion,* H^+, is simply a proton. Thus, we often refer to acids as *proton donors.* The reaction need not occur in water, and a Brønsted–Lowry acid need not give appreciable concentrations of H_3O^+ ions in water.

Brønsted–Lowry acid A substance that can donate a hydrogen ion, H^+, to another molecule or ion.

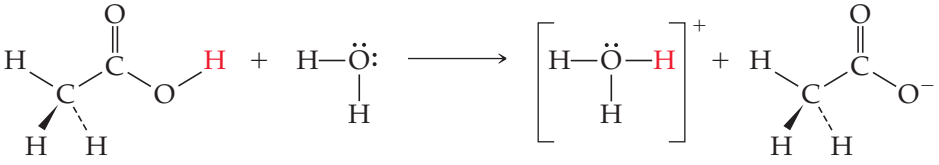
Different acids can supply different numbers of H^+ ions, as we saw in Section 3.11. Acids with one proton to donate, such as HCl or HNO_3, are called *monoprotic acids;* H_2SO_4 is a *diprotic acid* because it has two protons to donate, and H_3PO_4 is a *triprotic acid* because it has three protons to donate. Notice that the acidic H atoms (i.e., the H atoms that are donated as protons) are bonded to electronegative atoms, such as chlorine or oxygen.





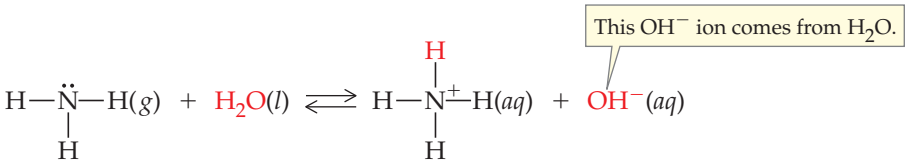
Acetic acid (CH_3CO_2H), an example of an organic acid, actually has a total of four hydrogens, but only the one bonded to the electronegative oxygen is positively polarized and therefore acidic. The three hydrogens bonded to carbon are not acidic. Most organic acids are similar in that they contain many hydrogen atoms, but only the one in the $—CO_2H$ group (blue in the electrostatic potential map) is acidic.

Acetic acid will react with water to produce H_3O^+ ions (Arrhenius acid definition) by donating a proton (Brønsted–Lowry acid definition) to water, as shown:

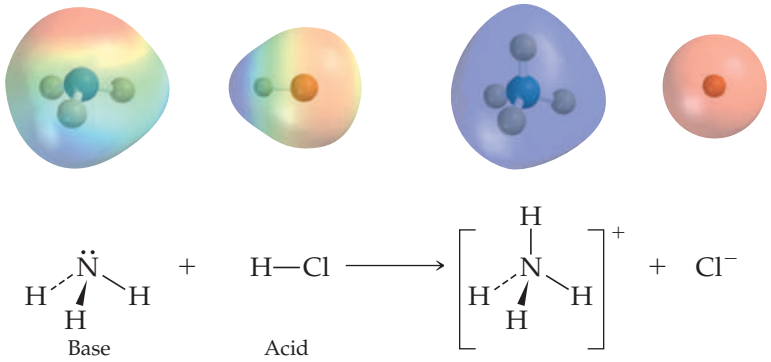


Brønsted–Lowry base A substance that can accept H^+ ions from an acid.

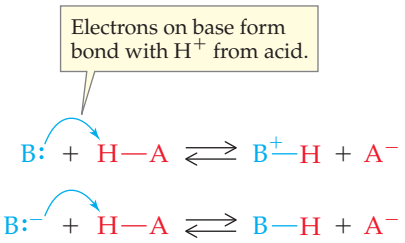
Whereas a Brønsted–Lowry acid is a substance that *donates* H^+ ions, a **Brønsted–Lowry base** is a substance that *accepts* H^+ ions from an acid. Ammonia will react with water to produce OH^- ions (Arrhenius base definition) by accepting a proton (Brønsted–Lowry base definition), as shown:



As with the acids, reactions involving Brønsted–Lowry bases need not occur in water, and the Brønsted–Lowry base need not give appreciable concentrations of OH^- ions in water. Gaseous NH_3, for example, acts as a base to accept H^+ from gaseous HCl and yield the ionic solid $NH_4^+ Cl^-$:



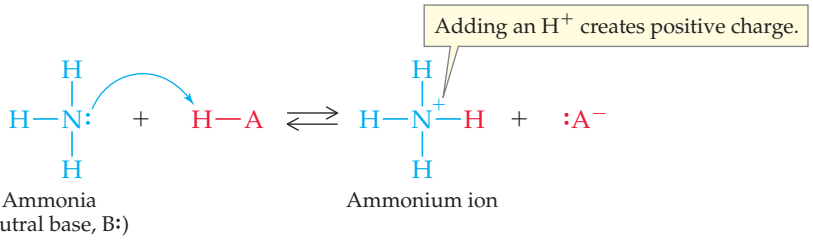
Putting the acid and base definitions together, *an acid-base reaction is one in which a proton is transferred.* The general reaction between proton-donor acids and proton-acceptor bases can be represented as



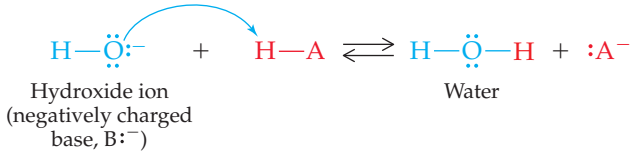
where the abbreviation HA represents a Brønsted–Lowry acid and B: or $B:^-$ represents a Brønsted–Lowry base. Notice in these acid-base reactions that both electrons in the product B—H bond come from the base, as indicated by the curved arrow flowing from the electron pair of the base to the hydrogen atom of the acid. Thus, the B—H bond that forms is a coordinate covalent bond. In fact, a Brønsted–Lowry base *must* have such a lone pair of electrons; without them, it could not accept H^+ from an acid.

A base can either be neutral (B:) or negatively charged ($B:^-$). If the base is neutral, then the product has a positive charge (BH^+) after H^+ has been added. Ammonia is an example:

CONCEPTS TO REVIEW Recall from Section 4.4 that a coordinate covalent bond is one where both electrons are donated by the same atom.

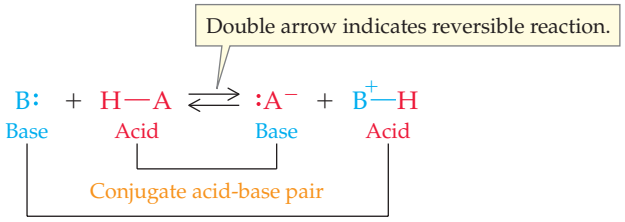


If the base is negatively charged, then the product is neutral (BH). Hydroxide ion is an example:



An important consequence of the Brønsted–Lowry definitions is that the *products* of an acid-base reaction can also behave as acids and bases. Many acid-base reactions are reversible, although in some cases the equilibrium constant for the reaction is quite large. For example, suppose we have as a forward reaction an acid HA donating a proton to a base B to produce A^-. This product A^- is a base because it can act as a proton acceptor in the reverse reaction. At the same time, the product BH^+ acts as an acid because it may donate a proton in the reverse reaction:

◀◀ When the equilibrium constant for a reaction is greater than 1, the forward reaction is favored. When the equilibrium constant is less than 1, the reverse reaction is favored (Section 7.8).

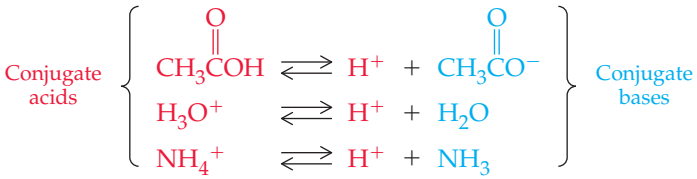


Conjugate acid-base pair Two substances whose formulas differ by only a hydrogen ion, H^+.

Conjugate base The substance formed by loss of H^+ from an acid.

Conjugate acid The substance formed by addition of H^+ to a base.

Pairs of chemical species such as B, BH^+ and HA, A^- are called **conjugate acid-base pairs.** They are species that are found on opposite sides of a chemical reaction whose formulas differ by only one H^+. Thus, the product anion A^- is the **conjugate base** of the reactant acid HA, and HA is the **conjugate acid** of the base A^-. Similarly, the reactant B is the conjugate base of the product acid BH^+, and BH^+ is the conjugate acid of the base B. The number of protons in a conjugate acid-base pair is always one greater than the number of protons in the base of the pair. To give some examples, acetic acid and acetate ion, the hydronium ion and water, and the ammonium ion and ammonia all make conjugate acid-base pairs:



Worked Example 10.1 Acids and Bases: Identifying Brønsted–Lowry Acids and Bases

Identify each of the following as a Brønsted–Lowry acid or base:

(a) PO_4^{3-} **(b)** $HClO_4$ **(c)** CN^-

ANALYSIS A Brønsted–Lowry acid must have a hydrogen that it can donate as H^+, and a Brønsted–Lowry base must have an atom with a lone pair of electrons that can bond to H^+. Typically, a Brønsted–Lowry base is an anion derived by loss of H^+ from an acid.

SOLUTION

(a) The phosphate anion (PO_4^{3-}) has no proton to donate, so it must be a Brønsted–Lowry base. It is derived by loss of 3 H^+ ions from phosphoric acid, H_3PO_4.

(b) Perchloric acid $(HClO_4)$ is a Brønsted–Lowry acid because it can donate an H^+ ion.

(c) The cyanide ion (CN^-) has no proton to donate, so it must be a Brønsted–Lowry base. It is derived by loss removal of an H^+ ion from hydrogen cyanide, HCN.

Worked Example 10.2 Acids and Bases: Identifying Conjugate Acid-Base Pairs

Write formulas for

(a) The conjugate acid of the cyanide ion, CN^-

(b) The conjugate base of perchloric acid, $HClO_4$

ANALYSIS A conjugate acid is formed by adding H^+ to a base; a conjugate base is formed by removing H^+ from an acid.

SOLUTION

(a) HCN is the conjugate acid of CN^-

(b) ClO_4^- is the conjugate base of $HClO_4$.

PROBLEM 10.1

Which of the following are Brønsted–Lowry acids?

(a) HCO_2H **(b)** H_2S **(c)** $SnCl_2$

PROBLEM 10.2

Which of the following are Brønsted–Lowry bases?

(a) SO_3^{2-} **(b)** Ag^+ **(c)** F^-

PROBLEM 10.3

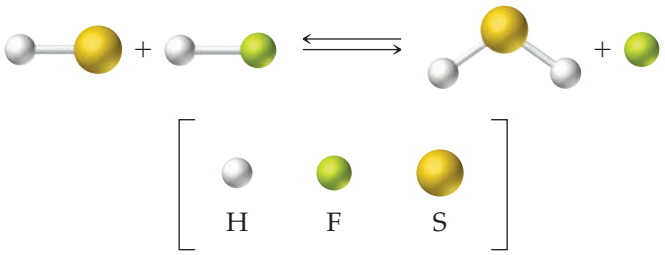
Write formulas for:

(a) The conjugate acid of HS^- **(b)** The conjugate acid of PO_4^{3-}

(c) The conjugate base of H_2CO_3 **(d)** The conjugate base of NH_4^+

KEY CONCEPT PROBLEM 10.4

For the reaction shown here, identify the Brønsted–Lowry acids, bases, and conjugate acid-base pairs.



10.2 Acid and Base Strength

Learning Objective:

- Identify substances as strong or weak acids or bases, and predict the direction of the proton transfer reaction based on the relative strength of the acids and bases involved.

Some acids and bases must be handled with caution because these substances are caustic or corrosive; contact with skin can cause severe burns. Other acids and bases are present in a variety of foods and consumer products. Acids generally have a sour taste, and nearly every sour food contains an acid: Lemons, oranges, and grapefruit contain citric acid, for instance, and sour milk contains lactic acid. Bases are not so obvious in foods, but most of us have them stored under the kitchen or bathroom sink. Bases are present in many household cleaning agents, from perfumed bar soap, to ammonia-based

▲ Common household cleaners typically contain bases (NaOH, NH_3). Soap is manufactured by the reaction of vegetable oils and animal fats with the bases NaOH and KOH.

window cleaners, to the substance you put down the drain to dissolve hair, grease, and other materials that clog it.

Some of the most common acids and bases are listed in Table 10.1. You should learn their names and formulas, because we will refer to them often throughout this chapter and the rest of the text.

Table 10.1 Common Acids and Bases

Common Acids	Information / Applications
Sulfuric acid, H_2SO_4	• The most important raw material in the chemical and pharmaceutical industries. • Over 45 million tons are prepared in the United States annually. • Used in the preparation of phosphate fertilizers, and is the acid found in automobile batteries.
Hydrochloric acid, HCl (*also* muriatic acid)	• Industrial applications include cleaning metal surfaces and manufacturing high-fructose corn syrup. • Component of "stomach acid" in the digestive systems of most mammals.
Phosphoric acid, H_3PO_4	• Used in the manufacturing of phosphate fertilizers, and as an additive in foods and toothpastes. • The tart taste of many soft drinks is due to the presence of phosphoric acid.
Nitric acid, HNO_3	• Strong oxidizing agent. • Used in the manufacturing of ammonium nitrate fertilizer and military explosives. • Contact with skin leaves a characteristic yellow coloration due to reaction with skin proteins.
Acetic acid, CH_3CO_2H	• Primary organic constituent of vinegar. • Occurs in all living cells. • Used in many industrial processes such as the preparation of solvents, lacquers, and coatings.
Common Bases	**Information / Applications**
Sodium hydroxide, NaOH (*also* caustic soda or lye)	• Most commonly used of all bases. • Industrially, used in the production of aluminum from its ore and in the production of glass; It is also used to manufacture soap from animal fat. • Drain cleaners often contain NaOH because it reacts with the fats and proteins found in grease and hair.
Calcium hydroxide, $Ca(OH)_2$ (*also* slaked lime)	• Made industrially by treating lime (CaO) with water. • A major component of mortars and cements. • Aqueous solution of $Ca(OH)_2$ often called *limewater.*
Magnesium hydroxide, $Mg(OH)_2$	• Aqueous suspensions called *milk of magnesia.* • Used as an additive in foods and toothpaste. • Component in many over-the-counter antacids such as Rolaids, Mylanta, and Maalox.
Ammonia, NH_3	• Used primarily as a fertilizer. • Other industrial applications include the manufacturing of pharmaceuticals and explosives. • Dilute solutions of ammonia are frequently used around the house as a glass cleaner.

Some acids and bases, such as sulfuric acid (H_2SO_4), hydrochloric acid (HCl), or sodium hydroxide (NaOH), are highly corrosive. They react readily and, in contact with skin, can cause serious burns. Other acids and bases are not nearly as reactive. Acetic acid (CH_3COOH, the major component in vinegar) and phosphoric acid (H_3PO_4) are found in many food products. Why are some acids and bases relatively "safe," while others must be handled with extreme caution? The answer lies in how easily they dissociate in water to produce the active ions for an acid (H^+) or a base (OH^-).

Strong acid An acid that gives up H^+ easily and completely dissociates in water.

As indicated in Table 10.2, acids differ in their ability to give up a proton. The six acids at the top of the table are **strong acids,** meaning that they give up a proton

easily and completely **dissociate,** or split apart into ions, in water. Those remaining are **weak acids,** meaning that they give up a proton with difficulty and do not completely dissociate in water. In a similar way, the conjugate bases at the top of the table are **weak bases** because they have little affinity for a proton, and the conjugate bases at the bottom of the table are **strong bases** because they have a strong affinity for a proton.

Dissociation The splitting apart of an acid in water to give H^+ and an anion.

Weak acid An acid that gives up H^+ with difficulty and does not completely dissociate in water.

Table 10.2 Relative Strengths of Acids and Conjugate Bases

	Acid		Conjugate base		
Increasing acid strength ↑	Strong acids: 100% dissociated	Perchloric acid	$HClO_4$	ClO_4^- Perchlorate ion	Little or no reaction as bases
		Sulfuric acid	H_2SO_4	HSO_4^- Hydrogen sulfate ion	
		Hydriodic acid	HI	I^- Iodide ion	
		Hydrobromic acid	HBr	Br^- Bromide ion	
		Hydrochloric acid	HCl	Cl^- Chloride ion	
		Nitric acid	HNO_3	NO_3^- Nitrate ion	
	Hydronium ion		**H_3O^+**	**H_2O** **Water**	
	Weak acids	Hydrogen sulfate ion	HSO_4^-	SO_4^{2-} Sulfate ion	Very weak bases
		Phosphoric acid	H_3PO_4	$H_2PO_4^-$ Dihydrogen phosphate ion	
		Nitrous acid	HNO_2	NO_2^- Nitrite ion	
		Hydrofluoric acid	HF	F^- Fluoride ion	
		Acetic acid	CH_3COOH	CH_3COO^- Acetate ion	
	Very weak acids	Carbonic acid	H_2CO_3	HCO_3^- Hydrogen carbonate ion	Weak bases
		Dihydrogen phosphate ion	$H_2PO_4^-$	HPO_4^{2-} Hydrogen phosphate ion	
		Ammonium ion	NH_4^+	NH_3 Ammonia	
		Hydrocyanic acid	HCN	CN^- Cyanide ion	
		Hydrogen carbonate ion	HCO_3^-	CO_3^{2-} Carbonate ion	
		Hydrogen phosphate ion	HPO_4^{2-}	PO_4^{3-} Phosphate ion	
	Water		**H_2O**	**OH^-** **Hydroxide ion**	Strong base

Increasing base strength ↓

Note that diprotic acids, such as sulfuric acid H_2SO_4, undergo two stepwise dissociations in water. The first dissociation yields HSO_4^- and occurs to the extent of nearly 100%, so H_2SO_4 is a strong acid. The second dissociation yields SO_4^{2-} and takes place to a much lesser extent because separation of a positively charged H^+ from the negatively charged HSO_4^- anion is difficult. Thus, HSO_4^- is a weak acid:

$$H_2SO_4(l) + H_2O(l) \longrightarrow H_3O^+(aq) + HSO_4^-(aq)$$
$$HSO_4^-(aq) + H_2O(l) \rightleftharpoons H_3O^+(aq) + SO_4^{2-}(aq)$$

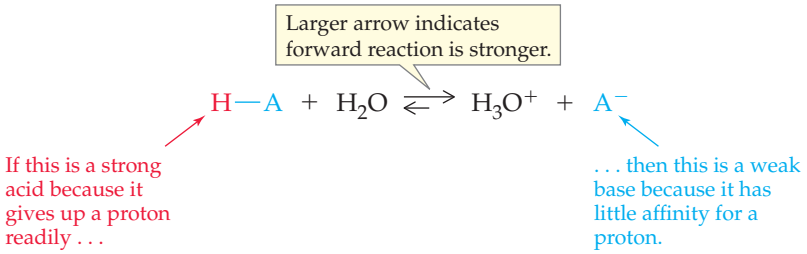
Perhaps the most striking feature of Table 10.2 is the inverse relationship between acid strength and base strength. **The stronger the acid, the weaker its conjugate base; the weaker the acid, the stronger its conjugate base.** HCl, for example, is a strong acid, so Cl^- is a very weak base. H_2O, however, is a very weak acid, so OH^- is a strong base.

Why is there an inverse relationship between acid strength and base strength? To answer this question, think about what it means for an acid or base to be strong or weak. A strong acid, HA, is one that readily gives up a proton, meaning that its conjugate base A^- has little affinity for the proton. But this is exactly the definition of a weak base—a substance that has little affinity for a proton. As a result, the reverse

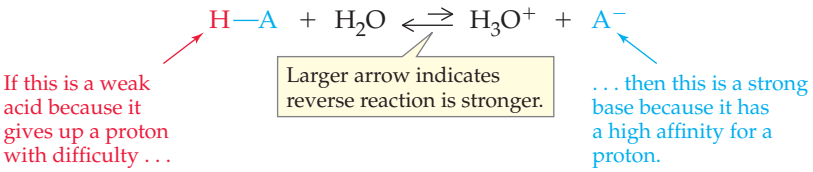
Weak base A base that has only a slight affinity for H^+ and holds it weakly.

Strong base A base that has a high affinity for H^+ and holds it tightly.

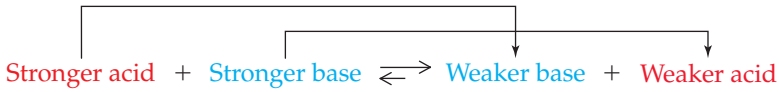
reaction occurs to a lesser extent, as indicated by the size of the forward and reverse arrows in the reaction:



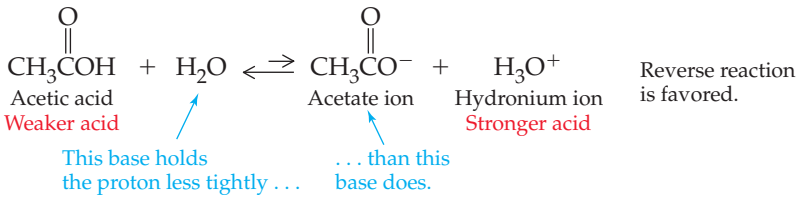
In the same way, a weak acid is one that gives up a proton with difficulty, meaning that its conjugate base has a high affinity for the proton. But this is just the definition of a strong base—a substance that has a high affinity for the proton. The reverse reaction now occurs more readily.



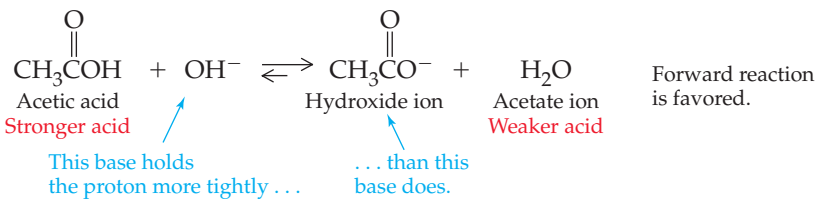
Knowing the relative strengths of different acids as shown in Table 10.2 makes it possible to predict the direction of proton-transfer reactions. *An acid-base proton-transfer equilibrium always favors reaction of the stronger acid with the stronger base and formation of the weaker acid and base.* That is, the proton always leaves the stronger acid (whose weaker conjugate base cannot hold the proton) and always ends up in the weaker acid (whose stronger conjugate base holds the proton tightly). Put another way, in a contest for the proton, the stronger base always wins.



To try out this rule, compare the reactions of acetic acid with water and with hydroxide ion. The idea is to write the equation, identify the acid on each side of the arrow, and then decide which acid is stronger and which is weaker. For example, the reaction of acetic acid with water to give acetate ion and hydronium ion is favored in the reverse direction, because acetic acid is a weaker acid than H_3O^+:



On the other hand, the reaction of acetic acid with hydroxide ion to give acetate ion and water is favored in the forward direction, because acetic acid is a stronger acid than H_2O:

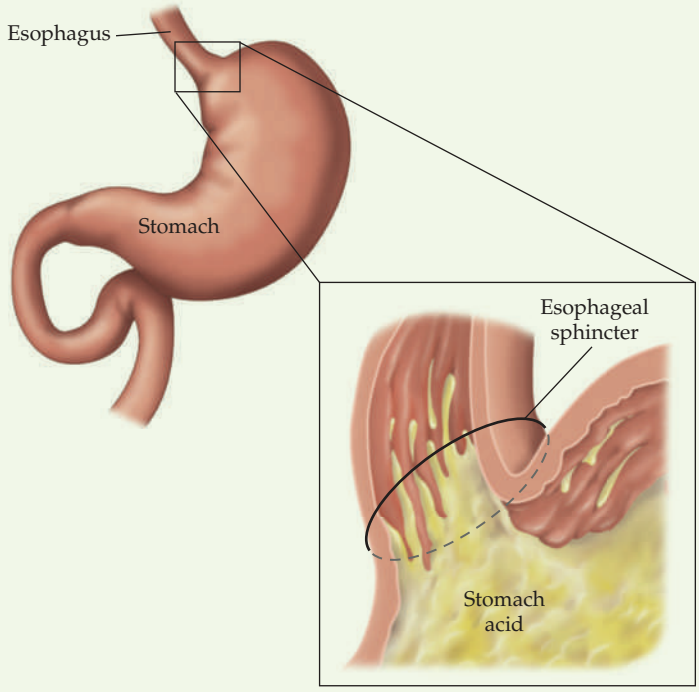


CHEMISTRY IN ACTION

GERD—Too Much Acid or Not Enough?

Strong acids are very caustic substances that can dissolve even metals, and no one would think of ingesting them. However, the major component of the gastric juices secreted in the stomach is hydrochloric acid—a strong acid—and the acidic environment in the stomach is vital to good health and nutrition.

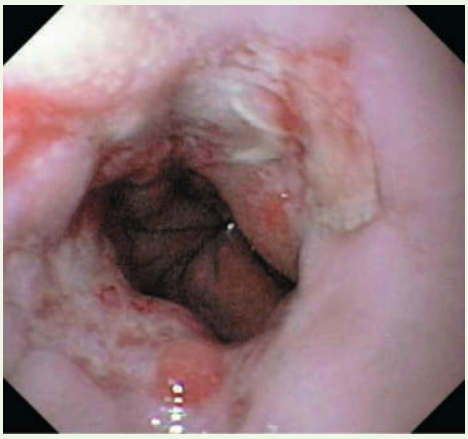
Stomach acid is essential for the digestion of proteins and for the absorption of certain micronutrients, such as calcium, magnesium, iron, and vitamin B_{12}. It also creates a sterile environment in the gut by killing yeast and bacteria that may be ingested. If these gastric juices leak up into the esophagus, the tube through which food and drink enter the stomach, they can cause the burning sensation in the chest or throat known as either heartburn or acid indigestion. Persistent irritation of the esophagus is known as gastro-esophageal reflux disease (GERD) and, if untreated, can lead to more serious health problems.



▲ The burning sensation and other symptoms associated with GERD are caused by the reflux of the acidic contents of the stomach into the esophagus.

Hydrogen ions and chloride ions are secreted separately from the cytoplasm of parietal cells lining the stomach and then combine to form HCl that is usually close to 0.10 *M*. The HCl is then released into the stomach cavity, where the concentration is diluted to about 0.01–0.001 *M*. Unlike the esophagus, the stomach is coated by a thick mucus layer that protects the stomach wall from damage by this caustic solution.

Those who suffer from acid indigestion can obtain relief by using over-the-counter antacids, such as TUMS or



▲ If not treated, GERD can cause ulcers and scarring of esophageal tissue.

Rolaids (see Section 10.8, p. 345). Chronic conditions such as GERD, however, are often treated with prescription medications. GERD can be treated by two classes of drugs. Proton-pump inhibitors (PPI), such as Prevacid and Prilosec, prevent the production of the H^+ ions in the parietal cells, while H_2-receptor blockers (Tagamet, Zantac, and Pepcid) prevent the release of stomach acid into the lumen. Both drugs effectively decrease the production of stomach acid to ease the symptoms of GERD.

Ironically, GERD can also be caused by not having enough stomach acid—a condition known as *hypochlorhydria.* The valve that controls the release of stomach contents to the small intestine is triggered by acidity. If this valve fails to open because the stomach is not acidic enough, the contents of the stomach can be churned back up into the esophagus.

CIA Problem 10.1 The concentration of HCl when released to the stomach cavity is diluted to between 0.01 and 0.001 *M*.

(a) Which of the two concentration of HCl cited above would require more antacid for neutralization? How much more?

(b) Write a balanced equation for the neutralization of stomach acid by $NaHCO_3$.

(c) How many grams of $NaHCO_3$ are required to neutralize 15.0 mL of a solution having a pH of 1.8?

CIA Problem 10.2 What are the functions of the acidic gastric juices in the stomach?

CIA Problem 10.3 Hydrochloric acid is the primary component of gastric juice in the stomach. The reaction between hydrochloric acid and the carbonate ion, the primary active ingredient in antacid tablets such as TUMS, can be written as

$$HCl(aq) + CO_3^{2-}(aq) \rightleftharpoons HCO_3^-(aq) + Cl^-(aq)$$

Identify the conjugate acid-base pairs in the reaction, and rewrite the arrows in the reaction to indicate if the forward or reverse reaction is favored.

Worked Example 10.3 Acid/Base Strength: Predicting Direction of H-transfer Reactions

Write a balanced equation for the proton-transfer reaction between phosphate ion (PO_4^{3-}) and water, and determine in which direction the equilibrium is favored.

ANALYSIS Look in Table 10.2 to see the relative acid and base strengths of the species involved in the reaction. The acid-base proton-transfer equilibrium will favor reaction of the stronger acid and formation of the weaker acid.

SOLUTION
Phosphate ion is the conjugate base of a weak acid (HPO_4^{2-}) and is, therefore, a relatively strong base. Table 10.2 shows that HPO_4^{2-} is a stronger acid than H_2O, and OH^- is a stronger base than PO_4^{3-}, so the reaction is favored in the reverse direction:

$$\underset{\text{Weaker base}}{PO_4^{3-}(aq)} + \underset{\text{Weaker acid}}{H_2O(l)} \rightleftharpoons \underset{\text{Stronger acid}}{HPO_4^{3-}(aq)} + \underset{\text{Stronger base}}{OH^-(aq)}$$

PROBLEM 10.5

Use Table 10.2 to identify the stronger acid in the following pairs:
(a) H_2O or NH_4^+ **(b)** H_2SO_4 or CH_3CO_2H **(c)** HCN or H_2CO_3

PROBLEM 10.6

Use Table 10.2 to identify the stronger base in the following pairs:
(a) F^- or Br^- **(b)** OH^- or HCO_3^-

PROBLEM 10.7

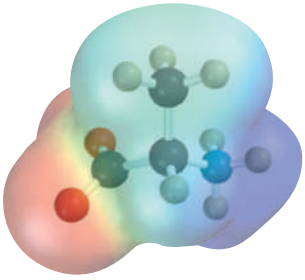
Write a balanced equation for the proton-transfer reaction between a hydrogen phosphate ion and a hydroxide ion. Identify each conjugate acid-base pair, and determine in which direction the equilibrium is favored.

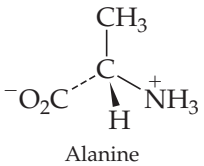
PROBLEM 10.8

Write a balanced equation for the proton transfer reaction between hydrofluoric acid (HF) and ammonia (NH_3). Identify each conjugate acid-base pair, and rewrite the equilibrium arrows to indicate if the forward or reverse reaction is favored.

KEY CONCEPT PROBLEM 10.9

From this electrostatic potential map of the amino acid alanine, identify the most acidic hydrogens in the molecule:





Alanine

10.3 Acid Dissociation Constants

Learning Objective:

- Write the expression for the acid dissociation constant (K_a), and use the value of K_a as a predictor of acid strength.

The reaction of a weak acid with water, like any chemical equilibrium, can be described by an equilibrium equation (Section 7.8), where square brackets indicate the concentrations of the enclosed species in molarity (moles per liter).

$$\text{For the reaction} \quad HA(aq) + H_2(l) \rightleftharpoons H_3^+(aq) + A^-(aq)$$

$$\text{we have} \quad K = \frac{[H_3O^+][A^-]}{[HA][H_2O]}$$

Because water is a solvent as well as a participant for the reaction, its concentration is essentially constant and has no effect on the equilibrium. Therefore, we usually put the equilibrium constant K and the water concentration $[H_2O]$ together to make a new constant called the **acid dissociation constant (K_a).** The acid dissociation constant is simply the hydronium ion concentration $[H_3O^+]$ times the conjugate base concentration $[A^-]$ divided by the undissociated acid concentration $[HA]$:

Acid dissociation constant (K_a) The equilibrium constant for the dissociation of an acid (HA), equal to $[H^+][A^-]/[HA]$.

$$\textit{Acid dissociation constant} \quad K_a = K[H_2O] = \frac{[H_3O^+][A^-]}{[HA]}$$

For a strong acid, the H_3O^+ and A^- concentrations are much larger than the HA concentration, so K_a is very large. In fact, the K_a values for strong acids such as HCl are so large that it is difficult and not very useful to measure them. For a weak acid, however, the H_3O^+ and A^- concentrations are smaller than the HA concentration, so K_a is small. Table 10.3 gives K_a values for some common acids and illustrates several important points:

- Strong acids have K_a values much greater than 1 because dissociation is favored.
- Weak acids have K_a values much less than 1 because dissociation is not favored.
- Donation of each successive H^+ from a polyprotic acid is more difficult than the one before it, so K_a values become successively lower (see K_a values for phosphoric acid in Table 10.3).
- Most organic acids, which contain the $-COOH$ group, have K_a values near 10^{-5}.

Table 10.3 Some Acid Dissociation Constants, K_a, at 25 °C (298 K)

Acid	K_a	Acid	K_a
Hydrofluoric acid (HF)	3.5×10^{-4}	*Polyprotic acids*	
Hydrocyanic acid (HCN)	4.9×10^{-10}	Sulfuric acid	
Ammonium ion (NH_4^+)	5.6×10^{-10}	H_2SO_4	Large
		HSO_4^-	1.2×10^{-2}
Organic acids		Phosphoric acid	
Formic acid (HCOOH)	1.8×10^{-4}	H_3PO_4	7.5×10^{-3}
Acetic acid (CH_3COOH)	1.8×10^{-5}	$H_2PO_4^-$	6.2×10^{-8}
Propanoic acid (CH_3CH_2COOH)	1.3×10^{-5}	HPO_4^{2-}	2.2×10^{-13}
Ascorbic acid (vitamin C)	7.9×10^{-5}	Carbonic acid	
		H_2CO_3	4.3×10^{-7}
		HCO_3^-	5.6×10^{-11}

PROBLEM 10.10

Benzoic acid ($C_6H_5CO_2H$) has $K_a = 6.5 \times 10^{-5}$ and citric acid ($C_6H_8O_7$) has $K_a = 7.2 \times 10^{-4}$. Which is the stronger conjugate base, benzoate ($C_6H_5CO_2^-$) or citrate ($C_6H_7O_7^-$)?

10.4 Water as Both an Acid and a Base

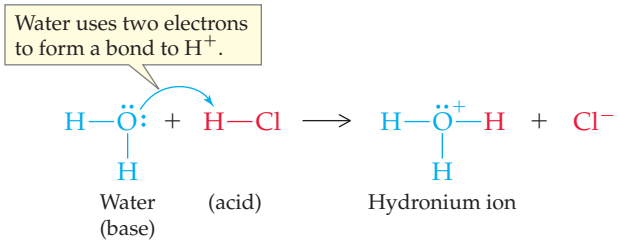
Learning Objectives:

- Identify the role of water as an acid or a base in hydrolysis reactions.
- Use the ion product constant for water (K_w) to calculate the relative concentrations of H_3O^+ and OH^- ions in aqueous solution.

Water is neither an acid nor a base in the Arrhenius sense because it does not contain appreciable concentrations of either H_3O^+ or OH^-. In the Brønsted–Lowry sense, however, water can act as *both* an acid and a base. When in contact with a base, water reacts as a Brønsted–Lowry acid and *donates* a proton to the base. In its reaction with ammonia, for example, water donates H^+ to ammonia to form the ammonium ion:

$$\underset{\text{Ammonia (base)}}{NH_3} + \underset{\text{Water (acid)}}{H_2O} \longrightarrow \underset{\text{Ammonium ion (acid)}}{NH_4^+} + \underset{\text{Hydroxide ion (base)}}{OH^-}$$

When in contact with an acid, water reacts as a Brønsted–Lowry base and *accepts* H^+ from the acid. This, of course, is exactly what happens when an acid such as HCl dissolves in water, as discussed in Section 10.1.



Amphoteric A substance that can react as either an acid or a base.

Substances like water, which can react as either an acid or a base depending on the circumstances, are said to be **amphoteric** (am-pho-**tare**-ic). When water acts as an acid, it donates H^+ and becomes OH^-; when it acts as a base, it accepts H^+ and becomes H_3O^+. (Note: HCO_3^-, $H_2PO_4^-$, and HPO_4^{2-} are also amphoteric.)

Dissociation of Water

We have learned how water can act as an acid when a base is present and as a base when an acid is present. But what about when no other acids or bases are present? In this case, one water molecule acts as an acid while another water molecule acts as a base, reacting to form the hydronium and hydroxide ions:

$$H_2O(l) + H_2O(l) \rightleftharpoons H_2O^+(aq) + OH^-(aq)$$

Because each dissociation reaction yields one H_3O^+ ion and one OH^- ion, the concentrations of the two ions are identical. Also, the equilibrium arrows indicate that this reaction favors reactants, so that not many H_3O^+ and OH^- ions are present at equilibrium. At 25 °C (298 K), the concentration of each is $1.00 \times 10^{-7}\,M$. We can write the equilibrium constant expression for the dissociation of water as

$$K = \frac{[H_3O^+][OH^-]}{[H_2O][H_2O]}$$

$$\text{where} \quad [H_3O^+] = [OH^-] = 1.00 \times 10^{-7}\,M \quad (\text{at } 25\,^\circ\text{C}/298\text{ K})$$

Refer to discussion of equilibria involving pure liquids and solids in Section 7.8.

As a pure substance the concentration of water is essentially constant. We can therefore put the water concentrations $[H_2O]$ together to make a new equilibrium constant called the **ion-product constant for water (K_w),** which is simply the H_3O^+ concentration times the OH^- concentration. At 25 °C (298 K), $K_w = 1.00 \times 10^{-14}$.

Ion-product constant for water (K_w) The product of the H_3O^+ and OH^- molar concentrations in water or any aqueous solution ($K_w = [H_3O^+][OH^-] = 1.00 \times 10^{-14}$).

Ion-product constant for water

$$\begin{aligned} K_w &= K[H_2O][H_2O] \\ &= [H_3O^+][OH^-] \\ &= 1.0 \times 10^{-14} \quad (\text{at } 25\,^\circ\text{C}/298\text{ K}) \end{aligned}$$

The importance of the equation $K_w = [H_3O^+][OH^-]$ is that it applies to all aqueous solutions, not just to pure water. Since the product of $[H_3O^+]$ times $[OH^-]$ is always constant for any solution, we can determine the concentration of one species if we know the concentration of the other. If an acid is present in solution, for instance, so that $[H_3O^+]$ is large, then $[OH^-]$ must be small. If a base is present in solution so

that $[OH^-]$ is large, then $[H_3O^+]$ must be small. For example, for a 0.10 *M* HCl solution, we know that $[H_3O^+] = 0.10\,M$ because HCl is 100% dissociated. Thus, we can calculate that $[OH^-] = 1.0 \times 10^{-13}\,M$:

$$\text{Since} \quad K_w \times [H_3O^+][OH^-] = 1.00 \times 10^{-14}$$

$$\text{we have} \quad [OH^-] = \frac{K_w}{[H_3O^+]} = \frac{1.00 \times 10^{-14}}{0.10} = 1.0 \times 10^{-13}\,M$$

Similarly, for a 0.10 *M* NaOH solution, we know that $[OH^-] = 0.10\,M$, so $[H_3O^+] = 1.0 \times 10^{-13}\,M$:

$$[H_3O^+] = \frac{K_w}{[OH^-]} = \frac{1.00 \times 10^{-14}}{0.10} = 1.0 \times 10^{-13}\,M$$

Solutions are identified as acidic, neutral, or basic *(alkaline)* according to the value of their H_3O^+ and OH^- concentrations:

Acidic solution: $[H_3O^+] > 10^{-7}\,M$ and $[OH^-] < 10^{-7}\,M$

Neutral solution: $[H_3O^+] = 10^{-7}\,M$ and $[OH^-] = 10^{-7}\,M$

Basic solution: $[H_3O^+] < 10^{-7}\,M$ and $[OH^-] > 10^{-7}\,M$

Worked Example 10.4 Water Dissociation Constant: Using K_w to Calculate $[OH^-]$

Milk has an H_3O^+ concentration of $4.5 \times 10^{-7}\,M$. What is the value of $[OH^-]$? Is milk acidic, neutral, or basic?

ANALYSIS The OH^- concentration can be found by dividing K_w by $[H_3O^+]$. An acidic solution has $[H_3O^+] > 10^{-7}\,M$, a neutral solution has $[H_3O^+] = 10^{-7}\,M$, and a basic solution has $[H_3O^+] < 10^{-7}\,M$.

BALLPARK ESTIMATE Since the H_3O^+ concentration is slightly *greater* than $10^{-7}\,M$, the OH^- concentration must be slightly *less* than $10^{-7}\,M$, on the order of 10^{-8}.

SOLUTION

$$[OH^-] = \frac{K_w}{[H_3O^+]} = \frac{1.00 \times 10^{-14}}{4.5 \times 10^{-7}} = 2.2 \times 10^{-8}\,M$$

Milk is slightly acidic because its H_3O^+ concentration is slightly larger than $1 \times 10^{-7}\,M$.

BALLPARK CHECK The OH^- concentration is of the same order of magnitude as our estimate.

PROBLEM 10.11

Identify the following solutions as either acidic or basic. What is the value of $[OH^-]$ in each?

(a) Household ammonia, $[H_3O^+] = 3.1 \times 10^{-12}\,M$

(b) Vinegar, $[H_3O^+] = 4.0 \times 10^{-3}\,M$

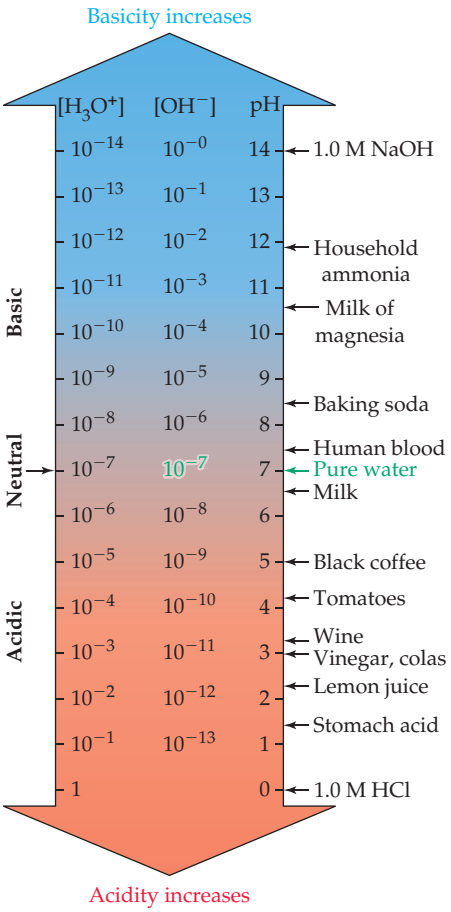
10.5 Measuring Acidity in Aqueous Solution: The pH Scale

Learning Objective:

- Calculate the pH of a solution from the H_3O^+ or OH^- concentration, and use the pH scale as an indication of the relative acidity/basicity of a solution.

In many fields, from medicine to chemistry to winemaking, it is necessary to know the exact concentration of H_3O^+ or OH^- in a solution. If, for example, the H_3O^+ concentration in blood varies only slightly from a value of $4.0 \times 10^{-8}\,M$, death can result.

Although correct, it is nevertheless awkward, or in some instances inconvenient, to refer to low concentrations of H_3O^+ using molarity. Fortunately, there is an easier way to express and compare H_3O^+ concentrations—the *pH scale*.



▲ Figure 10.1
The pH scale and the pH values of some common substances.
A low pH corresponds to a strongly acidic solution, a high pH corresponds to a strongly basic solution, and a pH of 7 corresponds to a neutral solution.

p function The negative common logarithm of some variable, $pX = -\log(X)$.

pH A measure of the acid strength of a solution; the negative common logarithm of the H_3O^+ concentration.

Acid-base indicator A dye that changes color depending on the pH of a solution.

The pH of an aqueous solution is a number, usually between 0 and 14, that indicates the H_3O^+ concentration of the solution. A pH smaller than 7 indicates an acidic solution, a pH larger than 7 indicates a basic solution, and a pH of exactly 7 indicates a neutral solution. The pH scale and pH values of some common substances are shown in Figure 10.1.

Mathematically, a **p function** is defined as the negative common logarithm of some variable. The **pH** of a solution, therefore, is the negative common logarithm of the H_3O^+ concentration:

$$\mathbf{pH} = -\log[H^+] \,(\text{or}\, [H_3O^+])$$

If you have studied logarithms, you may remember that the common logarithm of a number is the power to which 10 must be raised to equal the number. The pH definition can therefore be restated as

$$[H_3O^+] = 10^{-pH}$$

For example, in neutral water at 25 °C (298 K), where $[H_3O^+] = 1 \times 10^{-7}\,M$, the pH is 7; in a strong acid solution where $[H_3O^+] = 1 \times 10^{-1}\,M$, the pH is 1; and in a strong base solution where $[H_3O^+] = 1 \times 10^{-14}\,M$, the pH is 14:

Acidic solution: $\quad pH < 7, \quad [H_3O^+] > 1 \times 10^{-7}\,M$
Neutral solution: $\quad pH = 7, \quad [H_3O^+] = 1 \times 10^{-7}\,M$
Basic solution: $\quad pH > 7, \quad [H_3O^+] < 1 \times 10^{-7}\,M$

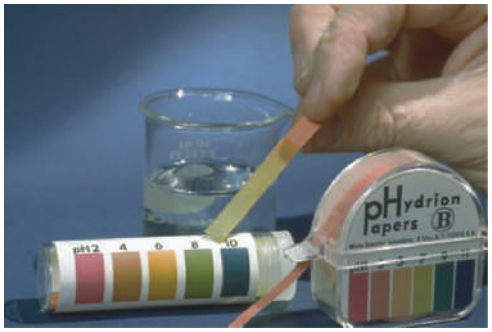
Keep in mind that the pH scale covers an enormous range of acidities because it is a *logarithmic* scale, which involves powers of 10 (Figure 10.2). A change of only 1 pH unit means a 10-fold change in $[H_3O^+]$, a change of 2 pH units means a 100-fold change in $[H_3O^+]$, and a change of 12 pH units means a change of 10^{12} (a trillion) in $[H_3O^+]$.

To get a feel for the size of the quantities involved, think of a typical backyard swimming pool, which contains about 100,000 L of water. You would have to add only 0.10 mol of HCl (3.7 g) to lower the pH of the pool from 7.0 (neutral) to 6.0, but you would have to add 10,000 mol of HCl (370 kg!) to lower the pH of the pool from 7.0 to 1.0.

The pH of water is an important indicator of water quality in applications ranging from swimming pool and spa maintenance to municipal water treatment. There are several ways to measure the pH of a solution. The simplest but least accurate method is to use an **acid-base indicator,** a dye that changes color depending on the pH of the solution. For example, the well-known dye *litmus* is red below pH 4.8 but blue above pH 7.8 and the indicator *phenolphthalein* (fee-nol-THAY-lean) is colorless below pH 8.2 but red above pH 10. To make pH determination particularly easy, test kits are available that contain a mixture of indicators known as *universal indicator* to give approximate pH measurements in the range 2–10 (Figure 10.2a). Also available are rolls of "pH paper," which make it possible to determine pH simply by putting a drop of solution on the paper and comparing the color that appears to the color on a calibration chart (Figure 10.2b).

▶ Figure 10.2
Finding pH.
(a) The color of universal indicator in solutions of known pH from 1 to 12. (b) Testing pH with a paper strip. Comparing the color of the strip with the code on the package gives the approximate pH.

(a)



(b)

A much more accurate way to determine pH uses an electronic pH meter like the one shown in Figure 10.3. Electrodes are dipped into the solution, and the pH is read from the meter.

The logarithmic pH scale is a convenient way of reporting the relative acidity of solutions, but using logarithms can also be useful when calculating H_3O^+ and OH^- concentrations. Remember that the equilibrium between H_3O^+ and OH^- in aqueous solutions is expressed by K_w, where

$$K_w = [H_3O^+][OH^-] = 1 \times 10^{-14} \quad (\text{at } 25\ ^\circ\text{C}/298\ \text{K})$$

If we convert this equation to its negative logarithmic form, we obtain

$$-\log(K_w) = -\log[H_3O^+] - \log[OH^-]$$
$$-\log(1 \times 10^{-14}) = -\log[H_3O^+] - \log[OH^-]$$
$$or \quad 14.00 = \text{pH} + \text{pOH}$$

The logarithmic form of the K_w equation can simplify the calculation of solution pH from OH^- concentration, as demonstrated in Worked Example 10.7.

▲ **Figure 10.3**
Using a pH meter to obtain an accurate reading of pH.
Is the blue solution acidic or basic?

Worked Example 10.5 Measuring Acidity: Calculating pH from $[H_3O^+]$

The H_3O^+ concentration in coffee is about $1 \times 10^{-5}\ M$. What pH is this?

ANALYSIS The pH is the negative common logarithm of the H_3O^+ concentration: $\text{pH} = -\log[H_3O^+]$.

SOLUTION
Since the common logarithm of $1 \times 10^{-5}\ M$ is –5.0, the pH is 5.0.

Worked Example 10.6 Measuring Acidity: Calculating $[H_3O^+]$ from pH

Lemon juice has a pH of about 2. What $[H_3O^+]$ is this?

ANALYSIS In this case, we are looking for the $[H_3O^+]$, where $[H_3O^+] = 10^{-\text{pH}}$.

SOLUTION
Since $\text{pH} = 2.0$, $[H_3O^+] = 10^{-2} = 1 \times 10^{-2}\ M$.

Worked Example 10.7 Measuring Acidity: Using K_w to Calculate $[H_3O^+]$ and pH

A cleaning solution is found to have $[OH^-] = 1 \times 10^{-3}\ M$. What is the pH?

ANALYSIS To find pH, we must first find the value of $[H_3O^+]$ by using the equation $[H_3O^+] = K_w/[OH^-]$. Alternatively, we can calculate the pOH of the solution and then use the logarithmic form of the K_w equation: $\text{pH} + \text{pOH} = 14.00$.

SOLUTION
Rearranging the K_w equation, we have

$$[H_3O^+] = \frac{K_w}{[OH^-]} = \frac{1.00 \times 10^{-14}}{1 \times 10^{-3}} = 1 \times 10^{-11}\ M$$
$$\text{pH} = -\log(1 \times 10^{-11}) = 11.0$$

Using the logarithmic form of the K_w equation, we have

$$\text{pH} = 14.0 - \text{pOH} = 14.0 - (-\log[OH^-])$$
$$\text{pH} = 14.0 - (-\log(1 \times 10^{-3}))$$
$$\text{pH} = 14.0 - 3.0 = 11.0$$

Worked Example 10.8 Measuring Acidity: Calculating pH of Strong Acid Solutions

What is the pH of a 0.01 *M* solution of HCl?

ANALYSIS To find pH, we must first find the value of $[H_3O^+]$.

SOLUTION
Since HCl is a strong acid (Table 10.1), it is 100% dissociated, and the H_3O^+ concentration is the same as the HCl concentration: $[H_3O^+] = 0.01\ M$, or $1 \times 10^{-2}\ M$, and pH = 2.0.

PROBLEM 10.12

Calculate the pH of the solutions in Problem 10.11.

PROBLEM 10.13

Give the hydronium ion and hydroxide ion concentrations of solutions with the following values of pH. Which of the solutions is most acidic? Which is most basic?

(a) pH 13.0 **(b)** pH 3.0 **(c)** pH 8.0

PROBLEM 10.14

Which solution would have the higher pH: 0.010 *M* HNO_2 or 0.010 *M* HNO_3? Explain.

10.6 Working with pH

Learning Objective:

- Calculate pH from $[H_3O^+]$ or $[OH^-]$, and calculate $[H_3O^+]$ from pH.

Converting between pH and H_3O^+ concentration is easy when the pH is a whole number, but how do you find the H_3O^+ concentration of blood, which has a pH of 7.4, or the pH of a solution with $[H_3O^+] = 4.6 \times 10^{-3}\ M$? Sometimes it is sufficient to make an estimate. The pH of blood (7.4) is between 7 and 8, so the H_3O^+ concentration of blood must be between 1×10^{-7} and $1 \times 10^{-8}\ M$. To be exact about finding pH values, though, requires a calculator.

Converting from pH to $[H_3O^+]$ requires finding the *antilogarithm* of the negative pH, which is done on many calculators with an "INV" key and a "log" key. Converting from $[H_3O^+]$ to pH requires finding the logarithm, which is commonly done with a "log" key and an "exp" or "EE" key for entering exponents of 10. Consult your calculator instructions if you are not sure how to use these keys. Remember that the sign of the number given by the calculator must be changed from minus to plus to get the pH.

The H_3O^+ concentration in blood with pH = 7.4 is

$$[H_3O^+] = \text{antilog}(-7.4) = 4 \times 10^{-8}\ M$$

The pH of a solution with $[H_3O^+] = 4.6 \times 10^{-3}\ M$ is

$$\text{pH} = -\log(4.6 \times 10^{-3}) = -(-2.34) = 2.34$$

If instead of $[H_3O^+]$ we are given $[OH^-]$, then we must first use the relationship $K_w = [H_3O^+]\,[OH^-]$; if $[OH^-]$ is known, we can rearrange to solve for the hydronium ion concentration and then calculate pH. Alternatively, we can calculate pOH and use the logarithmic form of K_w as discussed in the previous section:

$$14.00 = \text{pH} + \text{pOH}$$

A note about significant figures: an antilogarithm contains the same number of significant figures as the original number has to the right of the decimal point. A logarithm

contains the same number of digits to the right of the decimal point as the number of significant figures in the original number.

$$\text{antilog}(-7.4) = 4 \times 10^{-8} \qquad \log(4.6 \times 10^{-3}) = -2.34$$

1 digit after decimal point — 1 digit — 2 digits — 2 digits after decimal point

Worked Example 10.9 Working with pH: Converting a pH to $[H_3O^+]$

Soft drinks usually have a pH of approximately 3.1. What is the $[H_3O^+]$ concentration in a soft drink?

ANALYSIS To convert from a pH value to an $[H_3O^+]$ concentration requires using the equation $[H_3O^+] = 10^{-pH}$, which requires finding an antilogarithm on a calculator.

BALLPARK ESTIMATE Because the pH is between 3.0 and 4.0, the $[H_3O^+]$ must be between 1×10^{-3} and 1×10^{-4}. A pH of 3.1 is very close to 3.0, so the $[H_3O^+]$ must be just slightly below $1 \times 10^{-3}\,M$.

SOLUTION

Entering the negative pH on a calculator (-3.1) and pressing the "INV" and "log" keys gives the answer 7.943×10^{-4}, which must be rounded off to 8×10^{-4} because the pH has only one digit to the right of the decimal point.

BALLPARK CHECK The calculated $[H_3O^+]$ of $8 \times 10^{-4}\,M$ is between $1 \times 10^{-3}\,M$ and $1 \times 10^{-4}\,M$ and, as we estimated, just slightly below $1 \times 10^{-3}\,M$. (Remember, 8×10^{-4} is 0.8×10^{-3}.)

Worked Example 10.10 Working with pH: Calculating pH for Strong Acid Solutions

What is the pH of a 0.0045 M solution of $HClO_4$?

ANALYSIS Finding pH requires first finding $[H_3O^+]$ and then using the equation $pH = -\log[H_3O^+]$. Since $HClO_4$ is a strong acid (see Table 10.1), it is 100% dissociated, and so the H_3O^+ concentration is the same as the $HClO_4$ concentration.

BALLPARK ESTIMATE Because $[H_3O^+] = 4.5 \times 10^{-3}\,M$ is close to midway between $1 \times 10^{-2}\,M$ and $1 \times 10^{-3}\,M$, the pH must be close to the midway point between 2.0 and 3.0. (Unfortunately, because the logarithm scale is not linear, trying to estimate the midway point is not a simple process.)

SOLUTION

$[H_3O^+] = 0.0045\,M = 4.5 \times 10^{-3}\,M$. Taking the negative logarithm gives $pH = 2.35$.

BALLPARK CHECK The calculated pH is consistent with our estimate.

Worked Example 10.11 Working with pH: Calculating pH for Strong Base Solutions

What is the pH of a 0.0032 M solution of NaOH?

ANALYSIS Since NaOH is a strong base, the OH^- concentration is the same as the NaOH concentration. Starting with the OH^- concentration, finding pH requires either using the K_w equation to find $[H_3O^+]$ or calculating pOH and then using the logarithmic form of the K_w equation.

BALLPARK ESTIMATE Because $[OH^-] = 3.2 \times 10^{-3}\,M$ is close to midway between $1 \times 10^{-2}\,M$ and $1 \times 10^{-3}\,M$, the pOH must be close to the midway point between 2.0 and 3.0. Subtracting the pOH from 14 would therefore yield a pH between 11 and 12.

SOLUTION

$$[OH^-] = 0.0032\,M = 3.2 \times 10^{-3}\,M$$

$$[H_3O^+] = \frac{K_w}{(3.2 \times 10^{-3})} = 3.1 \times 10^{-12}\,M$$

—continued on next page

—continued from previous page

Taking the negative logarithm gives pH $= -\log(3.1 \times 10^{-12}) = 11.51$. Alternatively, we can calculate pOH and subtract from 14.00 using the logarithmic form of the K_w equation. For $[OH^-] = 0.0032\ M$,

$$\text{pOH} = -\log(3.2 \times 10^{-3}) = 2.49$$
$$\text{pH} = 14.00 - 2.49 = 11.51$$

Since the given OH^- concentration included two significant figures, the final pH includes two significant figures beyond the decimal point.

BALLPARK CHECK The calculated pH is consistent with our estimate.

CHEMISTRY IN ACTION

Acid Rain

As the water that evaporates from oceans and lakes condenses into raindrops, it dissolves small quantities of gases from the atmosphere. Under normal conditions, rain is slightly acidic, with a pH close to 5.6, because of atmospheric CO_2 that dissolves to form carbonic acid:

$$CO_2(aq) + H_2O(l) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons HCO_3^-(aq) + H_3O^+(aq)$$

In recent decades, however, the acidity of rainwater in many industrialized areas of the world has increased by a factor of over 100, to a pH between 3 and 3.5.

The primary cause of this so-called *acid rain* is industrial and automotive pollution. Each year, large power plants and smelters pour millions of tons of sulfur dioxide (SO_2) gas into the atmosphere, where some is oxidized by air to produce sulfur trioxide (SO_3). Sulfur oxides then dissolve in rain to form dilute sulfurous acid (H_2SO_3) and sulfuric acid (H_2SO_4):

$$SO_2(g) + H_2O(l) \longrightarrow H_2SO_3(aq)$$
$$SO_3(g) + H_2O(l) \longrightarrow H_2SO_4(aq)$$

Nitrogen oxides produced by the high-temperature reaction of N_2 with O_2 in coal-burning plants and in automobile engines further contribute to the problem. Nitrogen dioxide (NO_2) dissolves in water to form dilute nitric acid (HNO_3) and nitric oxide (NO):

$$3\,NO_2(g) + H_2O(l) \longrightarrow 2\,HNO_3(aq) + NO(g)$$

Oxides of both sulfur and nitrogen have always been present in the atmosphere, produced by such natural sources as volcanoes and lightning bolts, but their amounts have increased dramatically over the last century because of industrialization. The result is a notable decrease in the pH of rainwater in more densely populated regions, including Europe and the eastern United States.

Many processes in nature require such a fine pH balance that they are dramatically upset by the shift that has occurred in the pH of rain. Some watersheds contain soils that have the ability to neutralize acidic compounds in acid rain. Other areas, such as the northeastern United States and eastern Canada, where neutralizing capacity is poor, have experienced negative ecological effects. Acid rain releases aluminum salts from soil, and the ions then wash into streams. The low pH and increased aluminum levels are so toxic to fish and other organisms that many lakes and streams in these areas are devoid of aquatic life. Massive tree die-offs have occurred throughout central and eastern Europe as acid rain has lowered the pH of the soil and has leached nutrients from leaves.

▲ This limestone statue adorning the Rheims Cathedral in France has been severely eroded by acid rain.

Fortunately, acidic emissions in the United States have been greatly reduced in recent years as a result of the Clean Air Act Amendments of 1990, and cap-and-trade programs such as the Clean Air Interstate Rule (CAIR) and the Acid Rain

PROBLEM 10.15

Identify the following solutions as acidic or basic, estimate $[H_3O^+]$ and $[OH^-]$ values for each, and rank them in order of increasing acidity:

(a) Saliva, pH = 6.5
(b) Pancreatic juice, pH = 7.9
(c) Orange juice, pH = 3.7
(d) Wine, pH = 3.5

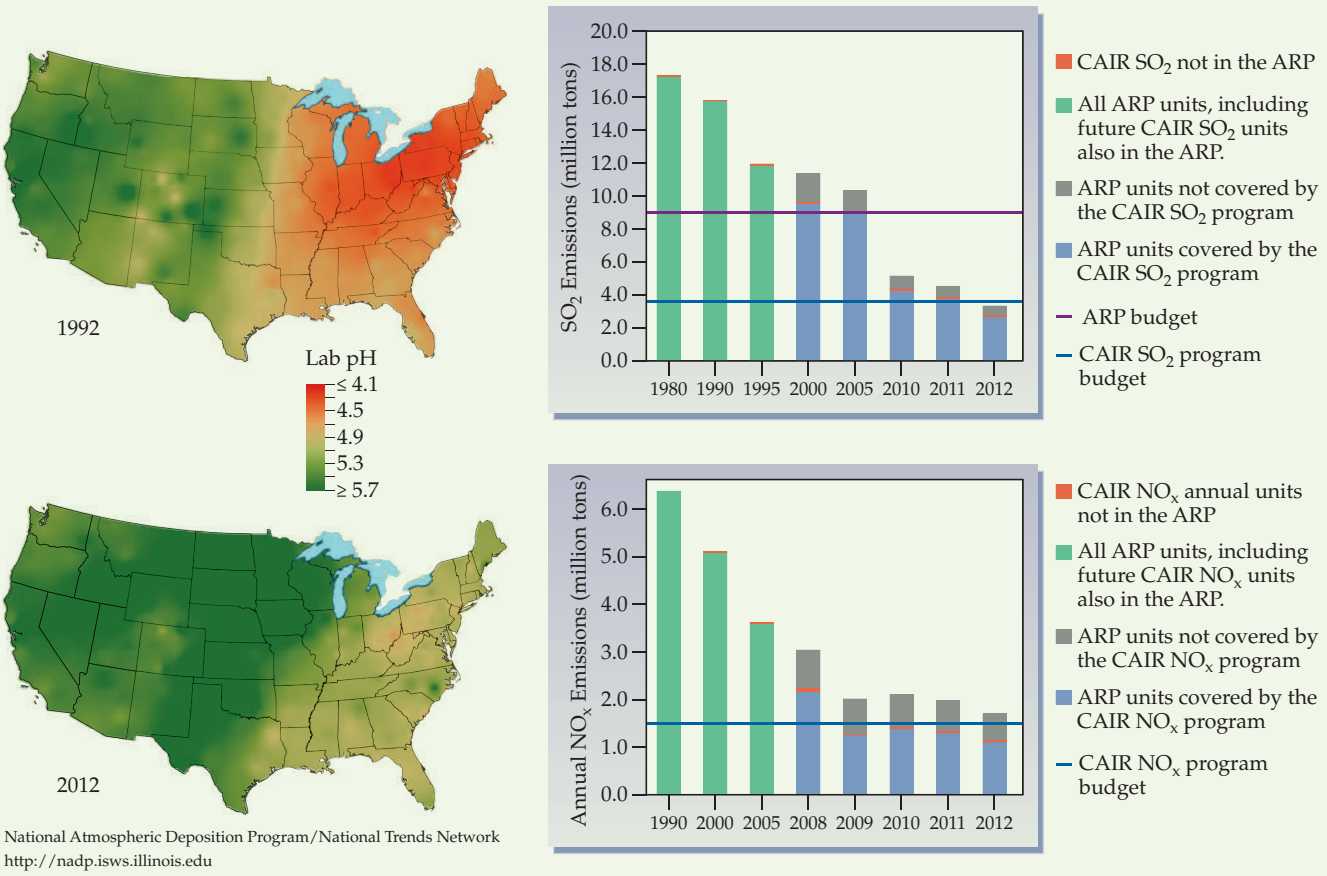
PROBLEM 10.16

Calculate the pH of the following solutions and report it to the correct number of significant figures:

(a) Seawater with $[H_3O^+] = 5.3 \times 10^{-9}\,M$
(b) A urine sample with $[H_3O^+] = 8.9 \times 10^{-6}\,M$

PROBLEM 10.17

What is the pH of a 0.0025 *M* solution of HCl?



▲ As illustrated on the pH maps (left side of figure), the decreased incidence of acid rain from 1992 to 2012 strongly correlates with decreases in SO_2 and NO_2 emissions over this same time frame (right side of figure).

Program (ARP) designed to reduce SO_2 and NO_x emissions from power plants. Emissions of SO_2 from participating industries decreased from 9.8 million tons in 2005 to 2.8 million tons in 2012, a decrease of 68%. Emissions of NO_x decreased by 53% over the same period. While these legislative actions have resulted in significant reductions in the United States, acid rain is a growing concern in many newly industrialized nations, including China and India.

CIA Problem 10.4 Rain typically has a pH of about 5.6. What is the H_3O^+ concentration in rain?

CIA Problem 10.5 Acid rain with a pH as low as 1.5 has been recorded in West Virginia.

(a) What is the H_3O^+ concentration in this acid rain?
(b) How many grams of HNO_3 must be dissolved to make 25 L of solution that has a pH of 1.5?

10.7 Acid and Base Equivalents

Learning Objective:

- Define normality (i.e., equivalent ion concentrations) for acids and bases, and the relationship between units of normality and molarity.

We said in Section 9.10 that it is sometimes useful to think in terms of ion *equivalents* (Eq) when we are primarily interested in an ion itself rather than the compound that produced the ion. For similar reasons, it can also be useful to consider acid or base equivalents.

When dealing with ions, the property of interest was the charge on the ion. Therefore, 1 Eq of an ion was defined as the number of ions that carry 1 mol of charge. For acids and bases, the property of interest is the number of H^+ ions (for an acid) or the number of OH^- ions (for a base) per formula unit. Thus, 1 **equivalent of acid** contains 1 mol of H^+ ions, and 1 **equivalent of base** contains 1 mol of OH^- ions.

Equivalent of acid Amount of an acid that contains 1 mole of H^+ ions.

Equivalent of base Amount of base that contains 1 mole of OH^- ions.

Using acid-base equivalents has a practical advantage when only the acidity or basicity of a solution is of interest rather than the identity of the acid or base. *One equivalent of any acid neutralizes one equivalent of any base.* Because acid-base equivalents are so useful, clinical chemists sometimes express acid and base concentrations in *normality* rather than molarity. The **normality (N)** of an acid or base solution is defined as the number of equivalents (or milliequivalents) of acid or base per liter of solution. For example, a solution made by dissolving 49.0 g of H_2SO_4 (or 0.50 mol) in water to give 1.0 L of solution has a concentration of 1.0 Eq/L, which is 1.0 N. Similarly, a solution that contains 0.010 Eq/L of acid is 0.010 N and has an acid concentration of 10 mEq/L:

Normality (N) A measure of acid (or base) concentration expressed as the number of acid (or base) equivalents per liter of solution.

$$\text{Normality (N)} = \frac{\text{Equivalents of acid or base}}{\text{Liters of solution}}$$

The values of molarity *(M)* and normality (N) are the same for monoprotic acids, such as HCl, but are not the same for diprotic or triprotic acids. For any acid or base, normality is always equal to molarity times the number of H^+ or OH^- ions produced per formula unit:

$$\text{Normality of acid} = (\text{Molarity of acid}) \times (\text{Number of } H^+ \text{ ions produced per formula unit})$$
$$\text{Normality of base} = (\text{Molarity of base}) \times (\text{Number of } OH^- \text{ ions produced per formula unit})$$

Worked Example 10.12 Equivalents: Mass to Equivalent Conversion for Diprotic Acid

How many equivalents are in 3.1 g of the diprotic acid H_2S? The molar mass of H_2S is 34.0 g.

ANALYSIS The number of acid or base equivalents is calculated by doing a gram to mole conversion using molar mass as the conversion factor and then multiplying by the number of H^+ ions produced.

BALLPARK ESTIMATE The 3.1 g is a little less than 0.10 mol of H_2S. Since it is a diprotic acid, (two H^+ per mole), this represents a little less than 0.2 Eq of H_2S.

SOLUTION

$$(3.1 \text{ g } \cancel{H_2S})\left(\frac{1 \text{ } \cancel{\text{mol } H_2S}}{34.0 \text{ g } \cancel{H_2S}}\right)\left(\frac{2 \text{ Eq } H_2S}{1 \text{ } \cancel{\text{mol } H_2S}}\right) = 0.18 \text{ Eq } H_2S$$

BALLPARK CHECK The calculated value of 0.18 is consistent with our prediction of a little less than 0.2 Eq of H_2S.

Worked Example 10.13 Equivalents: Calculating Equivalent Concentrations

What is the normality of a solution made by diluting 6.5 g of H_2SO_4 to a volume of 200 mL? What is the concentration of this solution in milliequivalents per liter? The molar mass of H_2SO_4 is 98.0 g.

ANALYSIS Calculate how many equivalents of H_2SO_4 are in 6.5 g by using the molar mass of the acid as a conversion factor and then determine the normality of the acid.

SOLUTION

STEP 1: Identify known information. We know the molar mass of H_2SO_4, the mass of H_2SO_4 to be dissolved, and the final volume of solution.

Molar mass of $H_2SO_4 = 98.0\ g/mol$
Mass of $H_2SO_4 = 6.5\ g$
Volume of solution $= 200\ mL$

STEP 2: Identify answer including units. We need to calculate the normality of the final solution.

$$\text{Normality} = \text{??}\ (\text{equiv.}/\text{L})$$

STEP 3: Identify conversion factors. We will need to convert the mass of H_2SO_4 to moles, and then to equivalents of H_2SO_4 . We will then need to convert volume from mL to L.

$$(6.5\ \text{g}\ \cancel{H_2SO_4})\left(\frac{1\ \text{mol}\ \cancel{H_2SO_4}}{98.0\ \text{g}\ \cancel{H_2SO_4}}\right)\left(\frac{2\ \text{Eq}\ H_2SO_4}{1\ \text{mol}\ \cancel{H_2SO_4}}\right)$$
$$= 0.132\ \text{Eq}\ H_2SO_4\ \text{(Don't round yet!)}$$
$$(200\ \cancel{\text{mL}})\left(\frac{1\ \text{L}}{1000\ \cancel{\text{mL}}}\right) = 0.200\ \text{L}$$

STEP 4: Solve. Dividing the number of equivalents by the volume yields the normality.

$$\frac{0.132\ \text{Eq}\ H_2SO_4}{0.200\ \text{L}} = 0.66\ \text{N}$$

The concentration of the sulfuric acid solution is 0.66 N, or 660 mEq/L.

PROBLEM 10.18

How many equivalents are in the following?

(a) 5.0 g HNO_3 **(b)** 12.5 g $Ca(OH)_2$ **(c)** 4.5 g H_3PO_4

PROBLEM 10.19

What are the normalities of the solutions if each sample in Problem 10.18 is dissolved in water and diluted to a volume of 300.0 mL?

10.8 Some Common Acid-Base Reactions

Learning Objective:

- Write balanced chemical equations for the common reactions of acids and bases.

Among the most common Brønsted–Lowry acid-base reactions are those of an acid with hydroxide ion, an acid with hydrogen carbonate or carbonate ion, and an acid with ammonia or a related nitrogen-containing compound. Let us look briefly at each of the three types.

Reaction of Acids with Hydroxide Ion

One equivalent of an acid reacts with 1 Eq of a metal hydroxide to yield water and a salt in a neutralization reaction:

$$\underset{\text{(acid)}}{HCl(aq)} + \underset{\text{(base)}}{KOH(aq)} \longrightarrow \underset{\text{(water)}}{H_2O(l)} + \underset{\text{(salt)}}{KCl(aq)}$$

In Section 5.4, we discussed neutralization reactions, and noted that the products were water, and a salt—an ionic compound formed from reaction of an acid with a base.

Such reactions are usually written with a single arrow because their equilibria lie far to the right and they have very large equilibrium constants ($K = 5 \times 10^{15}$; Section 7.8). The net ionic equation (Section 5.7) for all such reactions makes clear why acid-base equivalents are useful and why the properties of the acid and base disappear in neutralization reactions: The equivalent ions for the acid (H^+) and the base (OH^-) are used up in the formation of water.

$$H^+(aq) + OH^-(aq) \longrightarrow H_2O(l)$$

PROBLEM 10.20

Maalox, an over-the-counter antacid, contains aluminum hydroxide, $Al(OH)_3$, and magnesium hydroxide, $Mg(OH)_2$. Write balanced equations for the reaction of both with stomach acid (HCl).

Reaction of Acids with Hydrogen Carbonate and Carbonate Ion

Hydrogen carbonate ion reacts with acid by accepting H^+ to yield carbonic acid, H_2CO_3. Similarly, carbonate ion accepts two protons in its reaction with acid. Carbonic acid is unstable, however, rapidly decomposing to carbon dioxide gas and water:

$$H^+(aq) + HCO_3^-(aq) \longrightarrow [H_2CO_3(aq)] \longrightarrow H_2O(l) + CO_2(g)$$
$$2\,H^+(aq) + CO_3^{2-}(aq) \longrightarrow [H_2CO_3(aq)] \longrightarrow H_2O(l) + CO_2(g)$$

▲ **Figure 10.4**
Marble.
Marble, which is primarily $CaCO_3$, releases bubbles of CO_2 when treated with hydrochloric acid.

Most metal carbonates are insoluble in water—marble, for example, is almost pure calcium carbonate, $CaCO_3$ —but they nevertheless react easily with aqueous acid. In fact, geologists often test for carbonate-bearing rocks by putting a few drops of aqueous HCl on the rock and watching to see if bubbles of CO_2 form (Figure 10.4). This reaction is also responsible for the damage to marble and limestone artwork caused by acid rain (see the Chemistry in Action "Acid Rain" on p. 342). The most common application involving carbonates and acid, however, is the use of antacids that contain carbonates, such as TUMS or Rolaids, to neutralize excess stomach acid.

PROBLEM 10.21

Write a balanced equation for each of the following reactions:

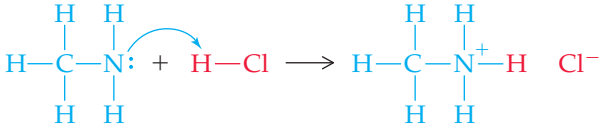
(a) $HCO_3^-(aq) + H_2SO_4(aq) \longrightarrow ?$ **(b)** $CO_3^{2-}(aq) + HNO_3(aq) \longrightarrow ?$

Reaction of Acids with Nitrogen-Containing Compounds

Acids react with ammonia to yield ammonium salts, such as ammonium chloride, NH_4Cl, most of which are water-soluble:

$$NH_3(aq) + HCl(aq) \longrightarrow NH_4Cl(aq)$$

Living organisms contain a group of compounds called *amines,* which contain nitrogen atoms bonded to carbon. Amines react with acids just as ammonia does, yielding water-soluble salts. Methanamine, for example, an organic compound found in rotting fish, reacts with HCl:



Methanamine Methylammonium chloride

LOOKING AHEAD In Chapter 16, we will see that amines occur in all living organisms, both plant and animal, as well as in many pharmaceutical agents. Amines called amino acids form the building blocks from which proteins are made, as we will see in Chapter 18.

PROBLEM 10.22

What products would you expect from the reaction of ammonia and sulfuric acid in aqueous solution?

$$2\,NH_3(aq) + H_2SO_4(aq) \longrightarrow ?$$

PROBLEM 10.23

Show how ethanamine ($C_2H_5NH_2$) reacts with hydrochloric acid to form an ethylammonium salt.

HANDS-ON CHEMISTRY 10.1

Assemble the following materials: vinegar (a 5% solution of acetic acid), baking soda (sodium hydrogen carbonate), a tall glass, a candle, and matches. Note: if you do not have baking soda, some antacid tablets containing calcium or magnesium carbonate will serve the same purpose.

1. Light the candle and place it on a clean, uncluttered surface.
2. Pour about ¼ cup of vinegar into the tall glass.
3. Slowly add about a tablespoon of baking soda, a little at a time. What do you observe? Try to avoid having the reaction solution bubble up higher than half the height of the glass. Based on the reactions discussed in this section, identify the gas that was produced in this reaction.
4. Now pick up the glass and position it about 15 cm above the candle flame. Tilt the glass so that the gas that has collected in the glass can flow out onto the candle flame. (Be careful not to allow any solution to pour from the glass.) What happens to the flame? How does this confirm the identity of the gas produced in the reaction?

10.9 Acidity and Basicity of Salt Solutions

Learning Objective:

- Predict whether a salt solution will be acidic, basic, or neutral.

It is tempting to think of all salt solutions as neutral; after all, they come from the neutralization reaction between an acid and a base. In fact, salt solutions can be neutral, acidic, or basic, depending on the ions present, because some ions react with water to produce H_3O^+ and some ions react with water to produce OH^-. To predict the acidity of a salt solution, it is convenient to classify salts according to the acid and base from which they are formed in a neutralization reaction. The classification and some examples are given in Table 10.4.

Table 10.4 Acidity and Basicity of Salt Solutions

Anion Derived from Acid That Is:	Cation Derived from Base That Is:	Solution	Example
Strong	Weak	Acidic	NH_4Cl, NH_4NO_3
Weak	Strong	Basic	$NaHCO_3$, KCH_3CO_2
Strong	Strong	Neutral	NaCl, KBr, $Ca(NO_3)_2$
Weak	Weak	More information needed	

The general rule for predicting the acidity or basicity of a salt solution is that the stronger partner from which the salt is formed dominates. That is, a salt formed from a strong acid and a weak base yields an acidic solution because the strong acid dominates; a salt formed from a weak acid and a strong base yields a basic solution because the base dominates; and a salt formed from a strong acid and a strong base yields a neutral solution because neither acid nor base dominates. Here are some examples.

Salt of Strong Acid + Weak Base ⟶ Acidic Solution

A salt such as NH_4Cl, which can be formed by reaction of a strong acid (HCl) with a weak base (NH_3), yields an acidic solution. The Cl^- ion does not react with water, but the NH_4^+ ion is a weak acid that gives H_3O^+ ions:

$$NH_4^+(aq) + H_2O(l) \rightleftharpoons NH_3(aq) + H_3O^+(aq)$$

Salt of Weak Acid + Strong Base ⟶ Basic Solution

A salt such as sodium hydrogen carbonate, which can be formed by reaction of a weak acid (H_2CO_3) with a strong base (NaOH), yields a basic solution. The Na^+ ion does not react with water, but the HCO_3^- ion is a weak base that gives OH^- ions:

$$HCO_3^-(aq) + H_2O(l) \rightleftharpoons H_2CO_3(aq) + OH^-(aq)$$

Salt of Strong Acid + Strong Base ⟶ Neutral Solution

A salt such as NaCl, which can be formed by reaction of a strong acid (HCl) with a strong base (NaOH), yields a neutral solution. Neither the Cl^- ion nor the Na^+ ion reacts with water.

Salt of Weak Acid + Weak Base

Both cation and anion in this type of salt react with water, so we cannot predict whether the resulting solution will be acidic or basic without quantitative information. The ion that reacts to the greater extent with water will govern the pH—it may be either the cation or the anion.

Worked Example 10.14 Acidity and Basicity of Salt Solutions

Predict whether the following salts produce an acidic, basic, or neutral solution:

(a) $BaCl_2$ **(b)** NaCN **(c)** NH_4NO_3

ANALYSIS Look in Table 10.2 to see the classification of acids and bases as strong or weak.

SOLUTION

(a) $BaCl_2$ gives a neutral solution because it is formed from a strong acid (HCl) and a strong base [$Ba(OH)_2$].

(b) NaCN gives a basic solution because it is formed from a weak acid (HCN) and a strong base (NaOH).

(c) NH_4NO_3 gives an acidic solution because it is formed from a strong acid (HNO_3) and a weak base (NH_3).

PROBLEM 10.24

Predict whether the following salts produce an acidic, basic, or neutral solution:

(a) K_2SO_4 **(b)** Na_2HPO_4 **(c)** MgF_2 **(d)** NH_4Br

10.10 Buffer Solutions

Learning Objective:

- Identify a buffer, and calculate the pH of a buffer solution.

Buffer A combination of substances that act together to prevent a drastic change in pH; usually a weak acid and its conjugate base.

Much of the body's chemistry depends on maintaining the pH of blood and other fluids within narrow limits. This is accomplished through the use of **buffers**—combinations of substances that act together to prevent a drastic change in pH.

Most buffers are mixtures of a weak acid and a roughly equal concentration of its conjugate base—for example, a solution that contains 0.10 *M* acetic acid and 0.10 *M* acetate ion. If a small amount of OH^- is added to a buffer solution, the pH increases, but not by much because the acid component of the buffer neutralizes the added OH^-. If a small amount of H_3O^+ is added to a buffer solution, the pH decreases, but again not by much because the conjugate base component of the buffer neutralizes the added H_3O^+.

To see why buffer solutions work, look at the equation for the acid dissociation constant of an acid HA.

$$\text{For the reaction: } HA(aq) + H_2O(l) \rightleftharpoons A^-(aq) + H_3O^+(aq)$$

$$\text{we have } \qquad K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

Rearranging this equation shows that the value of $[H_3O^+]$, and thus the pH, depends on the ratio of the undissociated acid concentration to the conjugate base concentration, $[HA]/[A^-]$:

$$[H_3O^+] = K_a\frac{[HA]}{[A^-]}$$

In the case of the acetic acid–acetate ion buffer, for instance, we have

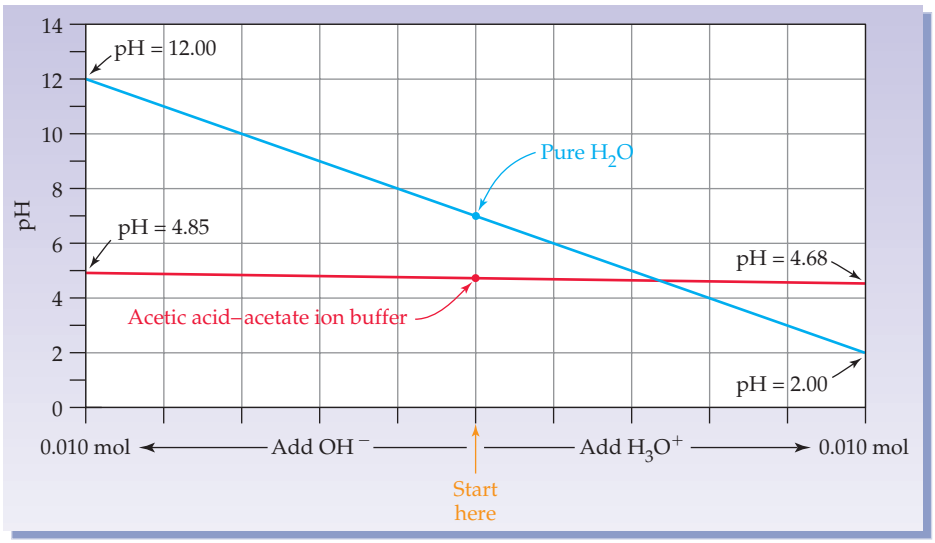
$$\underset{(0.10\,M)}{CH_3CO_2H(aq)} + H_2O(l) \rightleftharpoons H_3O^+(aq) + \underset{(0.10\,M)}{CH_3CO_2^-(aq)}$$

$$\text{and} \quad [H_3O^+] = K_a\frac{[CH_3CO_2H]}{[CH_3CO_2^-]}$$

Initially, the pH of the 0.10 *M* acetic acid–0.10 *M* acetate ion buffer solution is 4.74. When acid is added, most will be removed by reaction with $CH_3CO_2^-$. The equilibrium reaction shifts to the left, and as a result the concentration of CH_3CO_2H increases and the concentration of $CH_3CO_2^-$ decreases. As long as the changes in $[CH_3CO_2H]$ and $[CH_3CO_2^-]$ are relatively small, however, the ratio of $[CH_3CO_2H]$ to $[CH_3CO_2^-]$ changes only slightly, and there is little change in the pH.

When base is added to the buffer, most will be removed by reaction with CH_3CO_2H. The equilibrium shifts to the right, and so the concentration of CH_3CO_2H decreases and the concentration of $CH_3CO_2^-$ increases. Here too, though, as long as the concentration changes are relatively small, there is little change in the pH.

The ability of a buffer solution to resist changes in pH when acid or base is added is illustrated in Figure 10.5. Addition of 0.010 mol of H_3O^+ to 1.0 L of pure water changes the pH from 7 to 2, and addition of 0.010 mol of OH^- changes the pH from 7 to 12. A similar addition of acid to 1.0 L of a 0.10 *M* acetic acid–0.10 *M* acetate ion buffer, however, changes the pH from only 4.74 to 4.68, and addition of base changes the pH from only 4.74 to 4.85.



◀ Figure 10.5
A comparison of the change in pH. When 0.010 mol of strong acid (H_3O^+) or 0.00 mol of strong base (OH^-) are added to 1.0 L of pure water with an initial pH of 7.00, the pH of the solution varies between 12.00 (basic) and 2.000 (acidic) as indicated by the blue line. When the same amounts of strong acid or base is added to a 0.10 *M* acetic acid buffer solution having an initial pH of 4.74, the pH of the solution varies only between 4.85 and 4.68 (red line).

As we did with K_w, we can convert the rearranged K_a equation to its logarithmic form to obtain

$$\text{pH} = \text{p}K_a - \log\left(\frac{[\text{HA}]}{[\text{A}^-]}\right)$$

$$\text{or} \quad \text{pH} = \text{p}K_a + \log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right)$$

Henderson–Hasselbalch equation The logarithmic form of the K_a equation for a weak acid, used in applications involving buffer solutions.

This expression is known as the **Henderson–Hasselbalch equation** and is very useful in buffer applications, particularly in biology and biochemistry. Examination of the Henderson–Hasselbalch equation provides useful insights into how to prepare a buffer and into the factors that affect the pH of a buffer solution.

The effective pH range of a buffer will depend on the $\text{p}K_a$ of the acid HA and on the relative concentrations of HA and conjugate base A^-. In general, the most effective buffers meet the following conditions:

- The $\text{p}K_a$ for the weak acid should be close to the desired pH of the buffer solution.
- The ratio of $[\text{HA}]$ to $[\text{A}^-]$ should be close to 1, so that neither additional acid nor additional base changes the pH of the solution dramatically.
- The molar amounts of HA and A^- in the buffer should be approximately 10 times greater than the molar amounts of either acid or base you expect to add so that the ratio $[\text{A}^-]/[\text{HA}]$ does not undergo a large change.

The pH of body fluids is maintained by three major buffer systems. Two of these buffers, the carbonic acid–hydrogen carbonate ($H_2CO_3 - HCO_3^-$) system and the dihydrogen phosphate–hydrogen phosphate ($H_2PO_4^- - HPO_4^{2-}$) system, depend on weak acid–conjugate base interactions exactly like those of the acetate buffer system described previously:

$$H_2CO_3(aq) + H_2O(l) \rightleftharpoons HCO_3^-(aq) + H_3O^+(aq) \qquad \text{p}K_a = 6.37$$

$$H_2PO_4^-(aq) + H_2O(l) \rightleftharpoons HPO_4^{2-}(aq) + H_3O^+(aq) \qquad \text{p}K_a = 7.21$$

In Chapter 29, we will see how the regulation of blood pH by the hydrogen carbonate buffer system is particularly important in preventing *acidosis* and *alkalosis*.

The third buffer system depends on the ability of proteins to act as either proton acceptors or proton donors at different pH values.

Worked Example 10.15 Buffers: Selecting a Weak Acid for a Buffer Solution

Which of the organic acids in Table 10.3 would be the most appropriate for preparing a pH 4.15 buffer solution?

ANALYSIS The pH of the buffer solution depends on the $\text{p}K_a$ of the weak acid. Remember that $\text{p}K_a = -\log(K_a)$.

SOLUTION

The K_a and $\text{p}K_a$ values for the four organic acids in Table 10.3 are tabulated below. The ascorbic acid ($\text{p}K_a = 4.10$) will produce a buffer solution closest to the desired pH of 4.15.

Organic Acid	K_a	$\text{p}K_a$
Formic acid (HCOOH)	1.8×10^{-4}	3.74
Acetic acid (CH_3COOH)	1.8×10^{-5}	4.74
Propanoic acid (CH_3CH_2COOH)	1.3×10^{-5}	4.89
Ascorbic acid (vitamin C)	7.9×10^{-5}	4.10

Worked Example 10.16 Buffers: Calculating the pH of a Buffer Solution

What is the pH of a buffer solution that contains 0.100 *M* HF and 0.120 *M* NaF? The K_a of HF is 3.5×10^{-4}, and so $pK_a = 3.46$.

ANALYSIS The Henderson–Hasselbalch equation can be used to calculate the pH of a buffer solution:

$$pH = pK_a + \log\left(\frac{[F^-]}{[HF]}\right).$$

BALLPARK ESTIMATE If the concentrations of F^- and HF were equal, the log term in our equation would be zero, and the pH of the solution would be equal to the pK_a for HF, which means pH = 3.46. However, since the concentration of the conjugate base ($[F^-] = 0.120\ M$) is slightly higher than the concentration of the conjugate acid ($[HF] = 0.100\ M$), then the pH of the buffer solution will be slightly higher (more basic) than the pK_a.

SOLUTION

$$pH = pK_a + \log\left(\frac{[F^-]}{[HF]}\right)$$

$$pH = 3.46 + \log\left(\frac{0.120}{0.100}\right) = 3.46 + 0.08 = 3.54$$

BALLPARK CHECK The calculated pH of 3.54 is consistent with the prediction that the final pH will be slightly higher than the pK_a of 3.46.

Worked Example 10.17 Buffers: Measuring the Effect of Added Base on pH

What is the pH of 1.00 L of the 0.100 *M* hydrofluoric acid–0.120 *M* fluoride ion buffer system described in Worked Example 10.16 after 0.020 mol of NaOH is added?

ANALYSIS Initially, the 0.100 *M* HF–0.120 *M* NaF buffer has pH = 3.54, as calculated in Worked Example 10.16. The added base will react with the acid as indicated in the neutralization reaction,

$$HF(aq) + OH^-(aq) \longrightarrow H_2O(l) + F^-(aq)$$

which means $[HF]$ decreases and $[F^-]$ increases. With the pK_a and the concentrations of HF and F^- known, pH can be calculated using the Henderson–Hasselbalch equation.

BALLPARK ESTIMATE After the neutralization reaction, there is more conjugate base (F^-) and less conjugate acid (HF), and so we expect the pH to increase slightly from the initial value of 3.54.

SOLUTION

When 0.020 mol of NaOH is added to 1.00 L of the buffer, the HF concentration *decreases* from 0.100 *M* to 0.080 *M* as a result of an acid–base reaction. At the same time, the F^- concentration *increases* from 0.120 *M* to 0.140 *M* because additional F^- is produced by the neutralization. Using these new values gives

$$pH = 3.46 + \log\left(\frac{0.140}{0.080}\right) = 3.46 + 0.24 = 3.70$$

The addition of 0.020 mol of base causes the pH of the buffer to rise only from 3.54 to 3.70.

BALLPARK CHECK The final pH, 3.70, is slightly more basic than the initial pH of 3.54, consistent with our prediction.

PROBLEM 10.25

What is the pH of 1.00 L of the 0.100 *M* hydrofluoric acid–0.120 *M* fluoride ion buffer system described in Worked Example 10.16 after 0.020 mol of HNO_3 is added?

PROBLEM 10.26

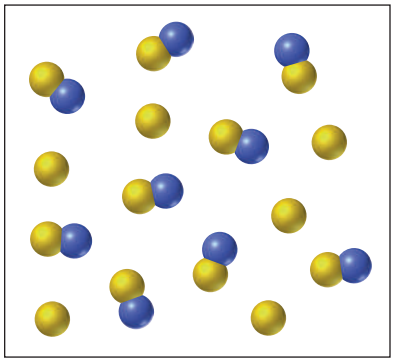
The ammonia/ammonium buffer system is sometimes used to optimize polymerase chain reactions (PCR) used in DNA studies. The equilibrium for this buffer can be written as

$$NH_4^+(aq) + H_2O(l) \rightleftharpoons H_3O^+(aq) + NH_3(aq)$$

Calculate the pH of a buffer that contains 0.050 M ammonium chloride and 0.080 M ammonia. The K_a of ammonium is 5.6×10^{-10}.

PROBLEM 10.27

What is the ratio of hydrogen carbonate ion to carbonic acid ($[HCO_3^-]/[H_2CO_3]$) in blood plasma that has a pH of 7.40? (see the Chemistry in Action "Buffers in the Body: Acidosis and Alkalosis" on p. 355).



= HCN = CN^-

KEY CONCEPT PROBLEM 10.28

A buffer solution is prepared using CN^- (from NaCN salt) and HCN in the amounts indicated in the margin. The K_a for HCN is 4.9×10^{-10}. Calculate the pH of the buffer solution.

10.11 Titration

Learning Objective:

- Use balanced neutralization reactions and titration data to determine the total acid or base concentration of a solution.

Titration A procedure for determining the total acid or base concentration of a solution.

Determining the pH of a solution gives the solution's H_3O^+ concentration but not necessarily its total acid concentration. That is because the two are not the same thing. The H_3O^+ concentration gives only the amount of acid that has dissociated into ions, whereas total acid concentration gives the sum of dissociated plus undissociated acid. In a 0.10 *M* solution of acetic acid, for instance, the total acid concentration is 0.10 *M*, yet the H_3O^+ concentration is only 0.0013 *M* (pH = 2.89) because acetic acid is a weak acid that is only about 1% dissociated.

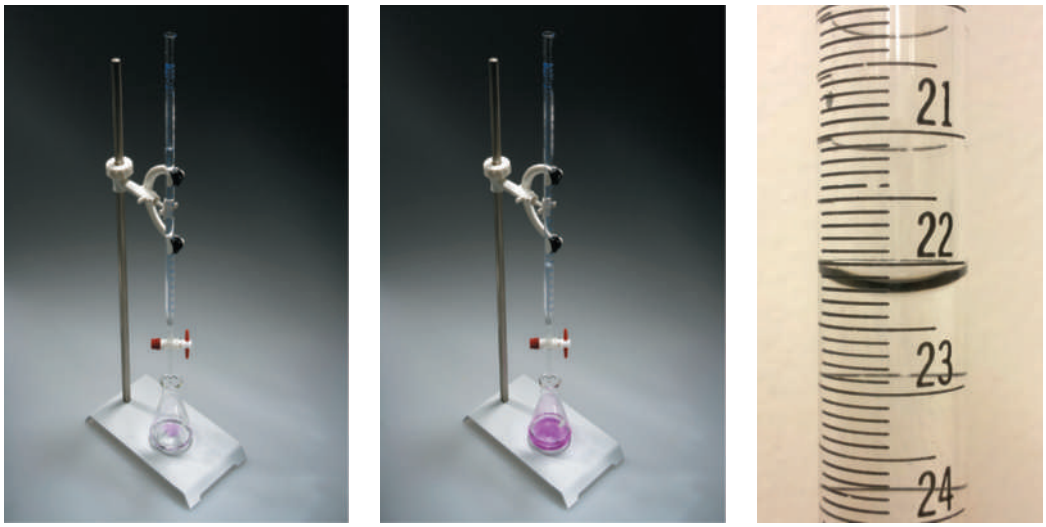
The total acid or base concentration of a solution can be found by carrying out a **titration** procedure, as shown in Figure 10.6. Let us assume, for instance, that we want to find the acid concentration of an HCl solution. (Likewise, we might need to find the base concentration of an NaOH solution.) We begin by measuring out a known volume of the HCl solution and adding an acid-base indicator. Next, we fill a calibrated glass tube called a *buret* with an NaOH solution of known concentration, and we slowly add the NaOH to the HCl until neutralization is complete (the *end point*), identified by a color change in the indicator.

Reading from the buret gives the volume of the NaOH solution that has reacted with the known volume of HCl. Knowing both the concentration and volume of the NaOH solution then allows us to calculate the molar amount of NaOH, and the coefficients in the balanced equation allow us to find the molar amount of HCl that has been neutralized. Dividing the molar amount of HCl by the volume of the HCl solution gives the concentration. The calculation thus involves mole–volume conversions just like those done in Section 9.6. Figure 10.7 shows a flow diagram of the strategy, and Worked Example 10.18 shows how to calculate total acid concentration.

When the titration involves a neutralization reaction in which one mole of acid reacts with one mole of base, such as that shown in Figure 10.7, then the moles of acid and base needed for complete reaction can be represented as

$$M_{acid} \times V_{acid} = M_{base} \times V_{base}$$

When the coefficients for the acid and base in the balanced neutralization reaction are not the same, such as in the reaction of a diprotic acid (H_2SO_4) with a monoprotic



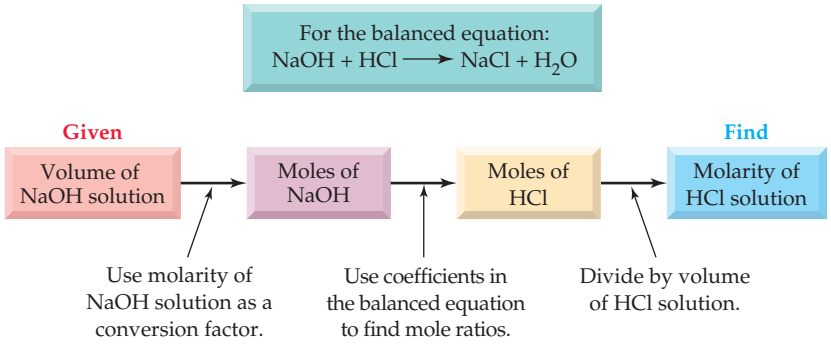
(a) (b) (c)

▲ **Figure 10.6**
Titration of an acid solution of unknown concentration with a base solution of known concentration.
(a) A measured volume of the acid solution is placed in the flask along with an indicator. (b) The base of known concentration is then added from a buret until the color change of the indicator shows that neutralization is complete (the *end point*). (c) Volume of base is calculated by difference, based on the initial and final volumes in the buret, measured at the meniscus.

base (NaOH), then we can use equivalents of acid and base instead of moles, and normality instead of molarity:

$$(\text{Eq})_{\text{acid}} = (\text{Eq})_{\text{base}}$$
$$N_{\text{acid}} \times V_{\text{acid}} = N_{\text{base}} \times V_{\text{base}}.$$

We can convert between normality and molarity as described in Section 10.7.



◀ **Figure 10.7**
A flow diagram for an acid-base titration.
This diagram summarizes the calculations needed to determine the concentration of an HCl solution by titration with an NaOH solution of known concentration. The steps are similar to those shown in Figure 9.7.

Worked Example 10.18 Titrations: Calculating Total Acid Concentration

When a 5.00 mL sample of household vinegar (dilute aqueous acetic acid) is titrated, 44.5 mL of 0.100 *M* NaOH solution is required to reach the end point. What is the acid concentration of the vinegar in moles per liter, equivalents per liter, and milliequivalents per liter? The neutralization reaction is

$$CH_3CO_2H(aq) + NaOH(aq) \longrightarrow CH_3CO_2^- Na^+(aq) + H_2O(l)$$

ANALYSIS To find the molarity of the vinegar, we need to know the number of moles of acetic acid dissolved in the 5.00 mL sample. Following a flow diagram similar to Figure 10.7, we use the volume and molarity of NaOH to find the number of moles. From the chemical equation, we use the mole ratio to find the number of moles of acid, and then divide by the volume of the acid solution. Because acetic acid is a monoprotic acid, the normality of the solution is numerically the same as its molarity.

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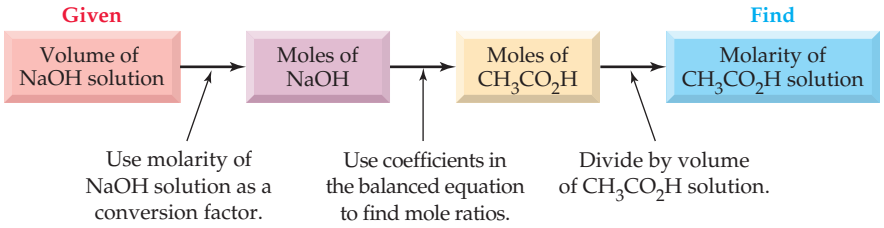


BALLPARK ESTIMATE The 5.00 mL of vinegar required nearly nine times as much NaOH solution (44.5 mL) for complete reaction. Since the neutralization stoichiometry is 1:1, the molarity of the acetic acid in the vinegar must be nine times greater than the molarity of NaOH, or approximately 0.90 *M*.

SOLUTION

Substitute the known information and appropriate conversion factors into the flow diagram, and solve for the molarity of the acetic acid:

$$(44.5 \text{ mL NaOH})\left(\frac{0.100 \text{ mol NaOH}}{1000 \text{ mL}}\right)\left(\frac{1 \text{ mol } CH_3CO_2H}{1 \text{ mol NaOH}}\right) \times \left(\frac{1}{0.00500 \text{ L}}\right) = 0.890 \text{ M } CH_3CO_2H$$

$$= 0.890 \text{ N } CH_3CO_2H$$

Expressed in milliequivalents, this concentration is

$$\frac{0.890 \text{ Eq}}{\text{L}} \times \frac{1000 \text{ m Eq}}{1 \text{ Eq}} = 890 \text{ m Eq/L}$$

BALLPARK CHECK The calculated result (0.890 *M*) is very close to our estimate of 0.90 *M*.

PROBLEM 10.29

A titration is carried out to determine the concentration of the acid in an old bottle of aqueous HCl whose label has become unreadable. What is the HCl concentration if 58.4 mL of 0.250 *M* NaOH is required to titrate a 20.0 mL sample of the acid?

PROBLEM 10.30

How many milliliters of 0.150 *M* NaOH are required to neutralize 50.0 mL of 0.200 M H_2SO_4? The balanced neutralization reaction is:

$$H_2SO_4(aq) + 2\,NaOH(aq) \longrightarrow Na_2SO_4(aq) + 2\,H_2O(l).$$

PROBLEM 10.31

A 21.5 mL sample of a KOH solution of unknown concentration requires 16.1 mL of 0.150 *M* H_2SO_4 solution to reach the end point in a titration.

(a) How many moles of H_2SO_4 were necessary to reach the end point? How many equivalents?

(b) What is the molarity of the KOH solution?

PROBLEM 10.32

Titration of a 50.00 mL sample of acid rain required 9.30 mL of 0.0012 *M* NaOH to reach the end point. What was the total $[H_3O^+]$ in the rain sample? What was the pH?

CHEMISTRY IN ACTION

Buffers in the Body: Acidosis and Alkalosis

Remember the diverse clinical cases introduced at the beginning of the chapter? All those individuals—the teenagers, the athlete, the diabetic patient, and the individuals taking aspirin or HIV medication—were all experiencing symptoms resulting from fluctuations in blood pH that produced clinical conditions known as *acidosis* ($pH < 7.35$) or *alkalosis* ($pH > 7.45$).

Each of the fluids in our bodies has a pH range suited to its function, as shown in the accompanying table. The stability of cell membranes, the shapes of huge protein molecules that must be folded in certain ways to function, and the activities of enzymes are all dependent on appropriate H_3O^+ concentrations. Blood plasma and the interstitial fluid surrounding cells, which together compose one-third of body fluids, have a slightly basic pH with a normal range of 7.35–7.45. The highly complex series of reactions and equilibria that take place throughout the body are very sensitive to pH—variations of even a few tenths of a pH unit can produce severe physiological symptoms.

pH of Body Fluids

Fluid	pH
Blood plasma	7.4
Interstitial fluid	7.4
Cytosol	7.0
Saliva	5.8–7.1
Gastric juice	1.6–1.8
Pancreatic juice	7.5–8.8
Intestinal juice	6.3–8.0
Urine	4.6–8.0
Sweat	4.0–6.8

Maintaining the pH of blood serum in its optimal range is accomplished by the carbonic acid–hydrogen carbonate buffer system (Section 10.10), which depends on the relative amounts of CO_2 and hydrogen carbonate dissolved in the blood. Because carbonic acid is unstable and therefore in equilibrium with CO_2 and water, there is an extra step in the hydrogen carbonate buffer mechanism:

$$CO_2(aq) + H_2O(l) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons HCO_3^-(aq) + H_3O^+(aq)$$

As a result, the hydrogen carbonate buffer system is intimately related to the elimination of CO_2, which is continuously produced in cells and transported to the lungs to be exhaled. Anything that significantly shifts the balance between dissolved CO_2 and HCO_3^- can upset these equilibria and raise or lower the pH. How does this happen, and how does the body compensate?

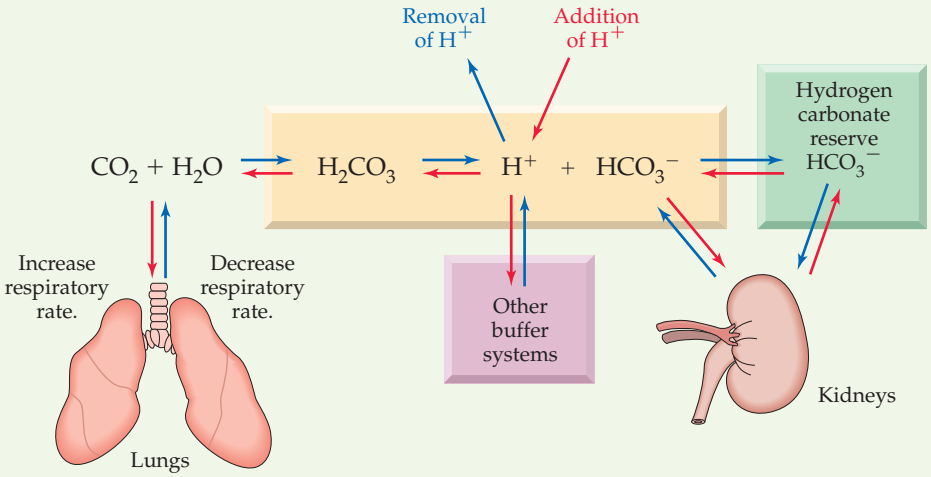
The relationships between the hydrogen carbonate buffer system, the lungs, and the kidneys are shown in the figure on the next page. Under normal circumstances, the reactions shown in the figure are in equilibrium. Addition of excess acid (red arrows) causes formation of H_2CO_3 and results in lowering of H_3O^+ concentration. Removal of acid (blue arrows) causes formation of more H_3O^+ by dissociation of H_2CO_3. The maintenance of pH by this mechanism is supported by a reserve of hydrogen carbonate ions in body fluids. Such a buffer can accommodate large additions of H_3O^+ before there is a significant change in the pH.

▲ Hyperventilation, the rapid breathing due to excitement or stress, removes CO_2 and increases blood pH resulting in respiratory alkalosis.

Additional backup to the hydrogen carbonate buffer system is provided by the kidneys. Each day a quantity of acid equal to that produced in the body is excreted in the urine. In the process, the kidney returns HCO_3^- to the extracellular fluids, where it becomes part of the hydrogen carbonate reserve.

Respiratory acidosis can be caused by a decrease in respiration, which leads to a buildup of excess CO_2 in the blood and a corresponding decrease in pH. This could be caused by a blocked air passage due to inhaled food—removal of the blockage restores normal breathing and a return to the optimal pH. *Metabolic acidosis* results from an excess of other acids in the blood that reduce the hydrogen carbonate concentration. High doses of aspirin (acetylsalicylic acid, Section 17.5), for example, increase the hydronium ion concentration and decrease the pH. Strenuous exercise generates excess lactate in the muscles, which is released into the bloodstream (Section 22.9). The liver converts lactate into glucose, which is the body's major source of energy; this process consumes hydrogen carbonate ions, which decreases the pH. Some HIV drug therapies can damage cellular mitochondria (Section 21.2), resulting in a buildup of lactic acid in the cells and bloodstream. In the case of a person with diabetes, lack of insulin causes the body to start burning fat, which generates ketones and keto acids (Chapter 15), organic compounds that lower the blood pH.

The body attempts to correct acidosis by increasing the rate and depth of respiration—breathing faster "blows off" CO_2, shifting the CO_2–hydrogen carbonate equilibrium to the left and



raising the pH. The net effect is rapid reversal of the acidosis. Although this may be sufficient for cases of respiratory acidosis, it provides only temporary relief for metabolic acidosis. A long-term solution depends on removal of excess acid by the kidneys, which can take several hours.

What about our teenage fans? In their excitement they have hyperventilated—their increased breathing rate has removed too much CO_2 from their blood and they are suffering from *respiratory alkalosis.* The body responds by "fainting" to decrease respiration and restore the CO_2 levels in the blood. When they regain consciousness, they will be ready to rock once again.

CIA Problem 10.6 Metabolic acidosis is often treated by administering hydrogen carbonate intravenously. Explain how this treatment can increase blood plasma pH.

CIA Problem 10.7 Which body fluid is most acidic? Which is most basic?

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Define the behavior of acids and bases in solution, and identify conjugate acid-base pairs.** According to the *Brønsted–Lowry definition,* an acid is a substance that donates a hydrogen ion (a proton, H^+) and a base is a substance that accepts a hydrogen ion. Thus, the generalized reaction of an acid with a base involves the reversible transfer of a proton: $B: + H{-}A \rightleftharpoons A:^- + H{-}B^+$. In aqueous solution, water acts as a base and accepts a proton from an acid to yield a *hydronium ion,* H_3O^+. Reaction of an acid with a metal hydroxide, such as KOH, yields water and a salt; reaction with hydrogen carbonate ion (HCO_3^-) or carbonate ion (CO_3^{2-}) yields water, a salt, and CO_2 gas; and reaction with ammonia yields an ammonium salt. The two substances that are related by the gain or loss of a proton in an acid-base reaction are called a *conjugate acid-base pair (see Problems 34–36, 39–41, 43, 46–49, 102, 106, 109, and 111).*

- **Identify substances as strong or weak acids or bases, and predict the direction of the proton transfer reaction based on the relative strength of the acids and bases involved.** Different acids and bases differ in their ability to give up or accept a proton. A *strong acid* gives up a proton easily and is 100% *dissociated* in aqueous solution; a *weak acid* gives up a proton with difficulty, is only slightly dissociated in water, and establishes an equilibrium between dissociated and undissociated forms. Similarly, a *strong base* accepts and holds a proton readily, whereas a *weak base* has a low affinity for a proton and establishes an equilibrium in aqueous solution. A proton-transfer reaction always takes place in the direction that favors formation of the weaker acid *(see Problems 34–36, 38–41, 44, and 45).*

- **Write the expression for the acid dissociation constant (K_a), and use the value of K_a as a predictor of acid strength.** The exact strength of an acid is defined by an *acid dissociation constant,* K_a: For the reaction $HA + H_2O \rightleftharpoons H_3O^+ + A^-$ we have $K_a = \dfrac{[H_3O^+][A^-]}{[HA]}$ *(see Problems 35, 50, 55, 56, 71, and 102).*

- **Use the ion product constant for water (K_w) to calculate the relative concentrations of H_3O^+ and OH^- ions in aqueous solution.** Water is *amphoteric;* that is, it can act as either an acid or a base. Water also dissociates slightly into H_3O^+ ions and OH^- ions; the product of whose concentrations in any aqueous solution is the *ion-product constant for water,* $K_w = [H_3O^+][OH^-] = 1.00 \times 10^{-14}$ at 25 °C (298 K) *(see Problems 51, 61, 62, and 64–66).*

- **Calculate the pH of a solution from the H_3O^+ or OH^- concentration, and use the pH scale as an indication of the relative acidity/basicity of a solution.** The acidity or basicity of an aqueous solution is given by its *pH,* defined as the negative logarithm of the hydronium ion concentration, $[H_3O^+]$. A pH below 7 means an acidic solution; a pH equal to 7 means a neutral solution; and a pH above 7 means a basic solution *(see Problems 52, 53, 61, 64, 98, 99, 102, and 108).*

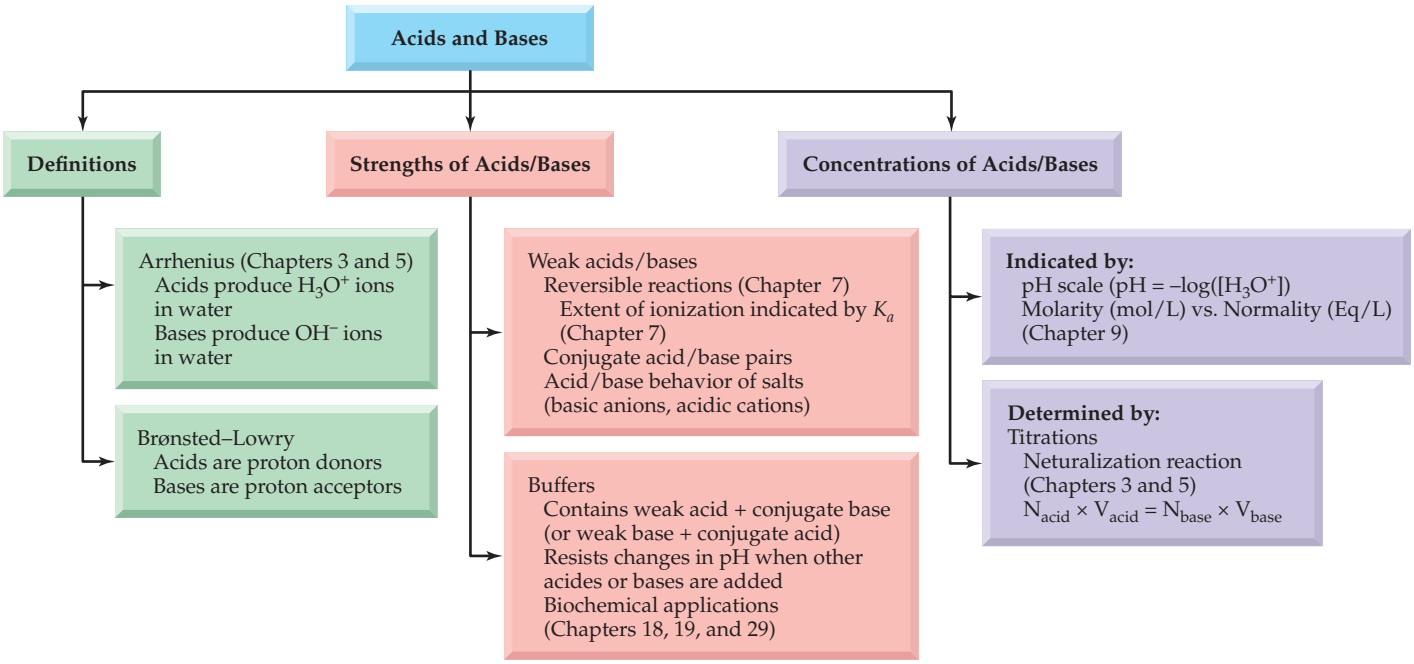
- **Calculate pH from $[H_3O^+]$ and $[OH^-]$, and calculate $[H_3O^+]$ from pH.** The pH of a solution is defined as $pH = -\log[H_3O^+]$. To determine hydronium ion concentration from a measured pH, the antilog function (or inverse log) would be used: $[H_3O^+] = 10^{-pH}$ *(see Problems 53, 54, 57–62, and 64–66).*

- **Define normality (i.e., equivalent ion concentrations) for acids and bases, and the relationship between units of normality and molarity.** Normality is a concentration unit defined as Eq./L. For acids, an equivalent is defined as the amount of acid that can produce one mole of H_3O^+ ions. For bases, an equivalent is defined as the amount of base that can produce one mole of OH^- ions. The relationship

between the two concentration units is Normality = Molarity × (Equiv. / mole) *(see Problems 33, 42, 82–95, and 104).*

- **Write balanced chemical equations for the common reactions of acids and bases.** Reactions between acids and bases typically involve direct reaction of the H_3O^+ and the OH^- ions to form water and a salt. However, acids can react with carbonate (CO_3^{2-}) compounds to form CO_2, and with NH_3 to form ammonium salts (see Section 10.8) *(see Problems 33, 36, 67–70, 79, 81, and 107–111).*
- **Predict whether a salt solution will be acidic, basic, or neutral.** The salt formed by the neutralization of a strong acid and strong base forms a neutral solution. The salt formed by the neutralization of a weak acid and a strong base forms a basic solution. The salt formed by the neutralization of a strong acid and a weak base forms an acidic solution *(see Problems 72, 73, 96, 97, and 111).*
- **Identify a buffer, and calculate the pH of a buffer solution.** The pH of a solution can be controlled through the use of a *buffer* that acts to remove either added H_3O^+ ions or added OH^- ions. Most buffer solutions consist of roughly equal amounts of a weak acid and its conjugate base. If the relative concentrations of the weak acid and its conjugate base are known, the pH can be calculated using the *Henderson–Hasselbalch equation* (see Section 10.10) *(see Problems 71, 74–81, 103, and 105).*
- **Use balanced neutralization reactions and titration data to determine the total acid or base concentration of a solution.** Acid (or base) concentrations are determined in the laboratory by *titration* of a solution of unknown concentration with a base (or acid) solution of known strength until an indicator signals that neutralization is complete *(see Problems 37, 86, 92–95, 101, 104, and 108).*

CONCEPT MAP: ACIDS AND BASES



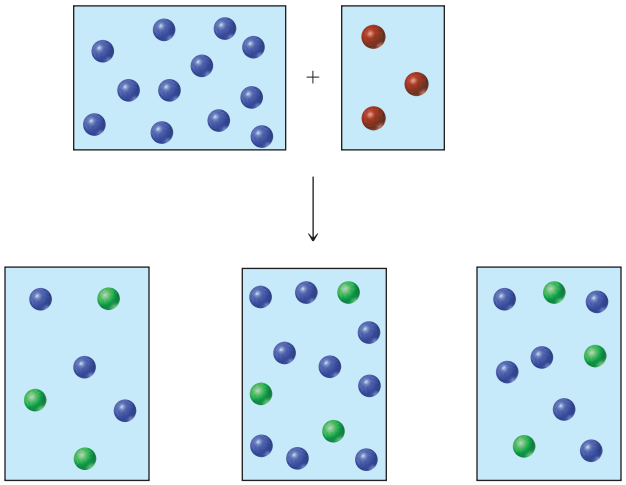
▲ **Figure 10.8 Concept Map.** Acids and bases play important roles in many chemical and biochemical processes, and many common substances are classified as acids or bases. Acid and base behavior is related to the ability to exchange protons, or to form H_3O^+ or OH^- ions, respectively, in water. Strong acids and bases ionize completely in aqueous solution, while weak acids/bases ionize only partially and establish an equilibrium with their conjugates. The relationship between these concepts and some of their practical and/or quantitative applications are illustrated in this concept map.

KEY WORDS

Acid dissociation constant (K_a), *p. 335*
Acid-base indicator, *p. 338*
Amphoteric, *p. 336*
Brønsted–Lowry acid, *p. 326*
Brønsted–Lowry base, *p. 326*
Buffer, *p. 348*
Conjugate acid, *p. 328*
Conjugate acid-base pair, *p. 328*
Conjugate base, *p. 328*
Dissociation, *p. 331*
Equivalent of acid, *p. 344*
Equivalent of base, *p. 344*
Henderson–Hasselbalch equation, *p. 350*
Hydronium ion, *p. 325*
Ion-product constant for water (K_w), *p. 336*
Normality (N), *p. 344*
p function, *p. 338*
pH, *p. 338*
Strong acid, *p. 330*
Strong base, *p. 331*
Titration, *p. 352*
Weak acid, *p. 331*
Weak base, *p. 331*

UNDERSTANDING KEY CONCEPTS

10.33 An aqueous solution of OH^-, represented as a blue sphere, is allowed to mix with a solution of an acid H_nA, represented as a red sphere. Three possible outcomes are depicted by boxes (1)–(3), where the green spheres represent A^{n-}, the anion of the acid:



(1) (2) (3)

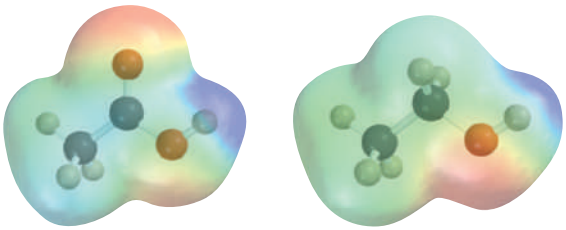
Which outcome corresponds to the following reactions?

(a) $HF + OH^- \longrightarrow H_2O + F^-$

(b) $H_2SO_3 + 2\ OH^- \longrightarrow 2\ H_2O + SO_3^{2-}$

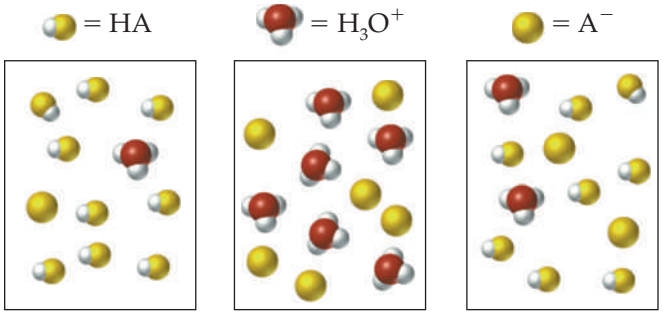
(c) $H_3PO_4 + 3\ OH^- \longrightarrow 3\ H_2O + PO_4^{3-}$

10.34 Electrostatic potential maps of acetic acid (CH_3CO_2H) and ethanol (CH_3CH_2OH) are shown. Identify the most acidic hydrogen in each, and tell which of the two is likely to be the stronger acid.



CH_3CO_2H CH_3CH_2OH

10.35 The following pictures represent aqueous acid solutions. Water molecules are not shown.



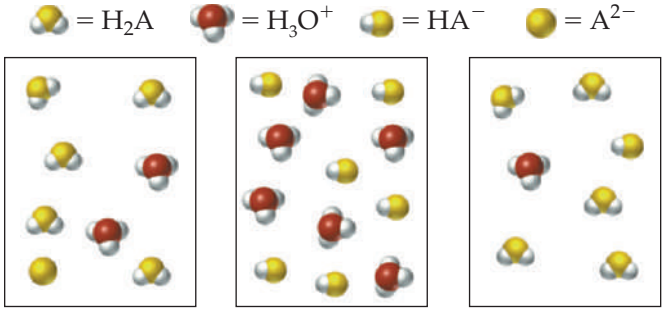
(1) (2) (3)

(a) Which picture represents the weakest acid?

(b) Which picture represents the strongest acid?

(c) Which picture represents the acid with the smallest value of K_a?

10.36 The following pictures represent aqueous solutions of a diprotic acid H_2A. Water molecules are not shown.

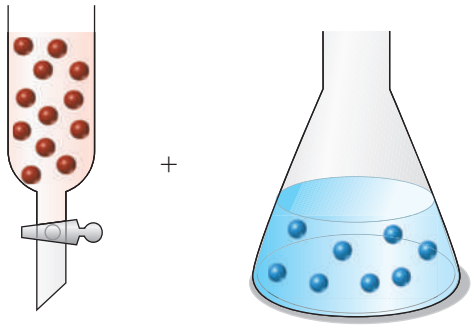


(1) (2) (3)

(a) Which picture represents a solution of a weak diprotic acid?

(b) Which picture represents an impossible situation?

10.37 Assume that the red spheres in the buret represent H_3O^+ ions, the blue spheres in the flask represent OH^- ions, and you are carrying out a titration of the base with the acid. If the volumes in the buret and the flask are identical and the concentration of the acid in the buret is 1.00 *M*, what is the concentration of the base in the flask?



ADDITIONAL PROBLEMS

ACIDS AND BASES (SECTIONS 10.1 AND 10.2)

10.38 What happens when a strong acid such as HBr is dissolved in water?

10.39 What happens when a weak acid such as CH_3CO_2H is dissolved in water?

10.40 What happens when a strong base such as KOH is dissolved in water?

10.41 What happens when a weak base such as NH_3 is dissolved in water?

10.42 What is the difference between a monoprotic acid and a diprotic acid? Give an example of each.

10.43 What is the difference between H^+ and H_3O^+?

10.44 Which of the following are strong acids? Look at Table 10.2 if necessary.

(a) $HClO_4$ **(b)** H_2CO_3 **(c)** H_3PO_4
(d) NH_4^+ **(e)** HI **(f)** $H_2PO_4^-$

10.45 Which of the following are weak bases? Look at Table 10.2 if necessary.

(a) NH_3 **(b)** $Ca(OH)_2$ **(c)** HPO_4^{2-}
(d) LiOH **(e)** CN^- **(f)** NH_2^-

10.46 Identify the following substances as a Brønsted–Lowry base, a Brønsted–Lowry acid, or neither:

(a) HCN **(b)** $CH_3CO_2^-$ **(c)** $AlCl_3$
(d) H_2CO_3 **(e)** Mg^{2+} **(f)** $CH_3NH_3^+$

10.47 Label the Brønsted–Lowry acids and bases in the following equations, and tell which substances are conjugate acid-base pairs.

(a) $CO_3^{2-}(aq) + HCl(aq) \longrightarrow HCO_3^-(aq) + Cl^-(aq)$

(b) $H_3PO_4(aq) + NH_3(aq) \longrightarrow H_2PO_4^-(aq) + NH_4^+(aq)$

(c) $NH_4^+(aq) + CN^-(aq) \rightleftharpoons NH_3(aq) + HCN(aq)$

(d) $HBr(aq) + OH^-(aq) \longrightarrow H_2O(l) + Br^-(aq)$

(e) $H_2PO_4^-(aq) + N_2H_4(aq) \rightleftharpoons HPO_4^{2-}(aq) + N_2H_5^+(aq)$

10.48 Write the formulas of the conjugate acids of the following Brønsted–Lowry bases:

(a) $ClCH_2CO_2^-$ **(b)** C_5H_5N
(c) SeO_4^{2-} **(d)** $(CH_3)_3N$

10.49 Write the formulas of the conjugate bases of the following Brønsted–Lowry acids:

(a) HCN **(b)** $(CH_3)_2NH_2^+$
(c) H_3PO_4 **(d)** $HSeO_3^-$

ACID AND BASE STRENGTH: K_a AND pH (SECTIONS 10.3–10.6)

10.50 How is K_a defined? Write the equation for K_a for the generalized acid HA.

10.51 How is K_w defined, and what is its numerical value at 25 °C (298 K)?

10.52 How is pH defined?

10.53 A solution of 0.10 *M* HCl has a pH = 1.00, whereas a solution of 0.10 *M* CH_3COOH has a pH = 2.88. Explain.

10.54 Calculate $[H_3O^+]$ for the 0.10 *M* CH_3COOH solution in Problem 10.53. What percent of the weak acid is dissociated?

10.55 Write the expressions for the acid dissociation constants for the three successive dissociations of phosphoric acid, H_3PO_4, in water.

10.56 Based on the K_a values in Table 10.3, rank the following solutions in order of increasing pH: 0.10 *M* HCOOH, 0.10 *M* HF, 0.10 *M* H_2CO_3, 0.10 *M* HSO_4^-, 0.10 *M* NH_4^+.

10.57 The electrode of a pH meter is placed in a sample of urine, and a reading of 7.9 is obtained. Is the sample acidic, basic, or neutral? What is the concentration of H_3O^+ in the urine sample?

10.58 A 0.10 *M* solution of the deadly poison hydrogen cyanide, HCN, has a pH of 5.2. Calculate the $[H_3O^+]$ of the solution. Is HCN a strong or a weak acid?

10.59 Human sweat can have a pH ranging from 4.0 to 6.8. Calculate the range of $[H_3O^+]$ in normal human sweat. How many orders of magnitude does this range represent?

10.60 Saliva has a pH range of 5.8–7.1. Approximately what is the H_3O^+ concentration range of saliva?

10.61 What is the approximate pH of a 0.02 *M* solution of a strong monoprotic acid? Of a 0.02 *M* solution of a strong base, such as KOH?

10.62 Calculate the pOH of each solution in Problems 10.57–10.61.

10.63 Without using a calculator, match the H_3O^+ concentrations of the following solutions, (a)–(d), to the corresponding pH, i–iv:

(a) Fresh egg white: $[H_3O^+] = 2.5 \times 10^{-8}\ M$

(b) Apple cider: $[H_3O^+] = 5.0 \times 10^{-4}\ M$

(c) Household ammonia: $[H_3O^+] = 2.3 \times 10^{-12}\ M$

(d) Vinegar (acetic acid): $[H_3O^+] = 4.0 \times 10^{-3}\ M$

i. pH = 3.30

ii. pH = 2.40

iii. pH = 11.64

iv. pH = 7.60

10.64 What are the OH^- concentration and pOH for each solution in Problem 10.63? Rank the solutions according to increasing acidity.

10.65 What are the H_3O^+ and OH^- concentrations of solutions that have the following pH values?

(a) pH 4 **(b)** pH 11 **(c)** pH 0
(d) pH 1.38 **(e)** pH 7.96

10.66 About 12% of the acid in a 0.10 *M* solution of a weak acid dissociates to form ions. What are the H_3O^+ and OH^- concentrations? What is the pH of the solution?

REACTIONS OF ACIDS AND BASES (SECTION 10.8)

10.67 The hydrogen-containing anions of many polyprotic acids are amphoteric. Write equations for HCO_3^- and $H_2PO_4^-$ acting as bases with the strong acid HCl and as acids with the strong base NaOH.

10.68 Write balanced equations for proton-transfer reactions between the listed pairs. Indicate the conjugate pairs, and determine the favored direction for each equilibrium.

(a) HCl and PO_4^{3-} **(b)** HCN and SO_4^{2-}

(c) $HClO_4$ and NO_2^- **(d)** CH_3O^- and HF

10.69 Sodium hydrogen carbonate ($NaHCO_3$), also known as baking soda, is a common home remedy for acid indigestion and is also used to neutralize acid spills in the laboratory. Write a balanced chemical equation for the reaction of sodium hydrogen carbonate with

(a) Gastric juice (HCl)

(b) Sulfuric acid (H_2SO_4)

10.70 Refer to Section 10.8 to write balanced equations for the following acid-base reactions:

(a) $LiOH + HNO_3 \longrightarrow$

(b) $BaCO_3 + HI \longrightarrow$

(c) $H_3PO_4 + KOH \longrightarrow$

(d) $Ca(HCO_3)_2 + HCl \longrightarrow$

(e) $Ba(OH)_2 + H_2SO_4 \longrightarrow$

(f) $NH_3 + HCl \longrightarrow$

10.71 Rearrange the equation you wrote in Problem 10.50 to solve for $[H_3O^+]$ in terms of K_a.

SALTS AND BUFFERS (SECTIONS 10.9 AND 10.10)

10.72 For each of the following salts, indicate if the solution would be acidic, basic or neutral.

(a) NH_4Cl **(b)** KBr

(c) Na_2CO_3 **(d)** $NaCH_3CO_2$

10.73 Which salt solutions in problem 10.72 could be used to prepare a buffer solution? In each case, indicate which acid or base must be added to create the buffer solution.

10.74 What are the two components of a buffer system? How does a buffer work to hold pH nearly constant?

10.75 Which system would you expect to be a better buffer: $HNO_3 + Na^+ NO_3^-$, or $CH_3CO_2H + CH_3CO_2^- Na^+$? Explain.

10.76 The pH of a buffer solution containing 0.10 *M* acetic acid and 0.10 *M* sodium acetate is 4.74.

(a) Write the Henderson–Hasselbalch equation for this buffer.

(b) Write the equations for reaction of this buffer with a small amount of HNO_3 and with a small amount of NaOH.

10.77 Which of the following buffer systems would you use if you wanted to prepare a solution having a pH of approximately 9.5?

(a) 0.08 *M* $H_2PO_4^-$/0.12 *M* HPO_4^{2-}

(b) 0.08 *M* NH_4^+/0.12 *M* NH_3

10.78 What is the pH of a buffer system that contains 0.200 *M* hydrocyanic acid (HCN) and 0.150 *M* sodium cyanide (NaCN)? The pK_a of hydrocyanic acid is 9.31.

10.79 Consider 1.00 L of the buffer system described in Problem 10.78.

(a) What are the $[HCN]$ and $[CN^-]$ after 0.020 mol of HCl is added? What is the pH?

(b) What are the $[HCN]$ and $[CN^-]$ after 0.020 mol of NaOH is added? What is the pH?

10.80 What is the pH of a buffer system that contains 0.15 *M* NH_4^+ and 0.10 *M* NH_3? The pK_a of NH_4^+ is 9.25.

10.81 How many moles of NaOH must be added to 1.00 L of the solution described in Problem 10.80 to increase the pH to 9.25? (Hint: What is the $[NH_3]/[NH_4^+]$ when the pH = pK_a?)

CONCENTRATIONS OF ACID AND BASE SOLUTIONS (SECTIONS 10.7 AND 10.11)

10.82 What does it mean when we talk about acid *equivalents* and base *equivalents*?

10.83 How does normality compare to molarity for monoprotic and polyprotic acids?

10.84 Identify the number of equivalents per mole for each of the following acids and bases.

(a) HNO_3 **(b)** H_3PO_4

(c) KOH **(d)** $Mg(OH)_2$

10.85 What mass of each of the acids and bases in Problem 10.84 is needed to prepare 500 mL of 0.15 N solution?

10.86 How many milliliters of 0.0050 N KOH are required to neutralize 25 mL of 0.0050 N H_2SO_4? To neutralize 25 mL of 0.0050 M H_2SO_4?

10.87 How many equivalents are in 75.0 mL of 0.12 *M* H_2SO_4 solution? In 75.0 mL of a 0.12 *M* H_3PO_4 solution?

10.88 How many equivalents of an acid or base are in the following?

(a) 0.25 mol $Mg(OH)_2$ **(b)** 2.5 g $Mg(OH)_2$

(c) 15 g CH_3CO_2H

10.89 What mass of citric acid (triprotic, $C_6H_5O_7H_3$) contains 152 mEq of citric acid?

10.90 What are the molarity and the normality of a solution made by dissolving 5.0 g of $Ca(OH)_2$ in enough water to make 500.0 mL of solution?

10.91 What are the molarity and the normality of a solution made by dissolving 25 g of citric acid (triprotic, $C_6H_5O_7H_3$) in enough water to make 800 mL of solution?

10.92 Titration of a 12.0 mL solution of HCl requires 22.4 mL of 0.12 *M* NaOH. What is the molarity of the HCl solution?

10.93 How many equivalents are in 15.0 mL of 0.12 *M* $Ba(OH)_2$ solution? What volume of 0.085 *M* HNO_3 is required to reach the end point when titrating 15.0 mL of this solution?

10.94 Titration of a 10.0 mL solution of NH_3 requires 15.0 mL of 0.0250 *M* H_2SO_4 solution. What is the molarity of the NH_3 solution?

10.95 If 35.0 mL of a 0.100 N acid solution is needed to reach the end point in titration of 21.5 mL of a base solution, what is the normality of the base solution?

10.96 For the titrations discussed in Problems 10.92 and 10.93, what is the pH of the solution at the equivalence point (acidic, basic, or neutral)? Explain.

10.97 For the titration discussed in Problem 10.94, what is the pH of the solution at the equivalence point (acidic, basic, or neutral)? Explain.

CONCEPTUAL PROBLEMS

10.98 A solution is prepared by bubbling 15.0 L of $HCl(g)$ at 25 °C (298 K) and 101,325 Pa into 250.0 mL of water.

(a) Assuming all the HCl dissolves in the water, how many moles of HCl are in solution?

(b) What is the pH of the solution?

10.99 The dissociation of water into H_3O^+ and OH^- ions depends on temperature. At 0 °C (273 K) the $[H_3O^+] = 3.38 \times 10^{-8}$ *M*, at 25 °C (298 K) the $[H_3O^+] = 1.00 \times 10^{-7}$ *M*, and at 50 °C (323 K) the $[H_3O^+] = 2.34 \times 10^{-7}$ *M*.

(a) Calculate the pH of water at 0 °C (273 K) and 50 °C (323 K).

(b) What is the value of K_w at 0 °C (273 K) and 50 °C (323 K)?

(c) Is the dissociation of water endothermic or exothermic?

10.100 The active ingredient in aspirin is acetylsalicylic acid (Molar mass = 180.2 g/mol). An aspirin tablet was dissolved in water and titrated with 0.100 *M* NaOH. If the titration required 13.87 mL of NaOH to reach the phenolphthalein endpoint, how many milligrams of acetylsalicylic acid were in the tablet?

10.101 How many milliliters of 0.50 *M* NaOH solution are required to titrate 40.0 mL of a 0.10 *M* H_2SO_4 solution to an end point?

10.102 Which solution contains more acid, 50 mL of a 0.20 N HCl solution or 50 mL of a 0.20 N acetic acid solution? Which has a higher hydronium ion concentration? Which has a lower pH?

10.103 One of the buffer systems used to control the pH of blood involves the equilibrium between $H_2PO_4^-$ and HPO_4^{2-}. The pK_a for $H_2PO_4^-$ is 7.21.

(a) Write the Henderson–Hasselbalch equation for this buffer system.

(b) What HPO_4^{2-} to $H_2PO_4^-$ ratio is needed to maintain the optimum blood pH of 7.40?

10.104 A 0.15 M solution of HCl is used to titrate 30.0 mL of a $Ca(OH)_2$ solution of unknown concentration. If 140.0 mL of HCl is required, what is the normality of the $Ca(OH)_2$ solution? What is the molarity?

10.105 Which of the following combinations produces an effective buffer solution? Assuming equal concentrations of each acid and its conjugate base, calculate the pH of each buffer solution.

(a) NaF and HF

(b) $HClO_4$ and $NaClO_4$

(c) NH_4Cl and NH_3

(d) KBr and HBr

10.106 One method of analyzing ammonium salts is to treat them with NaOH and then heat the solution to remove the NH_3 gas formed.

$$NH_4^+(aq) + OH^-(aq) \longrightarrow NH_3(g) + H_2O(l)$$

(a) Label the Brønsted–Lowry acid-base pairs.

(b) If 2.86 L of NH_3 at 60 °C (333 K) and 10^5 Pa is produced by the reaction of NH_4Cl, how many grams of NH_4Cl were in the original sample?

10.107 One method of reducing acid rain is "scrubbing" the combustion products before they are emitted from power plant smoke stacks. The process involves addition of an aqueous suspension of lime (CaO) to the combustion chamber and stack, where the lime reacts with SO_2 to give calcium sulfite $(CaSO_3)$: $CaO(aq) + SO_2(g) \longrightarrow CaSO_3(aq)$

(a) How much lime (in grams) is needed to remove 1 mol of SO_2?

(b) How much lime (in kilograms) is needed to remove 1 kg of SO_2?

10.108 Sodium oxide, Na_2O, reacts with water to give NaOH.

(a) Write a balanced equation for the reaction.

(b) What is the pH of the solution prepared by allowing 1.55 g of Na_2O to react with 500.0 mL of water? Assume that there is no volume change.

(c) How many milliliters of 0.0100 *M* HCl are needed to neutralize the NaOH solution prepared in (b)?

GROUP PROBLEMS

10.109 Obtain a package of Alka-Seltzer, an antacid, from the local drug store:

(a) List the ingredients.

(b) Why does Alka-Seltzer foam and bubble when dissolved in water? Which ingredient is the antacid?

(c) Write the reaction responsible for the formation of bubbles, and the reaction responsible for the antacid activity.

10.110 Research the composition of "smelling salts"—a product that is used to rouse people who have lost consciousness.

(a) What are the primary components?

(b) What are the chemical reactions that generate the "active" component?

10.111 Many allergy medications contain antihistamines, compounds that contain amine groups (R-NH_2, where R refers to an organic functional group). Would you expect these compounds to be acidic, basic or neutral? Explain.

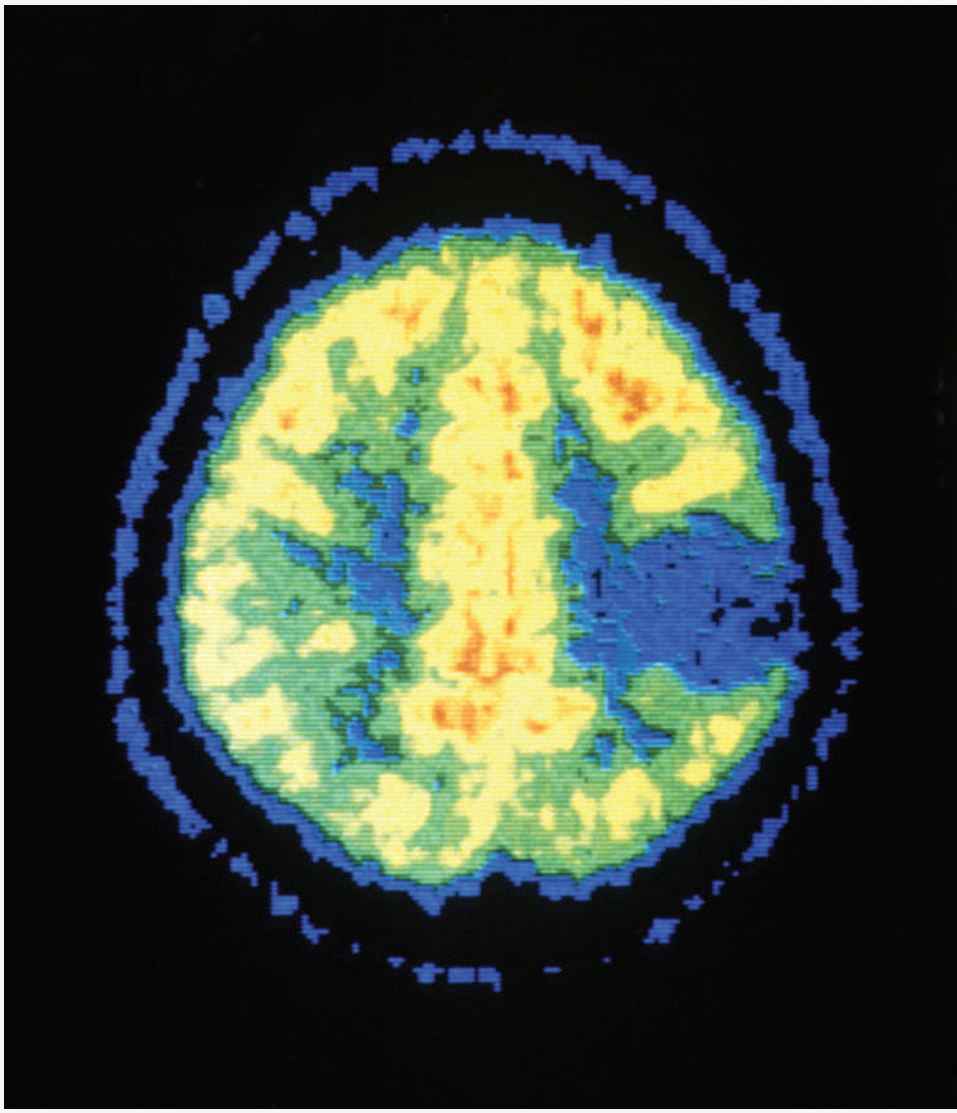
(a) One over-the-counter product lists the active ingredient as "diphenhydramine HCl." What does this designation mean?

(b) Write the acid-base reaction to illustrate how this compound is produced. When this product is dissolved in water would you expect the solution be acidic, basic, or neutral? Explain.

11

Nuclear Chemistry

CONTENTS



▲ This positron emission tomography (PET) scan takes advantage of the properties of radioactive isotopes to produce an image of a brain tumor. PET scans can also allow physicians to determine if a tumor is benign or malignant, and avoid unnecessary surgery.

CONCEPTS TO REVIEW

A. Atomic Theory (Section 2.1)
B. Elements and Atomic Number (Section 2.2)
C. Isotopes (Section 2.3)

A patient complaining of headaches and blurred vision on one side is referred to a regional research hospital for diagnostic tests. Thirty years ago, the standard diagnostic tool would have been X-ray imaging, but the use of 3-D *positron emission tomography* (PET) scans is becoming increasingly common. One advantage of PET technology is the ability to generate a 3-D image of tumors and body organs, including the brain, which enables physicians to more accurately diagnose the cause of medical symptoms. PET scans, and many other medical diagnostic techniques discussed in this chapter and in the Chemistry in Action "Body Imaging" on page 381, take advantage of the unique properties of radioisotopes—nuclei that undergo spontaneous nuclear decay reactions. Radioisotopes have practical applications far beyond medical diagnostics, including use in smoke detectors, in the determination of the age of archeological artifacts and geological formations, and as sources of energy in nuclear power plants.

But what is a "nuclear" reaction, and how is it different from the chemical reactions we have examined previously? In all of the reactions we have discussed thus far, only the *bonds* between atoms have changed; the chemical identities of atoms themselves have remained unchanged. Anyone who reads

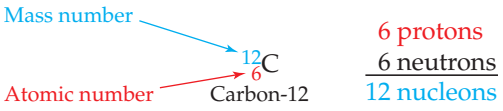
the paper or watches television knows, however, that atoms *can* change, often resulting in the conversion of one element into another. Atomic weapons, nuclear energy, and radioactive radon gas in our homes are all topics of societal importance, and all involve *nuclear chemistry*—the study of the properties and reactions of atomic nuclei.

11.1 Nuclear Reactions

Learning Objective:

- Identify reactants and products of nuclear reactions as elements, isotopes, or subatomic particles.

Recall from Section 2.2 that an atom is characterized by its *atomic number, Z,* and its *mass number, A*. The atomic number, written below and to the left of the element symbol, gives the number of protons in the nucleus and identifies the element. The mass number, written above and to the left of the element symbol, gives the total number of **nucleons,** a general term for both protons (p) and neutrons (n). The most common isotope of carbon, for example, has 12 nucleons: 6 protons and 6 neutrons: $^{12}_{6}C$.



Nucleon A general term for both protons and neutrons.

Atoms with identical atomic numbers but different mass numbers are called *isotopes,* and the nucleus of a specific isotope is called a **nuclide.** Thirteen isotopes of carbon are known—two occur commonly (^{12}C and ^{13}C) and one (^{14}C) is produced in small amounts in the upper atmosphere by the action of neutrons from cosmic rays on ^{14}N. The remaining 10 carbon isotopes have been produced artificially. Only the two commonly occurring isotopes are stable indefinitely; the others undergo spontaneous **nuclear reactions,** which change their nuclei. Carbon-14, for example, is an unstable isotope that slowly decomposes and is converted to nitrogen-14 plus an electron, a process we can write as

CONCEPTS TO REVIEW The different isotopes of an atom each have the same number of protons and only differ in their number of neutrons (Section 2.3).

Nuclide The nucleus of a specific isotope of an element.

Nuclear reaction A reaction that changes an atomic nucleus, usually causing the change of one element into another.

$$^{14}_{6}C \longrightarrow {}^{14}_{7}N + {}^{0}_{-1}e$$

The electron is often written as $^{0}_{-1}e$, where the superscript 0 indicates that the mass of an electron is essentially zero when compared with that of a proton or neutron, and the subscript -1 indicates that the charge is -1. (The subscript in this instance is not a true atomic number; in Section 11.4 the purpose of representing the electron this way will become clear.)

Nuclear reactions, such as the spontaneous decay of ^{14}C, are different from chemical reactions in several ways:

- A *nuclear* reaction involves a change in an atom's nucleus, usually producing a different element. A *chemical* reaction, by contrast, involves only a change in distribution of the outer-shell electrons around the atom and never changes the nucleus itself or produces a different element.
- Different isotopes of an element have essentially the same behavior in chemical reactions but often have completely different behavior in nuclear reactions.
- The rate of a nuclear reaction is unaffected by a change in temperature or pressure or by the addition of a catalyst.
- The nuclear reaction of an atom is essentially the same whether it is in a chemical compound or in an uncombined, elemental form.
- The energy change accompanying a nuclear reaction can be up to several million times greater than that accompanying a chemical reaction. The nuclear transformation of 1.0 g of uranium-235 releases 1.4×10^{9} kJ, for example, whereas the chemical combustion of 1.0 g of methane releases only 50 kJ.

11.2 The Discovery and Nature of Radioactivity

Learning Objective:

- Identify the different types of radiation and the properties of each type.

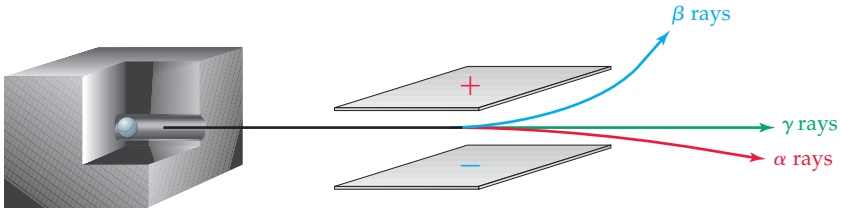
The discovery of *radioactivity* dates to the year 1896 when the French physicist Henri Becquerel made a remarkable observation. While investigating the nature of phosphorescence—the luminous glow of some minerals and other substances that remains when the lights are suddenly turned off—Becquerel happened to place a sample of a uranium-containing mineral on top of a photographic plate that had been wrapped in black paper and put in a drawer to protect it from sunlight. On developing the plate, Becquerel was surprised to find a silhouette of the mineral. He concluded that the mineral was producing some kind of unknown radiation, which passed through the paper and exposed the photographic plate.

Radioactivity The spontaneous emission of radiation from a nucleus.

Marie Sklodowska Curie and her husband, Pierre, began a series of investigations into this new phenomenon, which they termed **radioactivity.** They found that the source of the radioactivity was the element uranium (U) and that two previously unknown elements, which they named polonium (Po) and radium (Ra), were also radioactive. For these achievements, Becquerel and the Curies shared the 1903 Nobel Prize in physics.

Further work on radioactivity by the English scientist Ernest Rutherford established that there were at least two types of radiation, which he named *alpha* (α) and *beta* (β) after the first two letters of the Greek alphabet. Shortly thereafter, a third type of radiation was found and named for the third Greek letter, *gamma* (γ).

Subsequent studies showed that when the three kinds of radiation are passed between two plates with opposite electrical charges, each is affected differently. Alpha radiation bends toward the negative plate and must therefore have a positive charge. Beta radiation, by contrast, bends toward the positive plate and must have a negative charge, whereas gamma radiation does not bend toward either plate and has no charge (Figure 11.1).



▶ Figure 11.1
The effect of an electric field on α, β, γ radiation.
The radioactive source in the shielded box emits radiation, which passes between the two electrically charged plates. Alpha radiation is deflected toward the negative plate, β radiation is deflected toward the positive plate, and γ radiation is not deflected.

Gamma (γ) radiation Radioactivity consisting of high-energy light waves.

Beta (β) particle An electron (e^-), emitted as radiation.

Alpha (α) particle A helium nucleus (He^{2+}), emitted as α radiation.

Another difference among the three kinds of radiation soon became apparent when it was discovered that α and β radiations are composed of small particles with a measurable mass, whereas **gamma (γ) radiation** consists of high-energy electromagnetic waves and has no mass. Rutherford was able to show that a **beta (β) particle** is an electron (e^-) and that an **alpha (α) particle** is actually a helium nucleus, He^{2+}. (Recall that a helium *atom* consists of two protons, two neutrons, and two electrons. When the two electrons are removed, the remaining helium nucleus, or α particle, has only the two protons and two neutrons.).

Yet a third difference among the three kinds of radiation is their penetrating power. Because of their relatively large mass, α particles move slowly (up to about one-tenth the speed of light) and can be stopped by a few sheets of paper or by the top layer of skin. Beta particles, because they are much lighter, move at up to nine-tenth the speed of light and have about 100 times the penetrating power of α particles. A block of wood or heavy protective clothing is necessary to stop β radiation, which can otherwise penetrate the skin and cause burns and other damage. Gamma rays move at the speed of light $(3.00 \times 10^8 \text{ m/s})$ and have about 1000 times the penetrating power of α particles. A lead block several centimeters thick is needed to stop γ radiation, which can otherwise penetrate and damage the body's internal organs.

See the Chemistry in Action "Atoms and Light" on p. 100 in Chapter 2 for a discussion of gamma rays and the rest of the electromagnetic spectrum.

Table 11.1 summarizes the characteristics of the three kinds of radiation. Note that an α particle, even though it is an ion with a +2 charge, is usually written using the symbol $^{4}_{2}\text{He}$ without the charge. A β particle is usually written $^{0}_{-1}\text{e}$, as noted previously.

Table 11.1 Characteristics of α, β, and γ Radiation

Type of Radiation	Symbol	Charge	Composition	Mass (AMU)	Velocity	Relative Penetrating Power
Alpha	$\alpha, {}^{4}_{2}\text{He}$	+2	Helium nucleus	4	Up to 10% speed of light	Low (1)
Beta	$\beta, {}^{0}_{-1}\text{e}$	−1	Electron	1/1823	Up to 90% speed of light	Medium (100)
Gamma	$\gamma, {}^{0}_{0}\gamma$	0	High-energy radiation	0	Speed of light (3.00×10^{8} m/s)	High (1000)

11.3 Stable and Unstable Isotopes

Learning Objective:

- Identify natural isotopes, and distinguish between stable and unstable isotopes.

Every element in the periodic table has at least one radioactive isotope, or **radioisotope,** and more than 3300 radioisotopes are known. Their radioactivity is the result of having unstable nuclei, although the exact causes of this instability are not fully understood. Radiation is emitted when an unstable radioactive nucleus, or **radionuclide,** spontaneously changes into a more stable one.

Radioisotope A radioactive isotope.

Radionuclide The nucleus of a radioactive isotope.

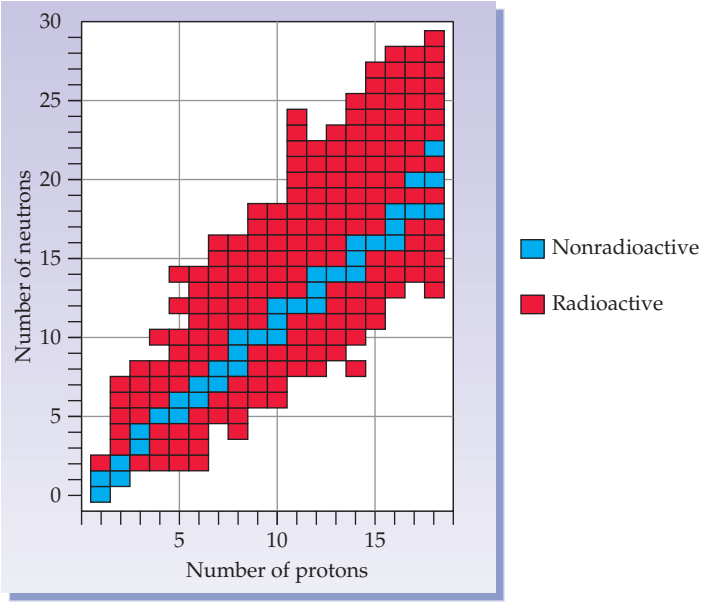
For elements in the first few rows of the periodic table, stability is associated with a roughly equal number of neutrons and protons (Figure 11.2). Hydrogen, for example, has stable $^{1}_{1}\text{H}$ (protium) and $^{2}_{1}\text{H}$ (deuterium) isotopes, but its $^{3}_{1}\text{H}$ isotope (tritium) is radioactive. As elements get heavier, the number of neutrons relative to protons in stable nuclei increases. Lead-208 ($^{208}_{82}\text{Pb}$), for example, the most abundant stable isotope of lead, has 126 neutrons and 82 protons in its nuclei. Nevertheless, of the 35 known isotopes of lead, only 3 are stable whereas 32 are radioactive. In fact, there are only 264 stable isotopes among all the elements. All isotopes of elements with atomic numbers higher than that of bismuth (83) are radioactive.

Most of the more than 3300 known radioisotopes have been made in high-energy particle accelerators by reactions that will be described in Section 11.8. Such isotopes are called **artificial radioisotopes** because they are not found in nature. All isotopes of the transuranium elements (those heavier than uranium) are artificial. The much smaller number of radioactive isotopes found in Earth's crust, such as $^{238}_{92}\text{U}$, are called **natural radioisotopes.**

Artificial radioisotope Radioactive isotopes not found in nature.

Natural radioisotopes Radioactive isotopes that occur naturally and are found in Earth's crust.

Aside from their radioactivity, different radioisotopes of the same element have the same chemical properties as stable isotopes, which accounts for their great usefulness as *tracers* (see the Chemistry in Action "Medical Uses of Radioactivity" on p. 372). A chemical compound tagged with a radioactive atom undergoes exactly the same reactions as its nonradioactive counterpart. The difference is that the tagged compound can be located with a radiation detector and its location determined, as discussed in the Chemistry in Action "Body Imaging" on page 381.



▶ **Figure 11.2**
A plot of the numbers of neutrons and protons for known isotopes of the first 18 elements.
Stable (nonradioactive) isotopes of these elements have equal or nearly equal numbers of neutrons and protons.

11.4 Nuclear Decay

Learning Objective:

- Write and balance nuclear reactions involving alpha, beta, and positron emission modes of radioactive decay.

Think for a minute about the consequences of α and β radiation. If radioactivity involves the spontaneous emission of a small particle from an unstable atomic nucleus, then the nucleus itself must undergo a change. With that understanding of radioactivity came the startling discovery that atoms of one element can change into atoms of another element, something that had previously been thought impossible. The spontaneous emission of a particle from an unstable nucleus is called **nuclear decay,** or *radioactive decay,* and the resulting change of one element into another is called **transmutation.**

Nuclear decay The spontaneous emission of a particle from an unstable nucleus.

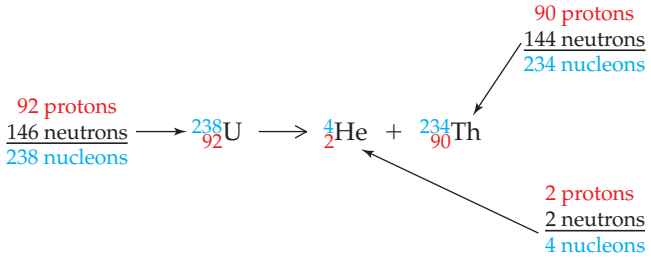
Transmutation The change of one element into another.

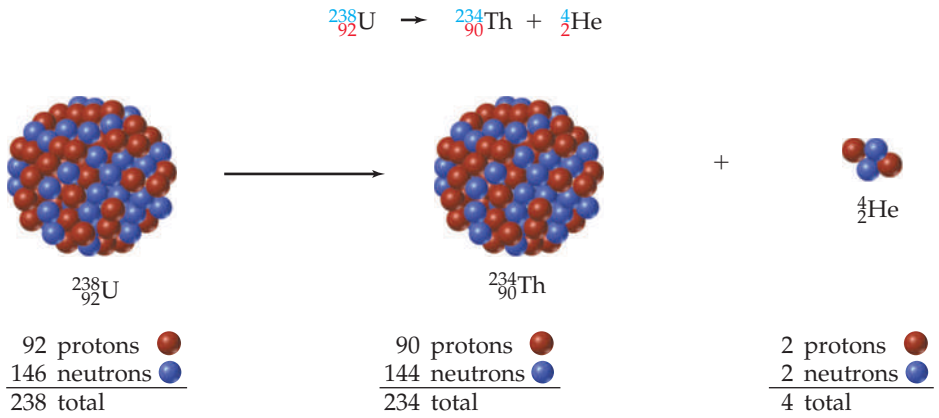
Nuclear decay: Radioactive element ⟶ New element + Emitted particle

Alpha Emission

When an atom of uranium-238 ($^{238}_{92}\text{U}$) emits an α particle (i.e., $^{4}_{2}\text{He}$), the nucleus loses 2 protons and 2 neutrons. Because the number of protons in the nucleus has now changed from 92 to 90, the *identity* of the atom has changed from uranium to thorium. Furthermore, since the total number of nucleons has decreased by 4, uranium-238 has become thorium-234 ($^{234}_{90}\text{Th}$) (Figure 11.3).

Note that the equation for a nuclear reaction is not balanced in the usual chemical sense because the kinds of atoms are not the same on both sides of the arrow. Instead, we say that a nuclear equation is balanced when the number of nucleons on both sides of the equation is the same and when the sums of the charges on the nuclei plus any ejected subatomic particles (protons or electrons) are same on both sides of the equation. In the decay of $^{238}_{92}\text{U}$ to give $^{4}_{2}\text{He}$ and $^{234}_{90}\text{Th}$, for example, there are 238 nucleons and 92 nuclear charges on both sides of the nuclear equation.





▶ Figure 11.3
Alpha emission.
Emission of an α particle from an atom of uranium-238 produces an atom of thorium-234.

Worked Example 11.1 Balancing Nuclear Reactions: Alpha Emission

Polonium-208 is one of the α emitters studied by Marie Curie. Write the equation for the α decay of polonium-208, and identify the element formed.

ANALYSIS Look up the atomic number of polonium (84) in the periodic table, and write the known part of the nuclear equation, using the standard symbol for polonium-208:

$$^{208}_{84}\text{Po} \longrightarrow {}^{4}_{2}\text{He} + \ ?$$

Then, calculate the mass number and atomic number of the product element, and write the final equation.

SOLUTION

The mass number of the product is $208 - 4 = 204$, and the atomic number is $84 - 2 = 82$. A look at the periodic table identifies the element with atomic number 82 as lead (Pb).

$$^{208}_{84}\text{Po} \longrightarrow {}^{4}_{2}\text{He} + {}^{204}_{82}\text{Pb}$$

Check your answer by making sure that the mass numbers and atomic numbers on the two sides of the equation are balanced:

Mass numbers: $208 = 4 + 204$ Atomic numbers: $84 = 2 + 82$

PROBLEM 11.1

High levels of radioactive radon-222 ($^{222}_{86}\text{Rn}$) have been found in many homes built on radium-containing rock, leading to the possibility of health hazards. What product results from α emission by radon-222?

PROBLEM 11.2

What isotope of radium (Ra) is converted into radon-222 by α emission?

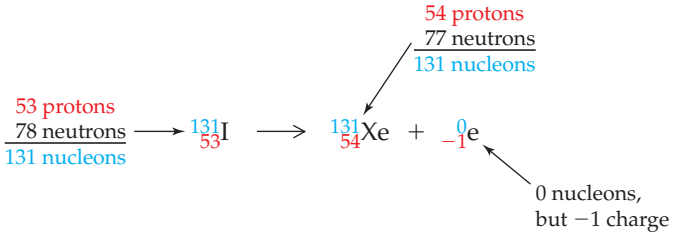
Beta Emission

Whereas α emission leads to the loss of two protons and two neutrons from the nucleus, β emission involves the *decomposition* of a neutron to yield an electron and a proton. This process can be represented as

$$^{1}_{0}\text{n} \longrightarrow {}^{1}_{1}\text{p} + {}^{0}_{-1}\text{e}$$

where the electron ($^{0}_{-1}\text{e}$) is ejected as a β particle, and the proton is retained by the nucleus. Note that the electrons emitted during β radiation come from the *nucleus* and not from the occupied orbitals surrounding the nucleus. The decomposition of carbon-14 to form nitrogen-14 in Section 11.1 is an example of beta decay.

The net result of β emission is that the atomic number of the atom increases by one because there is a new proton. The mass number of the atom remains the same, however, because a neutron has changed into a proton, leaving the total number of nucleons unchanged. For example, iodine-131 ($^{131}_{53}\text{I}$), a radioisotope used in detecting thyroid problems, undergoes nuclear decay by β emission to yield xenon-131 ($^{131}_{54}\text{Xe}$):



Note that the superscripts (mass numbers) are balanced in this equation because a β particle has a mass near zero, and the subscripts are balanced because a β particle has a charge of -1.

Worked Example 11.2 Balancing Nuclear Reactions: Beta Emission

Write a balanced nuclear equation for the β decay of chromium-55.

ANALYSIS Write the known part of the nuclear equation:

$$^{55}_{24}\text{Cr} \longrightarrow {}^{0}_{-1}\text{e} + ?$$

Then calculate the mass number and atomic number of the product element, and write the final equation.

SOLUTION

The mass number of the product stays at 55, and the atomic number increases by 1, $24 + 1 = 25$, so the product is manganese-55.

$$^{55}_{24}\text{Cr} \longrightarrow {}^{0}_{-1}\text{e} + {}^{55}_{25}\text{Mn}$$

Check your answer by making sure that the mass numbers and atomic numbers on the two sides of the equation are balanced:

Mass numbers: $55 = 0 + 55$ Atomic numbers: $24 = -1 + 25$

PROBLEM 11.3

Strontium-89 is a short-lived β emitter often used in the treatment of bone tumors. Write a nuclear equation for the decay of strontium-89.

PROBLEM 11.4

Write nuclear equations for the formation of each of the following nuclides by β emission.

(a) $^{3}_{2}\text{He}$ **(b)** $^{210}_{83}\text{Bi}$ **(c)** $^{20}_{10}\text{Ne}$

Gamma Emission

Emission of γ rays, unlike the emission of α and β particles, causes no change in mass or atomic number because γ rays are simply high-energy electromagnetic waves. Although γ emission can occur alone, it usually accompanies α or β emission as a mechanism for the new nucleus that results from a transmutation to release some extra energy.

Since γ emission affects neither mass number nor atomic number, it is often omitted from nuclear equations. Nevertheless, γ rays are of great importance. Their penetrating power makes them by far the most dangerous kind of external radiation for humans and also makes them useful in numerous medical applications. Cobalt-60, for example, is used in cancer therapy as a source of penetrating γ rays that kill cancerous tissue.

$$^{60}_{27}\text{Co} \longrightarrow {}^{60}_{28}\text{Ni} + {}^{0}_{-1}\text{e} + {}^{0}_{0}\gamma$$

Positron Emission

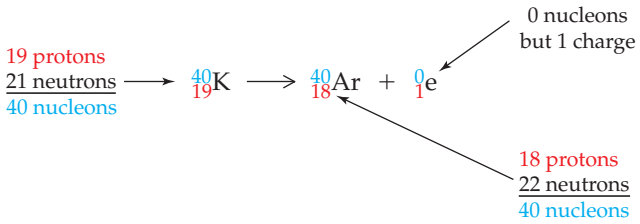
Positron A "positive electron," which has the same mass as an electron but a positive charge.

In addition to α, β, and γ radiation, there is another common type of radioactive decay process called *positron emission,* which involves the conversion of a proton in the nucleus into a neutron plus an ejected **positron,** $^{0}_{1}\text{e}$ or β^{+}. A positron, which can be thought of as a "positive electron," has the same mass as an electron but a positive charge. This process can be represented as

$$^{1}_{1}\text{p} \longrightarrow {}^{1}_{0}\text{n} + {}^{0}_{1}\text{e}$$

The result of positron emission is a decrease in the atomic number of the product nucleus because a proton has changed into a neutron, but no change in the mass number. Potassium-40, for example, undergoes positron emission to yield argon-40, a nuclear reaction important in geology for dating rocks. Note once again that the sum of the two

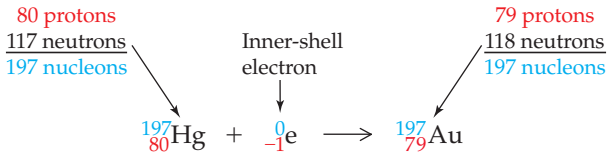
subscripts on the right of the nuclear equation $(18 + 1 = 19)$ is equal to the subscript in the $^{40}_{19}K$ nucleus on the left.



Electron Capture

Electron capture, symbolized E.C., is a process in which the nucleus captures an inner-shell electron from the surrounding electron cloud, thereby converting a proton into a neutron, and energy is released in the form of gamma rays. The mass number of the product nucleus is unchanged, but the atomic number decreases by one, just as in positron emission. The conversion of mercury-197 into gold-197 is an example:

Electron capture (E.C.) A process in which the nucleus captures an inner-shell electron from the surrounding electron cloud, thereby converting a proton into a neutron.



Do not plan on using this reaction to get rich, however. Mercury-197 is not one of the naturally occurring isotopes of Hg and is typically produced by transmutation reactions as discussed in Section 11.8.

In Figure 11.2, we see that most of the stable isotopes of the lighter elements have nearly the same number of neutrons and protons. With this fact in mind, we can often predict the most likely decay mode: unstable isotopes that have more protons than neutrons are more likely to undergo β decay to convert a proton to a neutron, whereas unstable isotopes having more neutrons than protons are more likely to undergo either positron emission or electron capture to convert a neutron to a proton. Also, the very heavy isotopes $(Z > 83)$ will most likely undergo α-decay to lose both neutrons and protons to decrease the atomic number. Characteristics of the five kinds of radioactive decay processes are summarized in Table 11.2.

Table 11.2 A Summary of Radioactive Decay Processes

Process	Symbol	Change in Atomic Number	Change in Mass Number	Change in Number of Neutrons
α emission	^4_2He or α	−2	−4	−2
β emission	$^0_{-1}e$ or β^-*	+1	0	−1
γ emission	$^0_0\gamma$ or γ	0	0	0
Positron emission	^0_1e or β^+*	−1	0	+1
Electron capture	E.C.	−1	0	+1

Superscripts are used to indicate the charge associated with the two forms of beta decay; β^-, or a beta particle, carries a −1 charge, while β^+, or a positron, carries a +1 charge.

Worked Example 11.3 Balancing Nuclear Reactions: Electron Capture, Positron Emission

Write balanced nuclear equations for the following processes:

(a) Electron capture by polonium-204: $^{204}_{84}Po + {}^0_{-1}e \longrightarrow ?$

(b) Positron emission from xenon-118: $^{118}_{54}Xe \longrightarrow {}^0_1e + ?$

—continued on next page

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ANALYSIS The key to writing nuclear equations is to make sure that the number of nucleons is the same on both sides of the equation and that the number of charges is the same.

SOLUTION

(a) In electron capture, the mass number is unchanged and the atomic number decreases by one, giving bismuth-204: $^{204}_{84}\text{Po} + {}^{0}_{-1}\text{e} \longrightarrow {}^{204}_{83}\text{Bi}$.

Check your answer by making sure that the number of nucleons and the number of charges are the same on both sides of the equation:

$$\text{Mass number: } 204 + 0 = 204 \qquad \text{Atomic number: } 84 + (-1) = 83$$

(b) In positron emission, the mass number is unchanged and the atomic number decreases by one, giving iodine-118: $^{118}_{54}\text{Xe} \longrightarrow {}^{0}_{1}\text{e} + {}^{118}_{53}\text{I}$.

CHECK!

$$\text{Mass number: } 118 = 0 + 118 \qquad \text{Atomic number: } 54 = 1 + 53$$

PROBLEM 11.5

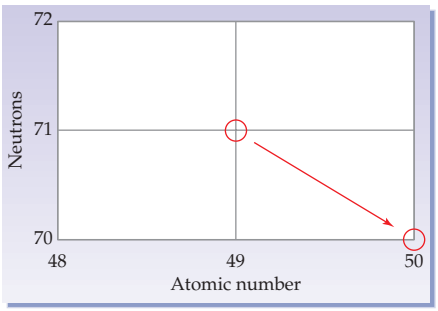
Write nuclear equations for positron emission from the following radioisotopes:

(a) $^{38}_{20}\text{Ca}$ **(b)** $^{118}_{54}\text{Xe}$ **(c)** $^{79}_{37}\text{Rb}$

PROBLEM 11.6

Write nuclear equations for the formation of the following radioisotopes by electron capture:

(a) $^{62}_{29}\text{Cu}$ **(b)** $^{110}_{49}\text{In}$ **(c)** $^{81}_{35}\text{Br}$



KEY CONCEPT PROBLEM 11.7

The red arrow in the graph (see margin) indicates the changes that occur in the nucleus of an atom during a nuclear reaction. Identify the isotopes involved as product and reactant, and name the type of decay process.

11.5 Radioactive Half-Life

Learning Objective:

- Determine the half-life of a radioactive isotope, and use the half-life to calculate the fraction of the isotope remaining as a function of time.

The rate of radioactive decay varies greatly from one radioisotope to another. Some radioisotopes, such as uranium-238, decay at a barely perceptible rate over billions of years, but others, such as carbon-17, decay within thousandths of a second.

Half-life ($t_{1/2}$) The amount of time required for one-half of a radioactive sample to decay.

Rates of nuclear decay are measured in units of **half-life ($t_{1/2}$)**, defined as the amount of time required for one-half of a radioactive sample to decay. For example, the half-life of iodine-131 is 8.021 days. If today, you have 1.000 g of $^{131}_{53}\text{I}$, then 8.021 days from now, you will have only 50% of that amount (0.500 g) because one-half of the sample will have decayed into $^{131}_{54}\text{Xe}$. After 8.021 more days (16.063 days total), you will have only 25% (0.250 g) of your original $^{131}_{53}\text{I}$ sample; after another 8.021 days (24.084 days total), you will have only 12.5% (0.125 g); and so on. Each passage of a half-life causes the decay of one-half of whatever sample remains. The half-life of any particular isotope is the same no matter what the size of the sample, the temperature, or any other external conditions. There is no known way to slow down, speed up, or otherwise change the characteristics of radioactive decay.

1.000 g $^{131}_{53}\text{I}$	$\xrightarrow{8\text{ days}}$	0.500 g $^{131}_{53}\text{I}$	$\xrightarrow{8\text{ days}}$	0.250 g $^{131}_{53}\text{I}$	$\xrightarrow{8\text{ days}}$	0.125 g $^{131}_{53}\text{I}$	$\longrightarrow$
		One half-life		Two half-lives (16 days total)		Three half-lives (24 days total)	
100%		50% remaining		25% remaining		12.5% remaining	

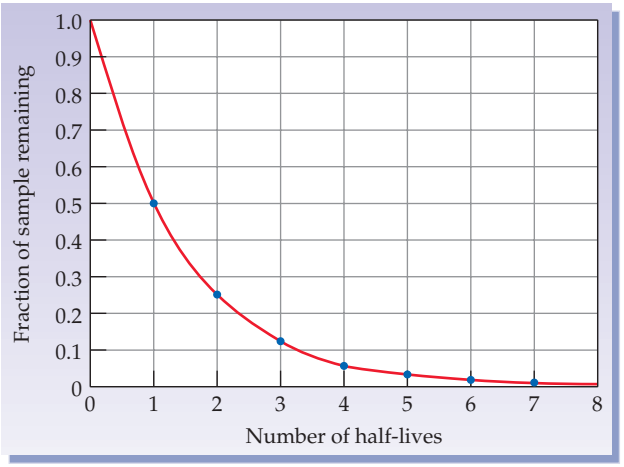
The fraction of radioisotope remaining after the passage of each half-life is represented by the curve in Figure 11.4 and can be calculated as

$$\text{fraction remaining} = (0.5)^n$$

where n is the number of half-lives that have elapsed.

One of the better known half-life applications is radiocarbon dating to determine the age of archaeological artifacts. The method is based on the slow and constant production of radioactive carbon-14 atoms in the upper atmosphere by bombardment of nitrogen atoms with neutrons from cosmic rays. Carbon-14 atoms combine with oxygen to yield $^{14}CO_2$, which slowly mixes with ordinary $^{12}CO_2$ and is then incorporated into plants during photosynthesis. When these plants are eaten by animals, carbon-14 enters the food chain and is distributed evenly throughout all living organisms.

As long as a plant or animal is living, a dynamic equilibrium is established in which the organism excretes or exhales the same amount of ^{14}C that it takes in. As a result, the ratio of ^{14}C to ^{12}C in the living organism is the same as that in the atmosphere—about one part in 10^{12}. When the plant or animal dies, however, it no longer takes in more ^{14}C. Thus, the $^{14}C/^{12}C$ ratio in the organism slowly decreases as ^{14}C undergoes radioactive decay. At 5730 years (one ^{14}C half-life) after the death of the organism, the $^{14}C/^{12}C$ ratio has decreased by a factor of 2; at 11,460 years after death, the $^{14}C/^{12}C$ ratio has decreased by a factor of 4; and so on. By measuring the amount of ^{14}C remaining in the traces of any once-living organism, archaeologists can determine how long ago the organism died. The accuracy of the technique lessens as a sample gets older, but artifacts with an age of 1000–20,000 years can be dated with reasonable accuracy.



▲ **Figure 11.4**
The decay of a radioactive nucleus over time.
All nuclear decays follow this curve, whether the half-lives are measured in years, days, minutes, or seconds. That is, the fraction of sample remaining after one half-life is 0.50, the fraction remaining after two half-lives is 0.25, the fraction remaining after three half-lives is 0.125, and so on.

Table 11.3 gives the half-lives of some useful radioisotopes. As you might expect, radioisotopes that are used internally for medical applications have fairly short half-lives so that they decay rapidly and do not remain in the body for prolonged periods.

Often, decay of a radioisotope produces a stable nucleus, but sometimes the product nucleus is itself radioactive and undergoes further decay. In fact, some of the heavier radioactive nuclei undergo an extended **decay series** of nuclear disintegrations before they ultimately reach a nonradioactive product. Uranium-238, for example, undergoes a series of 14 sequential nuclear reactions, ultimately stopping at lead-206 (Figure 11.5).

Decay series A sequential series of nuclear disintegrations leading from a heavy radioisotope to a nonradioactive product.

One of the intermediate radionuclides in the uranium-238 decay series is radon-222, a gas. Rocks, soil, and building materials that originally contained uranium are sources of radon-222, which can seep through cracks in basements and get into the air inside homes and other buildings. Radon-222 undergoes α decay to form a solid product, polonium-218, which also undergoes α decay. If radon-222 is inhaled, potential exposure to α radiation can damage lung tissue.

Table 11.3 Half-Lives of Some Useful Radioisotopes

Radioisotope	Symbol	Radiation	Half-Life	Use
Tritium	$^{3}_{1}H$	β	12.33 years	Biochemical tracer
Carbon-14	$^{14}_{6}C$	β	5730 years	Archaeological dating
Sodium-24	$^{24}_{11}Na$	β	14.959 hours	Examining circulation
Phosphorus-32	$^{32}_{15}P$	β	14.262 days	Leukemia therapy
Potassium-40	$^{40}_{19}K$	β, β^+	1.277×10^9 years	Geological dating
Cobalt-60	$^{60}_{27}Co$	β, γ	5.271 years	Cancer therapy
Arsenic-74	$^{74}_{33}As$	β^+	17.77 days	Locating brain tumors
Technetium-99*m**	$^{99m}_{43}Tc$	γ	6.01 hours	Brain scans
Iodine-131	$^{131}_{53}I$	β	8.021 days	Thyroid therapy
Uranium-235	$^{235}_{92}U$	α, γ	7.038×10^8 years	Nuclear reactors

**The m in technetium-99m stands for metastable, meaning that the nucleus undergoes γ emission but does not change its mass number or atomic number.*

CHEMISTRY IN ACTION

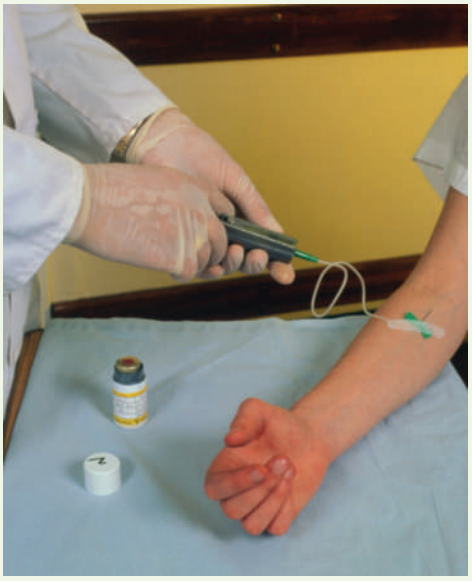
Medical Uses of Radioactivity

The origins of nuclear medicine date from 1901, when the French physician Henri Danlos first used radium in the treatment of a tubercular skin lesion. Since that time, the use of radioactivity has become a crucial part of modern medical care, both diagnostic and therapeutic. Current nuclear techniques can be grouped into three classes: (1) in vivo procedures, (2) radiation therapy, and (3) imaging procedures. The first two are described here, and the third one is described on page 381 in the Chemistry in Action "Body Imaging."

In Vivo Procedures

In vivo studies—those that take place inside the body—are carried out to assess the functioning of a particular organ or body system. A *radiopharmaceutical* agent is administered, and its path in the body—whether absorbed, excreted, diluted, or concentrated—is determined by analysis of blood or urine samples. Such compounds are called *tracers,* because their location or distribution can be tracked by monitoring the decay of the radioisotope incorporated in the radiopharmaceutical agent.

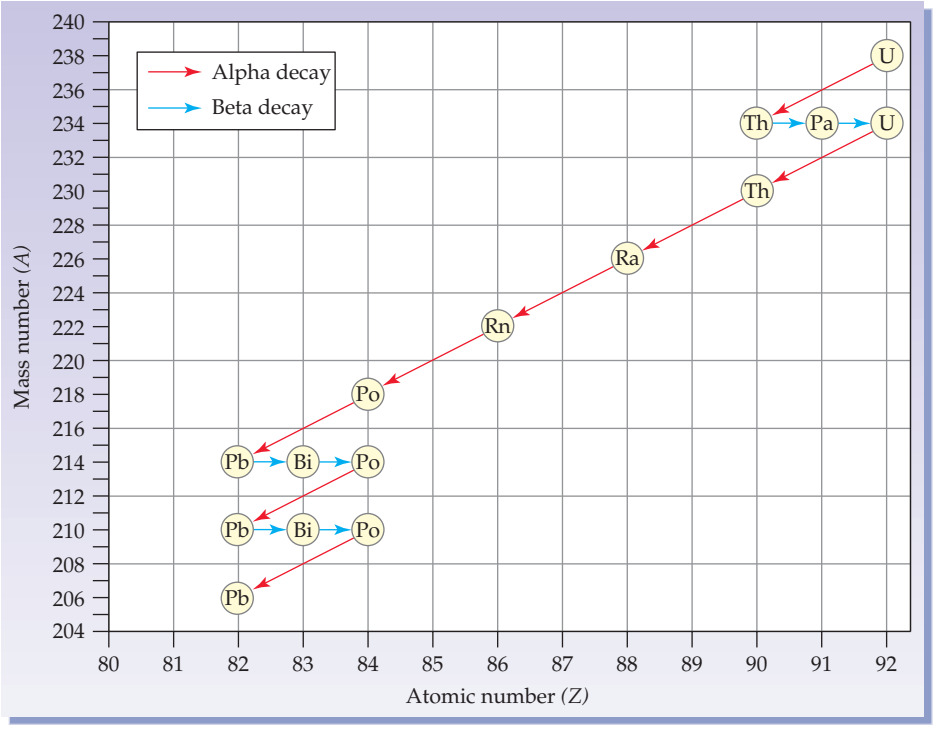
Among the many *in vivo* procedures utilizing radioactive agents is a simple method for the determination of whole-blood volume, a common indicator used in the diagnosis of congestive heart failure, hypertension, and renal failure. A known quantity of red blood cells labeled with radioactive chromium-51 is injected into the patient and allowed to circulate to be distributed evenly throughout the body. After a suitable interval, a blood sample is taken and blood volume is calculated by comparing the concentration of labeled cells in the blood with the quantity of labeled cells injected. This and similar procedures are known as *isotope dilution* and are described by



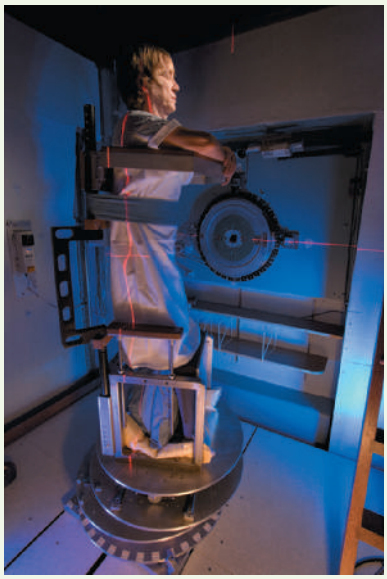
▲ A person's blood volume can be found by injecting a small amount of radioactive chromium-51 and measuring the dilution factor.

$$R_{sample} = R_{tracer}\left(\frac{W_{sample}}{W_{system} + W_{tracer}}\right)$$

where R_{sample} is the counting rate (a measure of radioactivity) of the analyzed sample, R_{tracer} is the counting rate of the tracer added to the system, and W refers to either the mass or volume of the analyzed sample, added tracer, or total system as indicated.



▶ **Figure 11.5**
The decay series from $^{238}_{92}U$ to $^{206}_{82}Pb$. Each isotope except for the last is radioactive and undergoes nuclear decay. The long slanted arrows represent α emissions, and the short horizontal arrows represent β emissions.



▲ Lasers are used to align and focus the neutron beam with the location of a patient's tumor at a neutron beam therapy facility at Fermilab.

Therapeutic Procedures

Therapeutic procedures—those in which radiation is purposely used as a weapon to kill diseased tissue—involve either external or internal sources of radiation. External radiation therapy for the treatment of cancer is often carried out with γ rays emanating from a cobalt-60 source. The highly radioactive source is shielded by a thick lead container and has a small opening directed toward the site of the tumor. By focusing the radiation beam on the tumor, the tumor receives the full exposure whereas exposure of surrounding parts of the body is minimized. Nevertheless, enough healthy tissue is affected so that most patients treated in this manner suffer the effects of radiation sickness discussed in Section 11.7.

Internal radiation therapy is a much more selective technique than external therapy. In the treatment of thyroid disease, for example, a radioactive substance such as iodine-131 is administered. This powerful β emitter is incorporated into the iodine-containing hormone thyroxine, which concentrates in the thyroid gland. Because β particles penetrate no farther than several millimeters, the localized ^{131}I produces a high radiation dose that destroys only the surrounding diseased tissue. To treat some tumors, such as those in the female reproductive system, a radioactive source is placed physically close to the tumor for a specific amount of time.

Boron neutron-capture therapy (BNCT) is a relatively new technique in which boron-containing drugs are administered to a patient and concentrate in the tumor site. The tumor is then irradiated with a neutron beam from a nuclear reactor. The boron absorbs a neutron and undergoes transmutation to produce an α particle and a lithium nucleus. These highly energetic particles have very low penetrating power and can kill nearby tumor tissue while sparing the healthy surrounding tissue. Because one disadvantage of BNCT is the need for access to a nuclear reactor, this treatment is available only in limited locations.

CIA Problem 11.1 What are the three main classes of techniques used in nuclear medicine? Give an example of each.

CIA Problem 11.2 A 2 mL solution containing 4.62×10^4 Bq/mL is injected into the bloodstream of a patient. After dilution, a 1.00 mL sample is withdrawn and found to have an activity of 9.62 Bq. Calculate total blood volume.

Worked Example 11.4 Nuclear Reactions: Half-Life

Phosphorus-32, a radioisotope used in leukemia therapy, has a half-life of about 14 days. Approximately what percentage of a sample remains after eight weeks?

ANALYSIS Determine how many half-lives have elapsed. For an integral number of half-lives, we can multiply the starting amount (100%) by 1/2 for each half-life that has elapsed.

SOLUTION

Since one half-life of $^{32}_{15}$P is 14 days (two weeks), eight weeks represents four half-lives. The fraction that remains after eight weeks is thus

$$\text{Final percentage} = 100\% \times (0.5)^4 = 100\% \times \underbrace{\left(\tfrac{1}{2} \times \tfrac{1}{2} \times \tfrac{1}{2} \times \tfrac{1}{2}\right)}_{\text{Four half-lives}}$$

$$= 100\% \times \tfrac{1}{16} = 6.25\%$$

Worked Example 11.5 Nuclear Reactions: Half-Life

As noted in Table 11.3, iodine-131 has a half-life of about eight days. Approximately what fraction of a sample remains after 20 days?

ANALYSIS Determine how many half-lives have elapsed. For a non-integral number (i.e., fraction) of half-lives, use the equation below to determine the fraction of radioisotope remaining.

$$\text{fraction remaining} = (0.5)^n$$

BALLPARK ESTIMATE Since the half-life of iodine-131 is eight days, an elapsed time of 20 days is 2.5 half-lives. The fraction remaining should be between 0.25 (fraction remaining after two half-lives) and 0.125 (fraction remaining after three half-lives). Since the relationship between the number of half-lives and fraction remaining is not linear (see Figure 11.4), the fraction remaining will not be exactly halfway between these values but instead will be slightly closer to the lower fraction, say 0.17.

SOLUTION

$$\text{fraction remaining} = (0.5)^n = (0.5)^{2.5} = 0.177$$

BALLPARK CHECK The fraction remaining is close to our estimate of 0.17.

Worked Example 11.6 Nuclear Reactions: Half-Life

For the phosphorus-32 radioisotope discussed in Worked Example 11.4, how long would it take for 85% of the ^{32}P to decay? (Note: $t_{1/2} = 14$ days.)

ANALYSIS If 85% of the original ^{32}P has decayed, then 15% remains. Knowing the fraction remaining (15%) the half-life relationship can be rearranged to solve for n (i.e., the number of half-lives). Multiplying n by 14 days yields the time required.

BALLPARK ESTIMATE Using exact half-lives as an estimate, we know that 25% would remain after two half-lives, and 12.5% would remain after three half-lives. Therefore, an elapsed time between two half-lives (28 days) and three half-lives (42 days) would be necessary. Since 15% is pretty close to 12.5% (three half-lives) the actual time is only slightly less than 42 days, so an estimate of 37 days is reasonable.

SOLUTION

Knowing the fraction remaining, we rearrange the half-life equation and solve for n. Because there is an exponential term involved, the mathematical solution can be simplified by applying the inverse function (i.e., a log function) to both sides, and rearranging:

$$\begin{aligned}
\text{fraction remaining} &= 0.15 = (0.5)^n \\
\log(0.15) &= \log(0.5)^n \\
\log(0.15) &= n\log(0.5) \\
-0.824 &= n(-0.301) \\
n &= (-0.824/-0.301) = 2.74 \text{ half-lives}
\end{aligned}$$

The time required is $(14 \text{ days} \times 2.74) = 38.3$ (38 days), close to our estimate.

PROBLEM 11.8

The half-life of carbon-14, an isotope used in archaeological dating, is 5730 years. What percentage of $^{14}_{6}C$ remains in a sample estimated to be 17,000 years old?

PROBLEM 11.9

A 1.00 mL sample of red blood cells containing chromium-51 as a tracer was injected into a patient. After several hours, a 5.00 mL sample of blood was drawn and its activity compared to the activity of the injected tracer sample. If the collected sample activity was 0.10% of the original tracer, calculate the total blood volume of the patient (see the Chemistry in Action "Medical Uses of Radioactivity," p. 372).

PROBLEM 11.10

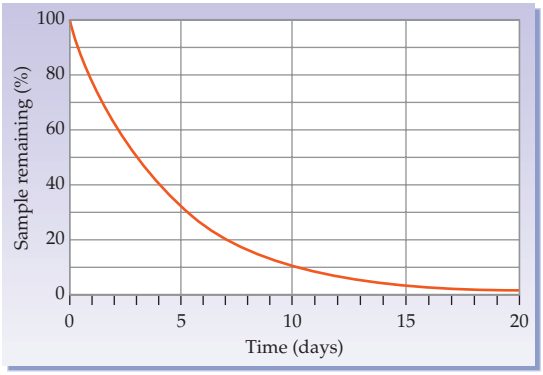
The first four radioisotopes in Table 11.3 are included in Figure 11.2. They all undergo β decay.

(a) Locate the position of these radioisotopes in Figure 11.2.

(b) Write the balanced decay reactions for these radioisotopes, and locate the position of the product nuclei in Figure 11.2.

KEY CONCEPT PROBLEM 11.11

What is the half-life of the radionuclide that shows the decay curve indicated in the graph (see margin)?



11.6 Ionizing Radiation

Learning Objective:

- Identify the types of ionizing radiation, and calculate the radiation intensity as a function of distance from the radiation source.

High-energy radiation of all kinds is often grouped together under the name **ionizing radiation.** This includes not only α particles, β particles, and γ rays but also *X rays* and *cosmic rays*. **X rays** are like γ rays; they have no mass and consist of high-energy electromagnetic radiation. The only difference between them is that the energy of X rays is somewhat less than that of γ rays (see the Chemistry in Action "Atoms and Light" in Chapter 2). **Cosmic rays** are not rays at all but are a mixture of high-energy particles that shower Earth from outer space. They consist primarily of protons, along with some α and β particles.

Ionizing radiation A general name for high-energy radiation of all kinds.

X rays Electromagnetic radiation with an energy somewhat less than that of γ rays.

Cosmic rays A mixture of high-energy particles—primarily of protons and various atomic nuclei—that shower Earth from outer space.

The interaction of any kind of ionizing radiation with a molecule knocks out an orbital electron, converting the atom or molecule into an extremely reactive ion:

$$\text{Molecule} \xrightarrow[\text{radiation}]{\text{ionizing}} \text{Ion} + e^-$$

This reactive ion can react with other molecules nearby, creating still other fragments that can cause further reactions. In this manner, a large dose of ionizing radiation can destroy the delicate balance of chemical reactions in living cells, ultimately causing the death of an organism.

A small dose of ionizing radiation may not cause visible symptoms but can nevertheless be dangerous if it strikes a cell nucleus and damages the genetic machinery inside. The resultant changes might lead to a genetic mutation, to cancer, or to cell death. The nuclei of rapidly dividing cells, such as those in bone marrow, the lymph system, the lining of the intestinal tract, or an embryo, are the most readily damaged. Because cancer cells are also rapidly dividing they are highly susceptible to the effects of ionizing radiation, which is why radiation therapy is an effective treatment for many types of cancer (see the Chemistry in Action "Medical Uses of Radioactivity" on p. 372). Table 11.4 summarizes some properties of ionizing radiation.

Table 11.4 Some Properties of Ionizing Radiation

Type of Radiation	Energy Range*	Penetrating Distance in Water**
α	3–9 MeV	0.02–0.04 mm
β	0–3 MeV	0–4 mm
X	100 eV–10 keV	0.01–1 cm
γ	10 keV–10 MeV	1–20 cm

**The energies of subatomic particles are often measured in electron volts (eV): 1 eV = 6.703×10^{-19} cal, or 2.805×10^{-18} J.*

***Distance at which one-half of the radiation is stopped.*

The effects of ionizing radiation on the human body vary with the energy of the radiation, its distance from the body, the length of exposure, and the location of the source outside or inside the body. When coming from outside the body, γ rays and X rays are potentially more harmful than α and β particles because they pass through clothing and skin and into the body's cells. Alpha particles are stopped by clothing and skin, and β particles are stopped by wood or several layers of clothing. These types of radiation are much more dangerous when emitted within the body, however, because all their radiation energy is given up to the immediately surrounding tissue. Alpha emitters are especially hazardous internally and are almost never used in medical applications.

Health professionals who work with X rays or other kinds of ionizing radiation protect themselves by surrounding the source with a thick layer of lead or other dense material. Protection from radiation is also afforded by controlling the distance between the worker and the radiation source because radiation intensity *(I)* decreases with the square of the distance from the source. The intensities of radiation at two different distances, 1 and 2, are given by the equation

$$\frac{I_1}{I_2} = \frac{{d_2}^2}{{d_1}^2}$$

For example, suppose a source delivers 16 units of radiation at a distance of 1.0 m. Doubling the distance to 2.0 m decreases the radiation intensity to one-fourth:

$$\frac{16 \text{ units}}{I_2} = \frac{(2 \text{ m})^2}{(1 \text{ m})^2}$$

$$I_2 = 16 \text{ units} \times \frac{1 \cancel{\text{m}^2}}{4 \cancel{\text{m}^2}} = 4 \text{ units}$$

Worked Example 11.7 Ionizing Radiation: Intensity versus Distance from the Source

If a radiation source gives 75 units of radiation at a distance of 2.4 m, at what distance does the source give 25 units of radiation?

ANALYSIS Radiation intensity *(I)* decreases with the square of the distance *(d)* from the source according to the equation

$$\frac{I_1}{I_2} = \frac{{d_2}^2}{{d_1}^2}$$

We know three of the four variables in this equation $(I_1, I_2, \text{and } d_1)$, and we need to find d_2.

BALLPARK ESTIMATE In order to decrease the radiation intensity from 75 units to 25 units (a factor of 3), the distance must *increase* by a factor of $\sqrt{3} = 1.7$. Thus, the distance should increase from 2.4 m to about 4 m.

SOLUTION

STEP 1: Identify known information. We know three of the four variables.

$I_1 = 75$ units
$I_2 = 25$ units
$d_1 = 2.4$ m

STEP 2: Identify answer and units.

$d_2 = ???$ m

STEP 3: Identify equation. Rearrange the equation relating intensity and distance to solve for d_2.

$$\frac{I_1}{I_2} = \frac{{d_2}^2}{{d_1}^2}$$

$${d_2}^2 = \frac{I_1 {d_1}^2}{I_2} \quad \Rightarrow \quad d_2 = \sqrt{\frac{I_1 {d_1}^2}{I_2}}$$

STEP 4: Solve. Substitute in known values so that unwanted units cancel.

$$d_2 = \sqrt{\frac{(75 \cancel{\text{ units}})(2.4 \text{ m})^2}{(25 \cancel{\text{ units}})}} = 4.2 \text{ m}$$

BALLPARK CHECK The calculated result is consistent with our estimate of about 4 m.

PROBLEM 11.12

A β-emitting radiation source gives 250 units of radiation at a distance of 4.0 m. At what distance does the radiation drop to one-tenth its original value?

11.7 Detecting and Measuring Radiation

Learning Objective:

- Identify methods for detecting radiation and the units used to measure radiation exposure.

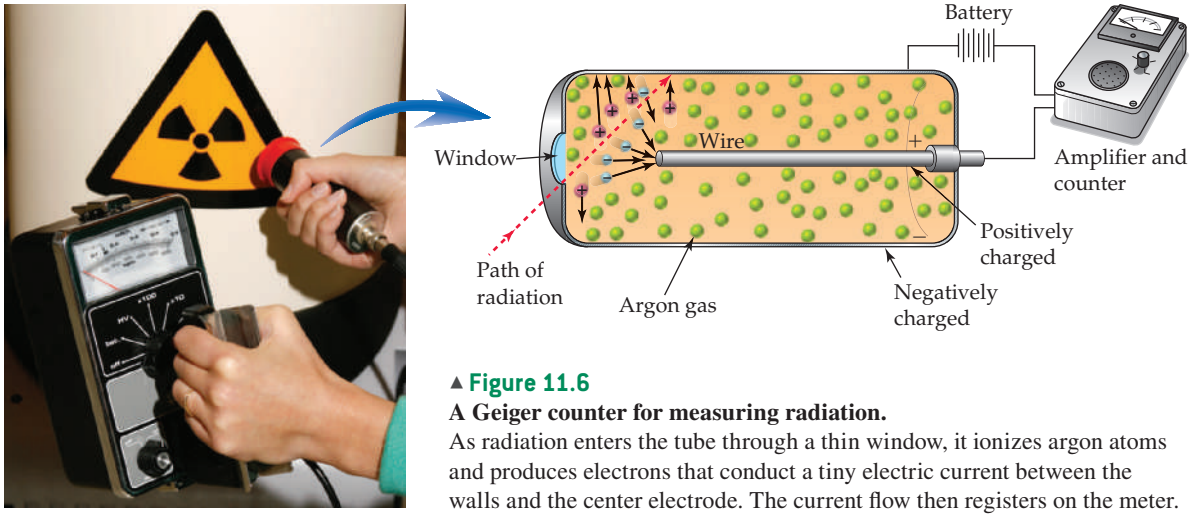
Small amounts of naturally occurring radiation have always been present, but people have been aware of it only within the past 100 years. The problem is that radiation is invisible. We cannot see, hear, smell, touch, or taste radiation, no matter how high the dose. We can, however, detect radiation by taking advantage of its ionizing properties.

The simplest device for detecting exposure to radiation is the photographic film badge worn by people who routinely work with radioactive materials. The film is protected from exposure to light, but any other radiation striking the badge causes the film to fog (remember Becquerel's discovery). At regular intervals, the film is developed and compared with a standard to indicate the radiation exposure.

▲ This photographic film badge is a common device for monitoring radiation exposure.

The most versatile method for measuring radiation in the laboratory is the *scintillation counter,* a device in which a substance called a *phosphor* emits a flash of light when struck by radiation. The number of flashes are counted electronically and converted into an electrical signal.

Perhaps the best-known method for detecting and measuring radiation is the *Geiger counter,* an argon-filled tube containing two electrodes (Figure 11.6). The inner walls of the tube are coated with an electrically conducting material and given a negative charge, and a wire in the center of the tube is given a positive charge. As radiation enters the tube through a thin window, it strikes and ionizes argon atoms, which briefly conduct a tiny electric current between the walls and the center electrode. The passage of the current is detected, amplified, and used to produce a clicking sound or to register on a meter. The more radiation that enters the tube, the more frequent the clicks. Geiger counters are useful for seeking out a radiation source in a large area and for gauging the intensity of emitted radiation.



▲ **Figure 11.6**
A Geiger counter for measuring radiation.
As radiation enters the tube through a thin window, it ionizes argon atoms and produces electrons that conduct a tiny electric current between the walls and the center electrode. The current flow then registers on the meter.

Measuring Radiation

Radiation intensity is expressed in different ways, depending on what characteristic of the radiation is measured (Table 11.5). Some units measure the number of nuclear decay events, while others measure exposure to radiation or the biological consequences of radiation.

Table 11.5 Common Units for Measuring Radiation

Unit	Quantity Measured	Description
Curie (Ci)	Decay events	Amount of radiation equal to 3.7×10^{10} disintegrations per second
Roentgen (R)	Ionizing intensity	Amount of radiation producing 2.1×10^9 charges per cubic centimeter of dry air
Rad	Energy absorbed per gram of tissue	1 rad = 1 R
Rem	Tissue damage	Amount of radiation producing the same damage as 1 R of X rays
Sievert (Sv)	Tissue damage	1 Sv = 100 rem

- **Curie** The *curie* (Ci), the *millicurie* (mCi), and the *microcurie* (μCi) measure the number of radioactive disintegrations occurring each second in a sample. One curie is the decay rate of 1 g of radium, equal to 3.7×10^{10} disintegrations per second; 1 mCi = 0.001 Ci = 3.7×10^7 disintegrations per second; and 1 μCi = 0.000 001 Ci = 3.7×10^4 disintegrations per second.

  The dosage of a radioactive substance administered orally or intravenously is usually given in millicuries. To calculate the size of a dose, it is necessary to determine the decay rate of the isotope solution per milliliter. Because the emitter concentration is constantly decreasing as it decays, the activity must be measured immediately before administration. Suppose, for example, that a solution containing iodine-131 for a thyroid-function study is found to have a decay rate of 0.020 mCi/mL and the dose administered is to be 0.050 mCi. The amount of the solution administered must be

$$\frac{0.05\ \cancel{\text{mCi}}}{\text{Dose}} \times \frac{1\ \text{mL}\ {}^{131}\text{I solution}}{0.020\ \cancel{\text{mCi}}} = 2.5\ \text{mL}\ {}^{131}\text{I solution/dose}$$

- **Roentgen** The *roentgen* (R) is a unit for measuring the ionizing intensity of γ or X radiation. In other words, the roentgen measures the capacity of the radiation for affecting matter. One roentgen is the amount of radiation that produces 2.1×10^9 units of charge in 1 cm^3 of dry air at atmospheric pressure. Each collision of ionizing radiation with an atom produces one ion, or one unit of charge.
- **Rad** The *rad* (radiation absorbed dose) is a unit for measuring the energy absorbed per gram of material exposed to a radiation source and is defined as the absorption of 1×10^{-5} J of energy per gram. The energy absorbed varies with the type of material irradiated and the type of radiation. For most purposes, though, the roentgen and the rad are so close that they can be considered identical when used for X rays and γ rays: 1 R = 1 rad.
- **Rem** The *rem* (roentgen equivalent for man) measures the amount of tissue damage caused by radiation. One rem is the amount of radiation that produces the same effect as 1 R of X rays. Rems are the preferred units for medical purposes because they measure equivalent doses of different kinds of radiation. The rem is calculated as

$$\text{Rems} = \text{rads} \times \text{RBE}$$

  where RBE is a *relative biological effectiveness* factor, which takes into account the differences in energy and of the different types of radiation. Although the actual biological effects of radiation depend greatly on both the source and the energy of the radiation, the RBE of X rays, γ rays, and β particles are essentially equivalent (RBE = 1), while the accepted RBE for α particles is 20. For example, 1 rad of α radiation causes 20 times more tissue damage than 1 rad of γ rays, but 1 rem of α radiation and 1 rem of γ rays cause the same amount of damage. Thus, the rem takes both ionizing intensity and biological effect into account, whereas the rad deals only with intensity.
- **SI Units** In the SI system, the *becquerel* (Bq) is defined as one disintegration per second. The SI unit for energy absorbed is the *gray* (Gy; 1 Gy = 100 rad). For radiation dose, the SI unit is the *sievert* (Sv), which is equal to 100 rem.

The biological consequences of different radiation doses are given in Table 11.6. Although the effects seem frightening, the average radiation dose received annually by most people is only about 0.62×10^{-2} Sv. Typical sources and percentage contribution to average background exposure are provided in Figure 11.7. About 50% of this *background radiation* comes from natural sources (rocks and cosmic rays); the remaining 50% comes from consumer products and from medical procedures such as X rays. The amount due to emissions from nuclear power plants and to fallout from testing of nuclear weapons in the 1950s is barely detectable.

Table 11.6 Biological Effects of Short-Term Radiation on Humans

Dose (Sv)	Biological Effects
0–0.25	No detectable effects
0.25–1	Temporary decrease in white blood cell count
1–2	Nausea, vomiting, longer-term decrease in white blood cells
2–3	Vomiting, diarrhea, loss of appetite, listlessness
3–6	Vomiting, diarrhea, hemorrhaging, eventual death in some cases
Above 6	Eventual death in nearly all cases

CHEMISTRY IN ACTION

Irradiated Food

The idea of irradiating food to kill harmful bacteria is not new; it goes back almost as far as the earliest studies on radiation. Not until the 1940s did serious work get under way, however, when U.S. Army scientists found that irradiation increased the shelf-life of ground beef. Nevertheless, widespread civilian use of the technique has been a long time in coming, spurred on in recent years by outbreaks of food poisoning that resulted in several deaths.

The principle of food irradiation is simple: exposure of contaminated food to ionizing radiation—usually γ rays produced by cobalt-60 or cesium-137—destroys the genetic material of any bacteria or other organisms present, thereby killing them. Irradiation will not, however, kill viruses or prions, the cause of "mad-cow" disease. The amount of radiation depends on the desired effect. For example, to delay ripening of fruit may require a dose of 0.25–0.75 kGy, while sterilization of packaged meat requires a much higher dose of 25–70 kGy. The food itself undergoes little if any change when irradiated and does not itself become radioactive. The only real argument against food irradiation, in fact, is that it is *too* effective. Knowing that irradiation will kill nearly all harmful organisms, a food processor might be tempted to cut back on normal sanitary practices!

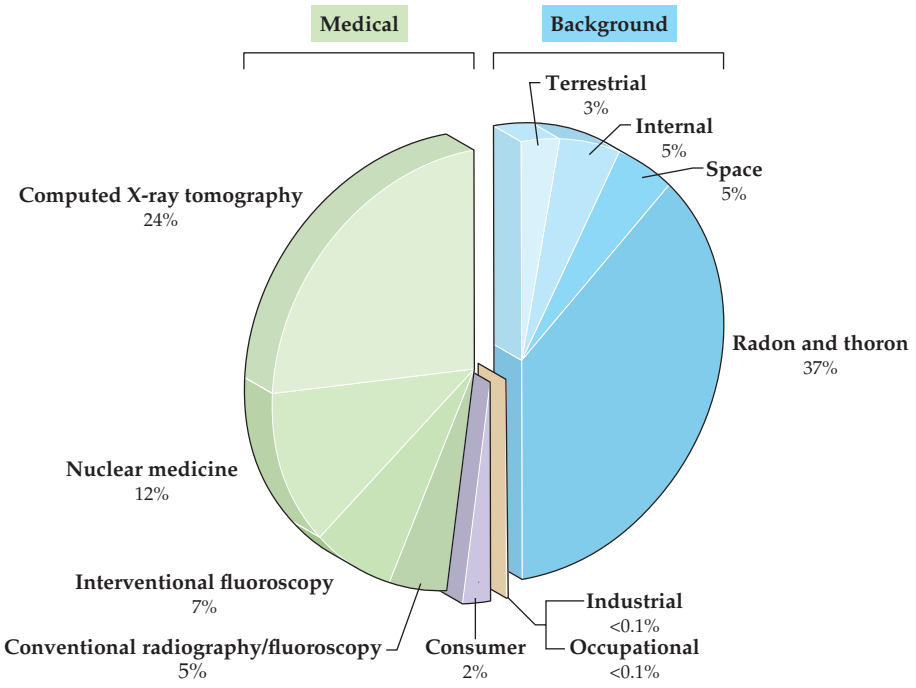
Food irradiation has been implemented to a much greater extent in Europe than in the United States. The largest marketers of irradiated food are Belgium, France, and the Netherlands, which irradiate between 10,000 and 20,000 tons of food per year. Currently, over 40 countries permit food irradiation and over 500,000 metric tons of food are treated annually worldwide. One of the major concerns in the United States is the possible generation of *radiolytic products,* compounds formed in food by exposure to ionizing radiation which some consumers fear may introduce radioactivity or degrade the nutritional value of the food. The U.S. Food and Drug Administration, after studying the matter extensively, has declared that food irradiation is safe and irradiated food products are nutritionally sound. Spices, fruits, pork, and vegetables were approved for irradiation in 1986, followed by poultry in 1990 and red meat, particularly ground beef, in 1997. In 2000, approval was extended to whole eggs and sprouting seeds. Should the food industry adopt irradiation of meat as its standard practice, occurrences of *Escherichia coli* and *salmonella* contaminations, resulting in either massive product recalls or serious health concerns for consumers will become a thing of the past.

▲ Irradiating food kills bacteria and extends shelf life. Most irradiated food products are labeled with the Radura symbol (in green) to inform the public that the food product was exposed to radiation.

CIA Problem 11.3 What is the purpose of food irradiation, and how does it work?

CIA Problem 11.4 What kind of radiation is used to treat food?

CIA Problem 11.5 A typical food irradiation application for the inhibition of sprout formation in potatoes applies a dose of 0.20 kGy. What is this dose in units of rem if the radiation is predominantly γ rays? If it is predominantly α particles? (Hint: 1 Gy = 100 rad)



▶ Figure 11.7
Average Radiation Exposure Sources.
This pie chart illustrates the sources of radiation exposure, expressed as percent of total average exposure. The greatest sources of radiation exposure are natural, background sources (radon, terrestrial, food) and medical applications.

PROBLEM 11.13

A solution of selenium-75, a radioisotope used in the diagnosis of pancreatic disease, is found just prior to administration to have an activity of 1.62×10^6 Bq/mL. If 3.98 mL were delivered intravenously to the patient, what dose of Se-75 (in μCi) did the patient receive?

PROBLEM 11.14

A typical chest X ray exposes a patient to an effective dose of 0.02 mSv. How many rem is this, and how many chest X rays would a patient have to receive before biological effects would be observed? (The limit from Table 11.6 is >0.25 Sv.)

11.8 Artificial Transmutation

Learning Objective:

- Write and balance equations for nuclear transmutation reactions.

Artificial transmutation The change of one atom into another brought about by a nuclear bombardment reaction.

Very few of the approximately 3300 known radioisotopes occur naturally. Most are made from stable isotopes by **artificial transmutation,** the change of one atom into another brought about by nuclear bombardment reactions.

When an atom is bombarded with a high-energy particle, such as a proton, a neutron, an α particle, or even the nucleus of another element, an unstable nucleus is created in the collision. A nuclear change then occurs, and a different element is produced. For example, transmutation of ^{14}N to ^{14}C occurs in the upper atmosphere when neutrons produced by cosmic rays collide with atmospheric nitrogen. In the collision, a neutron dislodges a proton (^{1}H) from the nitrogen nucleus as the neutron and nucleus fuse together:

$$^{14}_{7}\text{N} + {}^{1}_{0}\text{n} \longrightarrow {}^{14}_{6}\text{C} + {}^{1}_{1}\text{H}$$

▲ Smoke detectors contain a small amount of americium-241. The α particles emitted by this radioisotope ionize the air within the detector, causing it to conduct a tiny electric current. When smoke enters the chamber, conductivity drops and an alarm is triggered.

Artificial transmutation can lead to the synthesis of entirely new elements never before seen on Earth. In fact, all the *transuranium elements*—those elements with atomic numbers greater than 92—have been produced by bombardment reactions. For example, plutonium-241 (^{241}Pu) can be made by bombardment of uranium-238 with α particles:

$$^{238}_{92}\text{U} + {}^{4}_{2}\text{He} \longrightarrow {}^{241}_{94}\text{Pu} + {}^{1}_{0}\text{n}$$

Plutonium-241 is itself radioactive, with a half-life of 14.35 years, decaying by β emission to yield americium-241, which in turn, decays by α emission with a half-life

of 432.2 years. (If the name *americium* sounds vaguely familiar, it is because this radioisotope is used in smoke detectors.)

$$^{241}_{94}\text{Pu} \longrightarrow {}^{241}_{95}\text{Am} + {}^{0}_{-1}\text{e}$$

Note that all the equations just given for artificial transmutations are balanced. The sum of the mass numbers and the sum of the charges are the same on both sides of each equation.

CHEMISTRY IN ACTION

Body Imaging

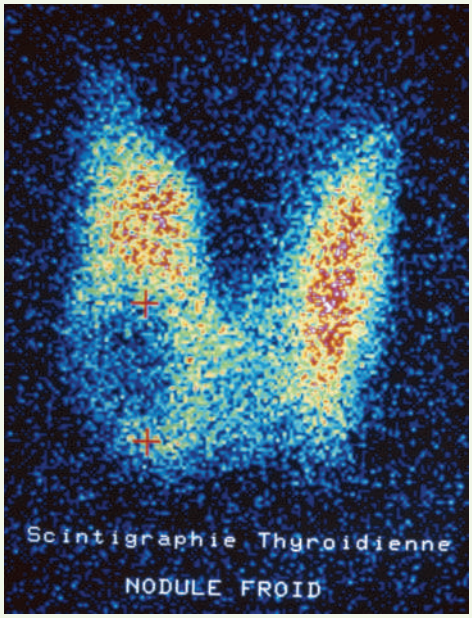
We are all familiar with the appearance of a standard X-ray image, produced when X rays pass through the body and the intensity of the radiation that exits is recorded on film. X-ray imaging is, however, only one of a host of noninvasive imaging techniques that are now in common use.

Among the most widely used imaging techniques are those that give diagnostic information about the health of various parts of the body by analyzing the distribution pattern of a radioactively tagged substance in the body. A radiopharmaceutical agent that is known to concentrate in a specific organ or other body part is injected into the body, and its distribution pattern is monitored by an external radiation detector such as a γ ray camera. Depending on the medical condition, a diseased part might concentrate more of the radiopharmaceutical than normal and thus show up on the film as a radioactive hot spot against a cold background. Alternatively, the diseased part might concentrate less of the radiopharmaceutical than normal and thus show up as a cold spot on a hot background.

Among the radioisotopes most widely used for diagnostic imaging is technetium-99*m,* whose short half-life of only six hours minimizes the patient's exposure to radioactivity. Enhanced body images, such as the thyroid scan shown in the accompanying photograph, are an important tool in the diagnosis of cancer and many other medical conditions.

Several other techniques now used in medical diagnosis are made possible by *tomography,* a technique in which computer processing allows production of images through "slices" of the body. In X-ray tomography, commonly known as *CAT* or *CT* scanning (computerized tomography), the X-ray source and an array of detectors move rapidly in a circle around a patient's body, collecting up to 90,000 readings. CT scans can detect structural abnormalities such as tumors without the use of radioactive materials.

Combining tomography with radioisotope imaging gives cross-sectional views of regions that concentrate a radioactive substance. We learned of one such technique, PET, in the opening of this chapter. PET utilizes radioisotopes that emit positrons and ultimately yield γ rays. Oxygen-15, nitrogen-13, carbon-11, and fluorine-18 are commonly used for PET because they can be readily incorporated into many physiologically active compounds. An ^{18}F-labeled glucose derivative, for instance, is useful for imaging brain regions that respond to various stimuli. The disadvantage of PET scans is that the necessary radioisotopes are so short-lived that they must be produced on-site immediately before use. The cost of PET is therefore high, because a hospital must install and maintain the necessary nuclear facility.



▲ A scintillation image obtained using I-131 indicates the presence of a "cold" thyroid nodule (lower left). A cold nodule, composed of tissue that does not absorb I-131, has a higher probability of being cancerous.

Magnetic resonance imaging (MRI) is a medical imaging technique that uses powerful magnetic and radio-frequency fields to interact with specific nuclei in the body (usually the nuclei of hydrogen atoms) to generate images in which the contrast between soft tissues is much better than that seen with CT. The original name for this technique was *nuclear* magnetic resonance imaging, but the *nuclear* was eliminated because in the public mind this word conjured up negative images of ionizing radiation. Ironically, MRI does not involve any nuclear radiation at all.

CIA Problem 11.6 What are the advantages of CT and PET relative to conventional X rays?

CIA Problem 11.7 What advantages does MRI have over CT and PET imaging?

CIA Problem 11.8 Technetium-99*m* (Tc-99*m*) is used extensively in diagnostic applications, including PET scans. The half-life of Tc-99*m* is six hours. How long will it take for the Tc-99*m* activity to decrease to 0.1% of its original activity?

Worked Example 11.8 Balancing Nuclear Reactions: Transmutation

Californium-246 is formed by bombardment of uranium-238 atoms. If 4 neutrons are also formed, what particle is used for the bombardment?

ANALYSIS First, write an incomplete nuclear equation incorporating the known information:

$$^{238}_{92}\text{U} + \text{?} \longrightarrow {}^{246}_{98}\text{Cf} + 4\,{}^{1}_{0}\text{n}$$

Then find the numbers of nucleons and charges necessary to balance the equation. In this instance, there are 238 nucleons on the left and 246 + 4 = 250 nucleons on the right, so the bombarding particle must have 250 − 238 = 12 nucleons. Furthermore, there are 92 nuclear charges on the left and 98 on the right, so the bombarding particle must have 98 − 92 = 6 protons.

SOLUTION
The missing particle is $^{12}_{6}\text{C}$.

$$^{238}_{92}\text{U} + {}^{12}_{6}\text{C} \longrightarrow {}^{246}_{98}\text{Cf} + 4\,{}^{1}_{0}\text{n}$$

PROBLEM 11.15

What isotope results from α decay of the americium-241 in smoke detectors?

PROBLEM 11.16

The element berkelium, first prepared at the University of California at Berkeley in 1949, is made by α bombardment of $^{241}_{95}\text{Am}$. Two neutrons are also produced during the reaction. What isotope of berkelium results from this transmutation? Write a balanced nuclear equation.

PROBLEM 11.17

Write a balanced nuclear equation for the reaction of argon-40 with a proton:

$$^{40}_{18}\text{Ar} + {}^{1}_{1}\text{H} \longrightarrow \text{?} + {}^{1}_{0}\text{n}$$

11.9 Nuclear Fission and Nuclear Fusion

Learning Objective:

- Write and balance equations for nuclear fission and nuclear fusion reactions.

Nuclear fission When heavy nuclei fragment into lighter nuclei.

Nuclear fusion When lighter nuclei combine to form a heavier nuclide.

In the preceding section, we learned that particle bombardment of various elements causes artificial transmutation and results in the formation of new, usually heavier elements. Under very special conditions with a very few isotopes, however, different kinds of nuclear events occur. Certain very heavy nuclei can split apart, and certain very light nuclei can fuse together. The two resultant processes—**nuclear fission** for the fragmenting of heavy nuclei and **nuclear fusion** for the joining together of light nuclei—have changed the world since their discovery in the late 1930s and early 1940s.

The huge amounts of energy that accompany these nuclear processes are the result of mass-to-energy conversions and are predicted by Einstein's equation

$$E = mc^2$$

where E = energy, m = mass change associated with the nuclear reaction, and c = the speed of light $(3.0 \times 10^8\ \text{m/s})$. Based on this relationship, a mass change as small as 1 μg results in a release of 9.00 × 104 kJ of energy!

Nuclear Fission

Uranium-235 is the only naturally occurring isotope that undergoes nuclear fission. When this isotope is bombarded by a stream of relatively slow-moving neutrons, its nucleus splits to give isotopes of other elements. The split can take place in more than 400 ways, and more than 800 different fission products have been identified. One of the

more frequently occurring pathways generates barium-142 and krypton-91, along with two additional neutrons plus the one neutron that initiated the fission:

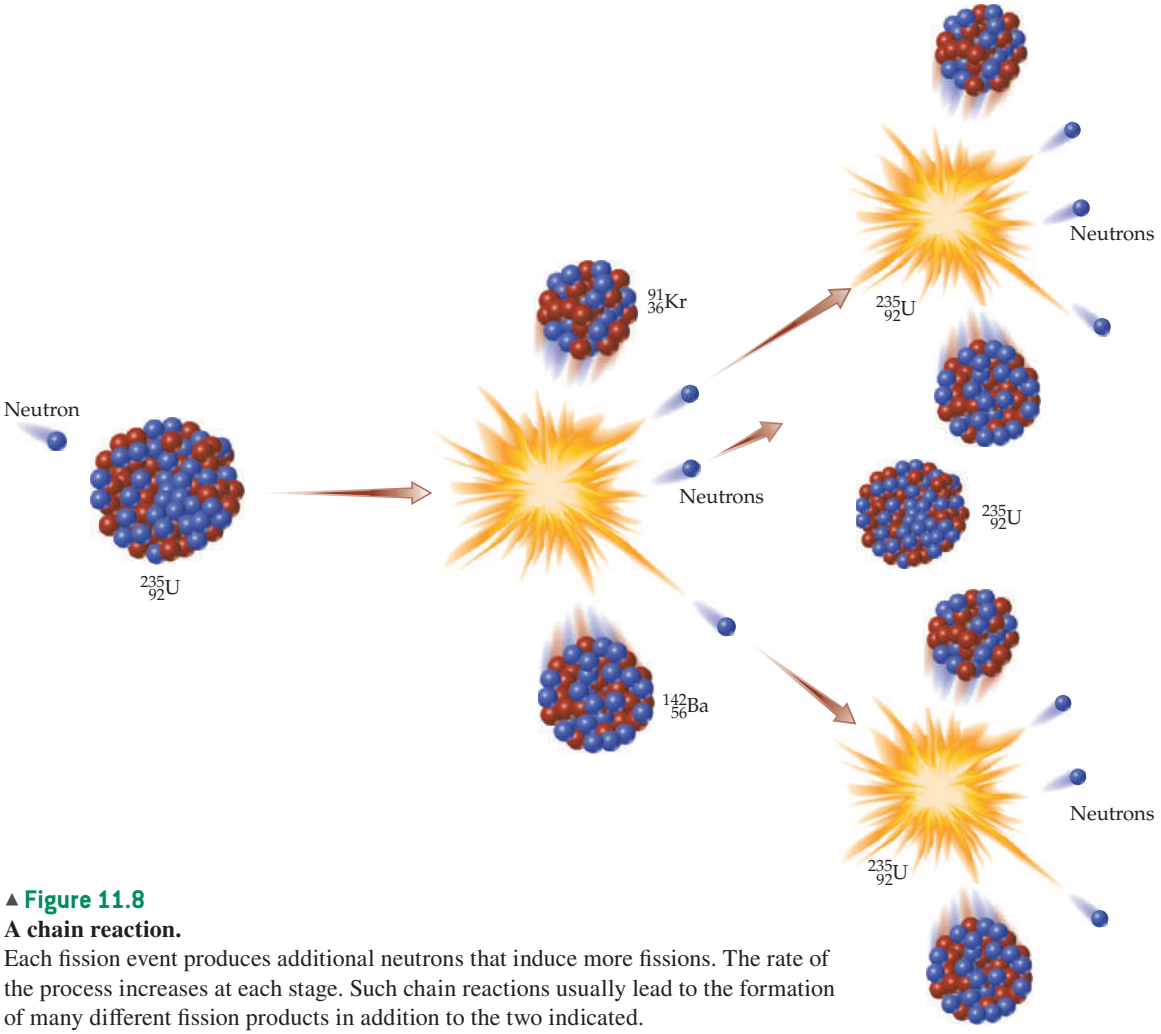
$$^{1}_{0}\text{n} + {}^{235}_{92}\text{U} \longrightarrow {}^{142}_{56}\text{Ba} + {}^{91}_{36}\text{Kr} + 3\,{}^{1}_{0}\text{n}$$

As indicated by the balanced nuclear equation above, *one* neutron is used to initiate fission of a ^{235}U nucleus, but *three* neutrons are released. Thus, a nuclear **chain reaction** can be started: one neutron initiates one fission that releases three neutrons. Those three neutrons initiate three new fissions that release nine neutrons. The nine neutrons initiate nine fissions that release 27 neutrons, and so on at an ever-faster pace (Figure 11.8). It is worth noting that the neutrons produced by fission reactions are highly energetic. They possess penetrating power greater than α and β particles, but less than γ rays. In a nuclear fission reactor, the neutrons must first be slowed down to allow them to react. If the sample size is small, many of the neutrons escape before initiating additional fission events, and the chain reaction stops. If a sufficient amount of ^{235}U is present, however—an amount called the **critical mass**—then the chain reaction becomes self-sustaining. Under high-pressure conditions that confine the ^{235}U to a small volume, the chain reaction occurs so rapidly that a nuclear explosion results. For ^{235}U, the critical mass is about 56 kg, although the amount can be reduced to approximately 15 kg by placing a coating of ^{238}U around the ^{235}U to reflect back some of the escaping neutrons.

Chain reaction A reaction that, once started, is self-sustaining.

Critical mass The minimum amount of radioactive material needed to sustain a nuclear chain reaction.

An enormous quantity of heat is released during nuclear fission—the fission of just 1.0 g of uranium-235 produces 1.4×10^{9} kJ for instance. This heat can be used to convert water to steam, which can be harnessed to turn huge generators and produce electric power. Although the United States, France, and Japan are responsible for nearly 50% of all nuclear power generated worldwide, only about 19% of the



▲ **Figure 11.8**
A chain reaction.
Each fission event produces additional neutrons that induce more fissions. The rate of the process increases at each stage. Such chain reactions usually lead to the formation of many different fission products in addition to the two indicated.

electricity consumed in the United States is nuclear-generated. In France, nearly 80% of electricity is generated by nuclear power plants.

Two major objections that have caused much public debate about nuclear power plants are safety and waste disposal. Although a nuclear explosion is not possible under the conditions that typically exist in a power plant, there is a serious potential radiation hazard should an accident rupture the containment vessel holding the nuclear fuel and release radioactive substances to the environment. There have been several such instances in the past 35 years, most notably Three Mile Island in Pennsylvania (1979), Chernobyl in the Ukraine (1986), and the more recent Fukushima reactor damaged by a tsunami in Japan (2011). Perhaps even more important is the problem posed by disposal of radioactive wastes from nuclear plants. Many of these wastes have such long half-lives that hundreds or even thousands of years must elapse before they will be safe for humans to approach. How to dispose of such hazardous materials safely is an unsolved problem.

PROBLEM 11.18

What other isotope besides tellurium-137 is produced by nuclear fission of uranium-235?

$$^{235}_{92}\text{U} + {}^{1}_{0}\text{n} \longrightarrow {}^{137}_{52}\text{Te} + 2\,{}^{1}_{0}\text{n} + \,?$$

PROBLEM 11.19

Uranium-238 is not used as a nuclear power source because it does not undergo nuclear fission. However, it can absorb a neutron and then undergo a series of β decays to produce plutonium-239, which is fissionable and can also be used as a nuclear fuel. Complete the following nuclear reaction:

$$^{238}_{92}\text{U} + {}^{1}_{0}n \longrightarrow \,?? \xrightarrow{\beta} \,?? \xrightarrow{\beta} {}^{239}_{94}\text{Pu}$$

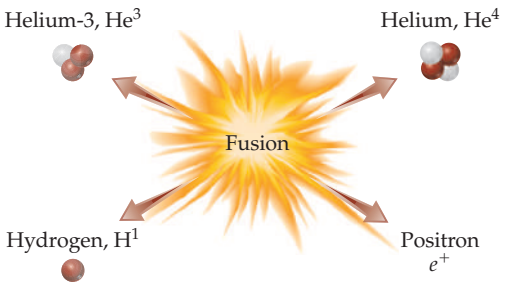
Nuclear Fusion

Just as heavy nuclei such as ^{235}U release energy when they undergo *fission,* very light nuclei such as the isotopes of hydrogen release enormous amounts of energy when they undergo *fusion*. In fact, it is just such a fusion reaction of hydrogen nuclei to produce helium that powers our sun and other stars. Among the processes thought to occur in the sun are those in the following sequence leading to helium-4:

$$^{1}_{1}\text{H} + {}^{2}_{1}\text{H} \longrightarrow {}^{3}_{2}\text{He}$$

$$^{3}_{2}\text{He} + {}^{3}_{2}\text{He} \longrightarrow {}^{4}_{2}\text{He} + 2\,{}^{1}_{1}\text{H}$$

$$^{3}_{2}\text{He} + {}^{1}_{1}\text{H} \longrightarrow {}^{4}_{2}\text{He} + {}^{0}_{1}e$$



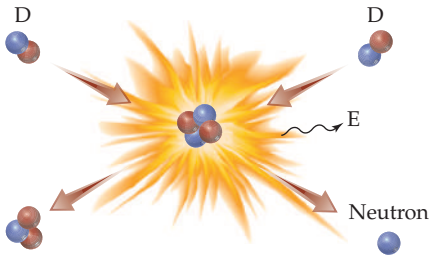
Under the conditions found in stars, where the temperature is on the order of 2×10^7 K and pressures approach 10^{10} Pa, nuclei are stripped of all their electrons and have enough kinetic energy that nuclear fusion readily occurs. The energy of our sun, and all the stars, comes from thermonuclear fusion reactions in their core that fuse hydrogen and other light elements, transmuting them into heavier elements. On Earth, however, the necessary conditions for nuclear fusion are not easily created. For more than 50 years, scientists have been trying to create the necessary conditions for fusion in laboratory reactors, including the Tokamak Fusion Test Reactor (TFTR) at Princeton, New Jersey, and the Joint European Torus (JET) at Culham, England. Recent advances in reactor design have raised hopes that a commercial fusion reactor will be realized within the next 20 years.

If the dream becomes reality, controlled nuclear fusion can provide the ultimate cheap, clean power source. The fuel is deuterium (^{2}H), available in the oceans in limitless amounts, and there are few radioactive by-products.

KEY CONCEPT PROBLEM 11.20

One of the possible reactions for nuclear fusion involves the collision of 2 deuterium nuclei. Complete the reaction by identifying the missing particle:

$$^{2}_{1}\mathrm{H} + {}^{2}_{1}\mathrm{H} \longrightarrow {}^{1}_{0}n + \ ?$$



HANDS-ON CHEMISTRY 11.1

Nuclear power plants provide about 20% of the electricity used in the United States. Nuclear reactors also serve as energy sources for U.S. Navy ships, including aircraft carriers and submarines. Perform a web search and respond to the following items:

a. Compare and contrast the two nuclear power sources (land-based vs. naval).

b. Locate a web site that provides a virtual tour of a nuclear power plant (such as at www.edfenergy.com/energyfuture/key-info/nuclear-power-plants/interactive-tour powered?) and identify the key components.

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Identify reactants and products of nuclear reactions as elements, isotopes, or subatomic particles.** A *nuclear reaction* is one that changes an atomic nucleus, causing the change of one element or isotope into another. Isotopes are atoms of a given element that have different atomic masses. Subatomic particles (protons, neutrons, electrons) can also be included as products or reactants in nuclear reactions *(see Problems 22, 24–27, 36, 37, 40, 41, and 44–53).*
- **Identify the different types of radiation and the properties of each type.** *Radioactivity* is the spontaneous emission of radiation from the nucleus of an unstable atom. The three major kinds of radiation are called *alpha* (α), *beta* (β), and gamma (γ). Alpha radiation consists of helium nuclei, small particles containing 2 protons and 2 neutrons $(^{4}_{2}\mathrm{He})$; β radiation consists of electrons $(^{0}_{-1}\mathrm{e})$; and γ radiation consists of high-energy light waves. Every element in the periodic table has at least one radioactive isotope, or *radioisotope (see Problems 22, 25, 27, 29, 30–32, 40, 41, 44–47, 49, 75, 76, and 86).*
- **Identify natural isotopes, and distinguish between stable and unstable isotopes.** *Natural* isotopes are found in the earth's crust, for elements with atomic numbers $Z \leq 92$. Stable isotopes are naturally occurring isotopes that do not undergo spontaneous radioactive decay *(see Problems 24, 26, 27, and 39).*
- **Write and balance nuclear reactions involving alpha, beta, and positron emission modes of radioactive decay.** Loss of an α particle leads to a new atom whose atomic number is 2 less than that of the starting atom. Loss of a β particle leads to an atom whose atomic number is 1 greater than that of the starting atom:

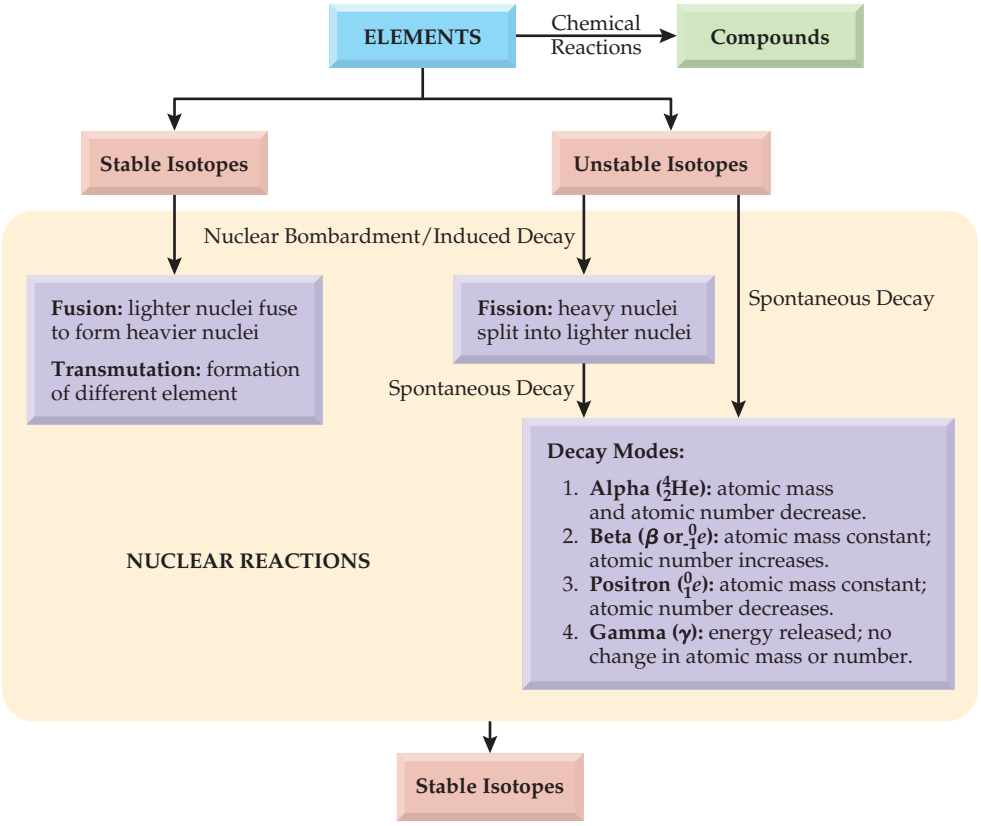
$$\alpha \text{ emission: } {}^{238}_{92}\mathrm{U} \longrightarrow {}^{234}_{90}\mathrm{Th} + {}^{4}_{2}\mathrm{He}$$

$$\beta \text{ emission: } {}^{131}_{53} \longrightarrow {}^{131}_{54}\mathrm{Xe} + {}^{0}_{-1}\mathrm{e}$$

A nuclear reaction is balanced when the sum of the *nucleons* (protons and neutrons) is the same on both sides of the reaction arrow and when the sum of the charges on the nuclei plus any ejected subatomic particles is the same *(see Problems 22, 24–27, 44–53, 59, 75–78, 81, and 83).*
- **Determine the half-life of a radioactive isotope, and use the half-life to calculate the fraction of the isotope remaining as a function of time.** The rate of a nuclear reaction is expressed in units of *half-life* $(t_{1/2})$, where one half-life is the amount of time necessary for one half of the radioactive sample to decay. The fraction of an isotope remaining after a given amount of time can be expressed as $(\text{fraction remaining} = (0.5)^{n})$, where n = number of half-lives *(see Problems 21, 23, 28, 29, 54–59, 71, 77,and 79).*
- **Identify the types of ionizing radiation, and calculate the radiation intensity as a function of distance from the radiation source.** High-energy radiation of all types—α particles, β particles, γ rays, and X rays—is called *ionizing radiation*. When any of these kinds of radiation strikes an atom, it dislodges an orbital electron and gives a reactive ion that can be lethal to living cells. Gamma rays and X rays are the most penetrating and most harmful types of external radiation; α and β particles are the most dangerous types of internal radiation because of their high energy and the resulting damage to surrounding tissue. Radiation intensity (I) decreases with the square of the distance from the source *(see Problems 33–37, 63, 65, 70, 78, 80, and 81).*
- **Identify methods for detecting radiation and the units used to measure radiation exposure.** Radiation intensity is expressed in different ways according to the property being measured. The *curie (Ci)* measures the number of radioactive disintegrations per second in a sample; the *roentgen (R)* measures the ionizing ability of radiation. The *rad* measures the amount of radiation energy absorbed per gram of tissue; and the *Sv* measures the amount of tissue damage caused by radiation. Radiation effects become noticeable with a human exposure of 0.25 Sv and become lethal at an exposure above 6.00 Sv *(see Problems 60–69, 73, and 74).*
- **Write and balance equations for nuclear transmutation reactions.** *Transmutation* is the change of one element into another brought about by a nuclear reaction. Most known radioisotopes do not occur naturally but are made by bombardment of an atom with a high-energy particle. In the ensuing collision between particle and atom, a nuclear change occurs and a new element is produced by *artificial transmutation (see Problems 38, 39, 48, 50, 51, 53, 84, 87, and 88).*

• **Write and balance equations for nuclear fission and nuclear fusion reactions.** With a very few isotopes, including $^{235}_{92}U$, the nucleus is split apart by neutron bombardment to give smaller fragments. A large amount of energy is released during this *nuclear fission*, leading to use of the reaction for generating electric power. *Nuclear fusion* results when small nuclei such as those of tritium ($^{3}_{1}H$) and deuterium ($^{2}_{1}H$) combine to give a heavier nucleus *(see Problems 42, 43, 48, 78, 84, and 85).*

CONCEPT MAP: SOLUTIONS



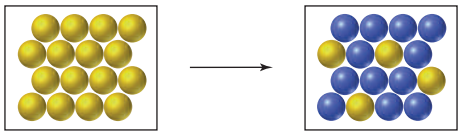
▲ **Figure 11.9 Concept Map.** Nuclear reactions involve changes in the composition of the nucleus of an atom, usually resulting in a change in the identity of the element. Some isotopes are stable, while other isotopes undergo spontaneous radioactive decay. Nuclei of a given element can also undergo transmutation, a nuclear reaction in which a nucleus is bombarded with light nuclei or subatomic particles to create a different nucleus.

KEY WORDS

Alpha (α) particle, *p. 364*
Artificial radioisotopes, *p. 365*
Artificial transmutation, *p. 380*
Beta (β) particle, *p. 364*
Chain reaction, *p. 383*
Cosmic rays, *p. 375*
Critical mass, *p. 383*
Decay series, *p. 371*
Electron capture (E.C.), *p. 369*
Gamma (γ) radiation, *p. 364*
Half-life ($t_{1/2}$) *p. 370*
Ionizing radiation, *p. 375*
Natural radioisotopes, *p. 365*
Nuclear decay, *p. 366*
Nuclear fission, *p. 382*
Nuclear fusion, *p. 382*
Nuclear reaction, *p. 363*
Nucleon, *p. 363*
Nuclide, *p. 363*
Positron, *p. 368*
Radioactivity, *p. 364*
Radioisotope, *p. 365*
Radionuclide, *p. 365*
Transmutation, *p. 366*
X rays, *p. 375*

UNDERSTANDING KEY CONCEPTS

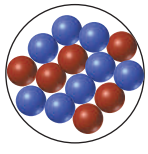
11.21 Magnesium-28 decays by β emission to give aluminum-28. If yellow spheres represent $^{28}_{12}Mg$ atoms and blue spheres represent $^{28}_{13}Al$ atoms, how many half-lives have passed in the following sample?



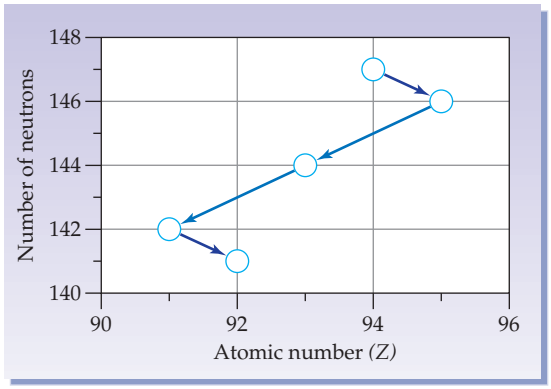
11.22 Write a balanced nuclear equation to represent the decay reaction described in Problem 11.21.

11.23 Refer to Figure 11.4 and then make a drawing similar to those in Problem 11.21 representing the decay of a sample of $^{28}_{12}Mg$ after approximately four half-lives have passed.

11.24 Write the symbol of the isotope represented by the following drawing. Blue spheres represent neutrons and red spheres represent protons. Based on Figure 11.2, would you expect this to be a stable or an unstable isotope?

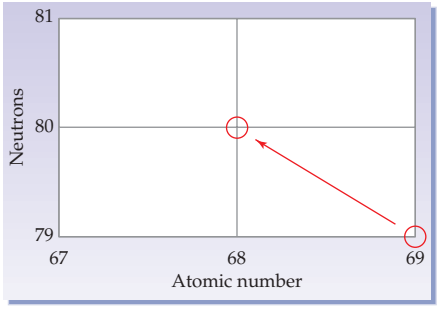


11.25 Shown in the following graph is a portion of the decay series for plutonium-241 ($^{241}_{94}Pu$). The series has two kinds of arrows: shorter arrows pointing right and longer arrows pointing left. Which arrow corresponds to an α emission, and which to a β emission? Explain.

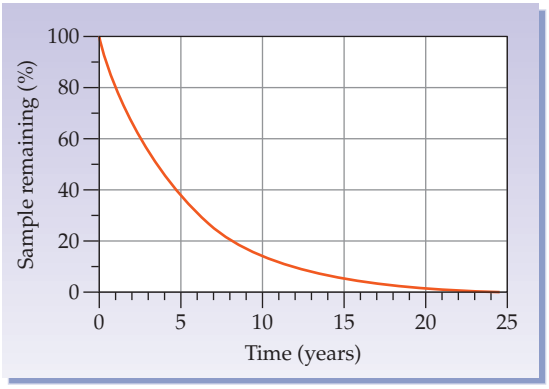


11.26 Identify and write the symbol for each of the five nuclides in the decay series shown in Problem 11.25.

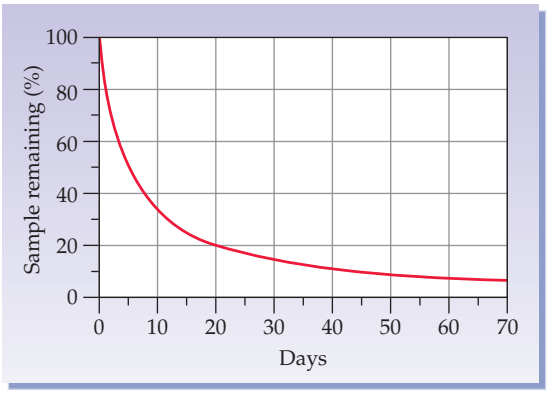
11.27 Identify the isotopes involved, and tell the type of decay process occurring in the following nuclear reaction:



11.28 What is the half-life of the radionuclide that shows the following decay curve?



11.29 What is wrong with the following decay curve? Explain.



ADDITIONAL PROBLEMS

RADIOACTIVITY (SECTIONS 11.1–11.4 AND 11.6)

11.30 What does it mean to say that a substance is radioactive?

11.31 Describe how α radiation, β radiation, γ radiation, positron emission, and electron capture differ.

11.32 List three of the five ways in which a nuclear reaction differs from a chemical reaction.

11.33 What happens when ionizing radiation strikes an atom in a chemical compound?

11.34 How does ionizing radiation lead to cell damage?

11.35 What are the main sources of background radiation?

11.36 How can a nucleus emit an electron during β decay when there are no electrons present in the nucleus to begin with?

11.37 What is the difference between an α particle and a helium atom?

NUCLEAR DECAY AND TRANSMUTATION (SECTIONS 11.4, 11.8, AND 11.9)

11.38 What does it mean to say that a nuclear equation is balanced?

11.39 What are transuranium elements, and how are they made? Are they stable or unstable?

11.40 What happens to the mass number and atomic number of an atom that emits an α particle? A β particle?

11.41 What happens to the mass number and atomic number of an atom that emits a γ ray? A positron?

11.42 How does nuclear fission differ from normal radioactive decay?

11.43 What characteristic of uranium-235 fission causes a chain reaction?

11.44 What products result from radioactive decay of the following β emitters?

(a) $^{35}_{16}S$ **(b)** $^{24}_{10}Ne$ **(c)** $^{90}_{38}Sr$

11.45 What radioactive nuclides will produce the following products following α decay?

(a) $^{186}_{76}Os$ **(b)** $^{204}_{85}At$ **(c)** $^{241}_{94}Pu$

11.46 Identify the starting radioisotopes needed to balance each of these nuclear reactions:

(a) $? + {}^{4}_{2}He \longrightarrow {}^{113}_{49}In$ **(b)** $? + {}^{4}_{2}He \longrightarrow {}^{13}_{7}N + {}^{1}_{0}n$

11.47 Identify the radioisotope product needed to balance each of these nuclear reactions:

(a) $^{26}_{11}Na \longrightarrow ? + {}^{0}_{-1}e$ **(b)** $^{212}_{83}Bi \longrightarrow ? + {}^{4}_{2}He$

11.48 Balance the following equations for the nuclear fission of $^{235}_{92}U$:

(a) $^{235}_{92}U + {}^{1}_{0}n \longrightarrow {}^{160}_{62}Sm + {}^{72}_{30}Zn + ? \, {}^{1}_{0}n$

(b) $^{235}_{92}U + {}^{1}_{0}n \longrightarrow {}^{87}_{35}Br + ? + 3 \, {}^{1}_{0}n$

11.49 Complete the following nuclear equations and identify each as α decay, β decay, positron emission, or electron capture:

(a) $^{126}_{50}Sn \longrightarrow ? + {}^{126}_{51}Sb$ **(b)** $^{210}_{88}Ra \longrightarrow ? + {}^{206}_{86}Rn$

(c) $^{76}_{36}Kr + ? \longrightarrow {}^{76}_{35}Br$

11.50 For centuries, alchemists dreamed of turning base metals into gold. The dream finally became reality when it was shown that mercury-198 can be converted into gold-198 when bombarded by neutrons. What small particle is produced in addition to gold-198? Write a balanced nuclear equation for the reaction.

11.51 Cobalt-60 (half-life = 5.3 years) is used to irradiate food, to treat cancer, and to disinfect surgical equipment. It is produced by irradiation of cobalt-59 in a nuclear reactor. It decays to nickel-60. Write nuclear equations for the formation and decay reactions of cobalt-60.

11.52 Bismuth-212 attaches readily to monoclonal antibodies and is used in the treatment of various cancers. This bismuth-212 is formed after the parent isotope undergoes a decay series consisting of four α decays and one β decay (the decays could be in any order). What is the parent isotope for this decay series?

11.53 Meitnerium-266 ($^{266}_{109}Mt$) was prepared in 1982 by bombardment of bismuth-209 atoms with iron-58. What other product must also have been formed? Write a balanced nuclear equation for the transformation.

HALF-LIFE (SECTION 11.5)

11.54 What does it mean when we say that strontium-90, a waste product of nuclear power plants, has a half-life of 28.8 years?

11.55 How many half lives must pass for the mass of a radioactive sample to decrease to 35% of the original mass? To 10%?

11.56 Selenium-75, a β emitter with a half-life of 120 days, is used medically for pancreas scans.

(a) Approximately how long would it take for a 0.050 g sample of selenium-75 to decrease to 0.010 g?

(b) Approximately how much selenium-75 would remain from a 0.050 g sample that has been stored for one year? (Hint: How many half-lives are in one year?)

11.57 Approximately how long would it take a sample of selenium-75 to lose 75% of its radioactivity? To lose 99%? (See Problem 11.56.)

11.58 The half-life of mercury-197 is 64.1 hours. If a patient undergoing a kidney scan is given 5.0 ng of mercury-197, how much will remain after 7 days? After 30 days?

11.59 Gold-198, a β emitter used to treat leukemia, has a half-life of 2.695 days. The standard dosage is about 37 MBq/kg body weight.

(a) What is the product of the β emission of gold-198?

(b) How long does it take a 11.1×10^8 Bq sample of gold-198 to decay so that only 1.39×10^8 Bq remains?

(c) How many becquerels are required in a single dosage administered to a 70.0 kg adult?

MEASURING RADIOACTIVITY (SECTION 11.7)

11.60 Describe how a Geiger counter works.

11.61 Describe how a film badge works.

11.62 Describe how a scintillation counter works.

11.63 Why are rems the preferred units for measuring the health effects of radiation?

11.64 Approximately what amount (in Sv) of short-term exposure to radiation produces noticeable effects in humans?

11.65 Match each unit in the left column with the property being measured in the right column:

1. curie	(a) Ionizing intensity of radiation
2. rem	(b) Amount of tissue damage
3. rad	(c) Number of disintegrations per second
4. roentgen	(d) Amount of radiation per gram of tissue

11.66 Technetium-99*m* is used for radioisotope-guided surgical biopsies of certain bone cancers. A patient must receive an injection of 10.4×10^8 Bq of technetium-99*m* 6–12 hours before surgery. If the activity of the solution is 5.55×10^8 Bq/mL, what volume should be injected?

11.67 Sodium-24 is used to study the circulatory system and to treat chronic leukemia. It is administered in the form of saline (NaCl) solution, with a therapeutic dosage of 6.66 MBq/kg body weight.

(a) What dosage (in MBq) would be administered to a 68 kg adult patient?

(b) How many milliliters of a 2.40×10^8 Bq/mL solution are needed to treat a 68 kg adult?

11.68 A selenium-75 source is producing 3 Sv at a distance of 2.0 m?

(a) What is its intensity at 16 m?

(b) What is its intensity at 25 m?

11.69 If a radiation source has an intensity of 6.50 Sv at 1.0 m, what distance is needed to decrease the intensity of exposure to below 0.25 Sv, the level at which no effects are detectable?

CONCEPTUAL PROBLEMS

11.70 Film badge dosimeters typically include filters to target specific types of radiation. A film badge is constructed that includes a region containing a tin foil filter, a region containing a plastic film filter, and a region with no filter. Which region monitors exposure to α-radiation? Which monitors exposure to β-radiation? Which monitors γ-radiation? Explain.

11.71 Some dried beans with a $^{14}C/^{12}C$ ratio one-eighth of the current value are found in an old cave. How old are the beans?

11.72 Harmful chemical spills can often be cleaned up by treatment with another chemical. For example, a spill of H_2SO_4 might be neutralized by addition of $NaHCO_3$. Why is it that the harmful radioactive wastes from nuclear power plants cannot be cleaned up as easily?

11.73 Why is a scintillation counter or Geiger counter more useful for determining the existence and source of a new radiation leak than a film badge?

11.74 A Geiger counter records an activity of 28 counts per minute (cpm) when located at a distance of 10 m. What will be the activity (in cpm) at a distance of 5 m?

11.75 Most of the stable isotopes for elements lighter than Ca-40 have equal numbers of protons and neutrons in the nucleus. What would be the most probable decay mode for an isotope that had more protons than neutrons? More neutrons than protons?

11.76 Technetium-99*m,* used for brain scans and to monitor heart function, is formed by decay of molybdenum-99.

(a) By what type of decay does ^{99}Mo produce ^{99m}Tc?

(b) Molybdenum-99 is formed by neutron bombardment of a natural isotope. If one neutron is absorbed and there are no other by-products of this process, from what isotope is ^{99}Mo formed?

11.77 The half-life of technetium-99*m* (Problem 11.76) is 6.01 hours. If a sample with an initial activity of 5.55×10^5 Bq is injected into a patient, what is the activity in 24 hours, assuming that none of the sample is excreted?

11.78 Plutonium-238 is an α emitter used to power batteries for heart pacemakers.

(a) Write the balanced nuclear equation for this emission.

(b) Why is a pacemaker battery enclosed in a metal case before being inserted into the chest cavity?

11.79 Sodium-24, a beta-emitter used in diagnosing circulation problems, has a half-life of 15 hours.

(a) Write the balanced nuclear equation for this emission.

(b) What fraction of sodium-24 remains after 50 hours?

11.80 High levels of radioactive fallout after the 1986 accident at the Chernobyl nuclear power plant in what is now Ukraine resulted in numerous miscarriages in humans and many instances of farm animals born with severe defects. Why are embryos and fetuses particularly susceptible to the effects of radiation?

11.81 Iodine-131 is a radioactive isotope used to treat thyroid conditions.

(a) What is the mode of radioactive decay for I-131? Write a balanced nuclear reaction to illustrate.

(b) The half-life of I-131 is eight days. What fraction of I-131 remains after four weeks? After eight weeks?

11.82 What are the main advantages of nuclear fission relative to nuclear fusion as an energy source? What are the drawbacks?

11.83 Although turning lead into gold in a nuclear reactor is technologically feasible (Problem 11.50), it is not economical. It is far easier to convert gold into lead. The process involves a series of neutron bombardments, and can be summarized as

$$^{197}_{79}\text{Au} + ?\ ^{1}_{0}n \longrightarrow {}^{204}_{82}\text{Pb} + ?\ ^{0}_{-1}e$$

How many neutrons and β particles are involved?

11.84 Balance the following transmutation reactions:

(a) $^{253}_{99}\text{Es} + ? \longrightarrow {}^{256}_{101}\text{Md} + {}^{1}_{0}\text{n}$

(b) $^{250}_{98}\text{Cf} + {}^{11}_{5}\text{B} \longrightarrow ? + 4\ {}^{1}_{0}\text{n}$

11.85 Boron is used in *control rods* for nuclear reactors because it can absorb neutrons to keep a chain reaction from becoming supercritical, and decays by emitting α particles (i.e., a He-4 nucleus). Balance the equation by supplying the missing product:

$$^{10}_{5}\text{B} + {}^{1}_{0}\text{n} \longrightarrow ? + {}^{4}_{2}\text{He}$$

11.86 Thorium-232 decays by a 10-step series, ultimately yielding lead-208. How many α particles and how many β particles are emitted?

11.87 Californium-246 is formed by bombardment of uranium-238 atoms. If four neutrons are formed as by-products, what particle is used for the bombardment?

11.88 The most recently discovered element 117 (Ununseptium, Uus) was synthesized by nuclear transmutation reactions in which berkelium-249 was bombarded with calcium-48. Two isotopes of Uus were identified:

$$^{48}_{20}\text{Ca} + {}^{249}_{97}\text{Bk} \longrightarrow {}^{294}_{117}\text{Uus} + ?\ {}^{1}_{0}n$$
$$^{48}_{20}\text{Ca} + {}^{249}_{97}\text{Bk} \longrightarrow {}^{293}_{117}\text{Uus} + ?\ {}^{1}_{0}n$$

How many neutrons are produced in each reaction?

GROUP PROBLEMS

11.89 One way to demonstrate the dose factor of ionizing radiation (penetrating distance $\times$ ionizing energy) is to think of radiation as cookies. Imagine that you have four cookies—an α cookie, a β cookie, a γ cookie, and a neutron cookie. Which one would you eat, which would you hold in your hand, which would you put in your pocket, and which would you throw away? Explain your reasoning.

11.90 One approach for treating cancerous tumors is **B**oron **N**eutron **C**apture **T**herapy (BNCT). Perform an internet search on BNCT and answer the following:

(a) How is boron introduced to the tumors?

(b) How are neutrons generated and directed to the tumor site?

(c) What nuclear reactions occur? What are the products of the nuclear reaction, and why is this a particularly effective treatment for tumors?

11.91 The nuclear disasters at the Chernobyl nuclear power plant disaster in 1986 and in Fukushima in 2011 resulted in significant releases of radioactive nuclear materials into the environment. Perform a web search to find information about one or both of these disasters and answer the following questions:

(a) What was the primary nuclear fuel? What other radioactive materials besides the fuel were released during the accident?

(b) What is the estimated amount of radioactive material released into the environment, and in what form was it released?

(c) How much additional radiation exposure would be expected for a person living near the power plant? How much additional radiation exposure would be expected for someone living at a considerable distance from the plant? How do these levels compare to the average background radiation dose for the average person? Express your answer as a percentage.

12

Introduction to Organic Chemistry: Alkanes

CONTENTS

CONCEPTS TO REVIEW

A. Covalent Bonds (Sections 4.1 and 4.2)

B. Multiple Covalent Bonds (Section 4.3)

C. Drawing Lewis Structures (Section 4.7)

D. VSEPR and Molecular Shapes (Section 4.8)

E. Polar Covalent Bonds (Section 4.9)

F. Polar Molecules (Section 4.10)

▲ As a mother attends to her daughter's scrape, organic chemistry aids in the healing process, in the form of the antibiotic cream she is using.

Think back to the days when you first learned to ride a bike; at some time you undoubtedly fell off and scraped an elbow or knee. Your mom or dad came to the rescue, picking you up, dusting you off, and putting some antibacterial ointment and a bandage on your scrape. Or think of the times you went camping or to the beach and your lips got so chapped that the lip balm you had so fortuitously brought with you felt like it saved your life. Both of these instances are examples of organic chemistry at work. Organic chemistry

impacts your life on a daily basis and is the foundation upon which biochemistry, the chemistry of life, is built. In Chapters 12–17 of this book, we will discuss organic chemistry, then later, in Chapters 18–29, the biochemistry that is built upon it. We will look at how organic molecules form, the reactions they undergo, and how those molecules, with their unique shapes, structures, and chemistries, affect our bodies and those of other living organisms.

The term *organic chemistry* was first introduced to describe the study of compounds derived from living organisms, whereas *inorganic chemistry* was used to refer to the study of compounds obtained from minerals. Scientists long believed that organic compounds could only be obtained from a living source; this concept, known as *vitalism,* hindered the study of these types of molecules because vitalist chemists believed that organic materials could not be synthesized from inorganic components. In 1828, Friedrich Wöhler prepared an organic compound, urea, from an inorganic salt, ammonium cyanate, disproving the theory of vitalism and truly pioneering the field of organic chemistry. Since compounds from living sources contain carbon as their primary component, organic chemistry is now defined as the study of carbon-based compounds.

Carbon is special because it can readily form strong bonds with both other carbon atoms and atoms of other elements (primarily hydrogen, oxygen, nitrogen, and halogens) to produce long chains and rings of organic compounds. Only carbon is able to form such a diverse and immense array of compounds; chemists have discovered or prepared more than 18 million organic compounds (versus less than 2 million inorganic compounds), the simplest class of which are called the hydrocarbons, or *alkanes,* compounds composed of only carbon and hydrogen connected by single bonds.

So, how does any of this relate to a scraped knee or chapped lips? While hydrocarbons themselves are important from an industrial and energy standpoint (being responsible for waxes, lubricants, and fuels, so-called *petrochemicals*), their biological and medical significance is sometimes lost at first glance. One of the hydrocarbon products obtained from petroleum is *petrolatum* (petroleum jelly; commonly known as Vaseline). This product is the footing upon which many medically useful ointments are based. Neosporin, a common antibiotic cream, is composed of a mixture of three different antibiotics in a petrolatum-based matrix. Lip balms (such as ChapStick or Carmex) also heavily rely on the presence of petroleum jelly for their healing properties, which, because of their *hydrophobic* nature, seal moisture in allowing the chapped skin to heal quickly. In fact, petroleum jelly alone, with no additives, is believed to be just as effective as either antibiotic ointments or lip balms in promoting the healing of wounded or dry skin. We will learn more about petrochemicals and petroleum jelly in the Chemistry in Action on page 428. As you can see, hydrocarbons play such a fundamental role in our everyday world it is appropriate that we begin our study of organic chemistry with alkanes.

12.1 The Nature of Organic Molecules

Learning Objective:

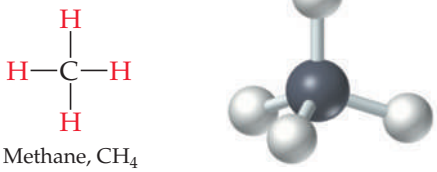
- Identify the general structural characteristics of organic molecules, in particular, the tetravalent nature of carbon and the different ways in which it can be expressed.

Let us begin our study of **organic chemistry**—the chemistry of carbon compounds—by reviewing what we have learned in earlier chapters about covalent bonds and molecular compounds and seeing how this applies to organic molecules in general (as you go through this section, take note of the three-dimensional shapes these molecules possess):

Organic chemistry The study of carbon compounds.

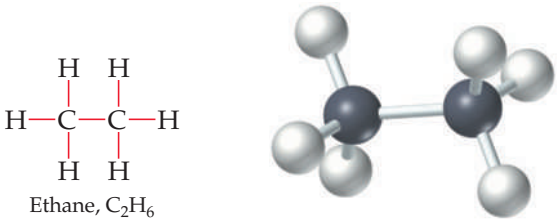
- **Carbon is tetravalent; it always forms four bonds** (Section 4.2). With the four valence electrons it already possesses, carbon has the ability to pick up four more from other atoms to fill out its octet. In the organic compound methane, for example, carbon is connected to four hydrogen atoms, with each hydrogen donating its valence electron to carbon to fill out its octet. Because it has groups attached to the carbon, methane is both tetrahedral (Section 4.8) and tetravalent.

CONCEPTS TO REVIEW Recall that a bond is formed when two electrons are shared between atoms.



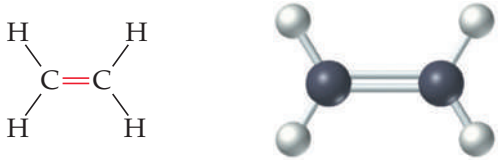
Methane, CH_4

- **Organic molecules, which are primarily composed of nonmetals, have covalent bonds** (Section 4.2). In ethane, for example, the bonds result from the sharing of two electrons, either between two C atoms or a C and an H atom.



Ethane, C_2H_6

- **Carbon forms multiple covalent bonds by sharing more than two electrons with a neighboring atom** (Section 4.3). In ethene, for example, the two carbon atoms share four electrons to form a double bond; in ethyne, the two carbons share six electrons to form a triple bond. Notice, however, that each carbon still possesses an octet: in ethene, four shared between the two carbons and two each shared with the hydrogens; in ethyne, six shared between the carbons and two with the hydrogen. The carbons in ethene and ethyne are not tetrahedral, but they are tetravalent.



Ethene

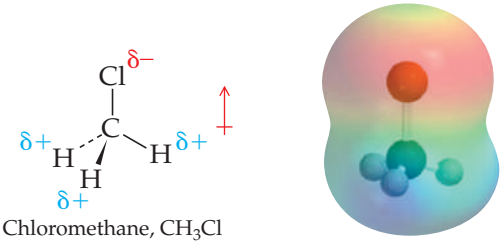
Ethyne, C_2H_2

In general, we can make the following statements:

A group is any atom or collection of atoms attached to the carbon.

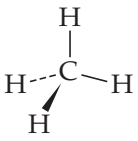
1. A carbon that has four groups attached will be tetrahedral (e.g., methane or ethane);
2. A carbon that has three groups attached will be trigonal planar (e.g., ethene);
3. A carbon that has two groups attached will be linear (e.g., ethyne).

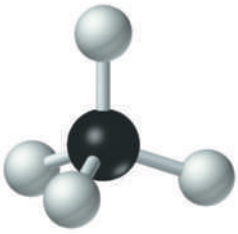
- **When carbon bonds to a more electronegative element, polar covalent bonds result** (Section 4.9). C—H bonds are considered nonpolar, as are most C—C bonds; however, if you replace a hydrogen with an oxygen or a halogen, for example, a polar covalent bond results. In chloromethane, for example, the electronegative chlorine atom attracts electrons more strongly than carbon, resulting in polarization of the C—Cl bond so that carbon and hydrogens have a partial positive charge, $\delta+$, and chlorine has a partial negative charge, $\delta-$. It is useful to think of polar covalent bonds in this manner, as it will later help to explain their reactivity. In electrostatic potential maps (Section 4.9), the chlorine atom is therefore in the red region of the map and the carbon atom in the blue region.



Chloromethane, CH_3Cl

- **Organic molecules have specific three-dimensional shapes** (Section 4.8). For example, when carbon is bonded to four atoms, as in methane, CH_4, the bonds are oriented toward the four corners of a regular tetrahedron with carbon in the center. Such three-dimensionality is commonly shown using normal lines for bonds in the plane of the page, dashed lines for bonds receding behind the page, and wedged lines for bonds coming out of the page.





- In addition to carbon, most **organic molecules always contain hydrogen and often also contain nitrogen and oxygen** (Section 4.7). Nitrogen can form single, double, and triple bonds to carbon, whereas oxygen can form single and double bonds. Hydrogen can only form single bonds to carbon because hydrogen can only hold two electrons in its valence shell:

C—N C—O C—H
C=N C=O
C≡N

Covalent bonding makes organic compounds quite different from the inorganic compounds we have been concentrating on up to this point. For example, inorganic compounds such as NaCl have high melting points and high boiling points because they consist of a large network of oppositely charged ions held together by strong electrical attractions. By contrast, organic compounds consist of atoms joined by covalent bonds, forming individual molecules. Because the organic molecules are attracted to one another only by weak nonionic intermolecular forces, organic compounds generally have lower melting and boiling points than inorganic salts. As a result, many simple organic compounds are liquids or low melting solids at room temperature, and a few are gases.

Other important differences between organic and inorganic compounds include solubility and electrical conductivity. Whereas many inorganic compounds dissolve in water to yield solutions of ions that conduct electricity, most organic compounds are insoluble in water, and almost all of those that are soluble do not conduct electricity. Only small polar organic molecules, such as glucose and ethanol, or large molecules with many polar groups, such as some proteins, interact with water molecules through both dipole–dipole interactions and/or hydrogen bonding and, thus, dissolve in water. This lack of water solubility for organic compounds has important practical consequences, varying from the difficulty in removing greasy dirt and cleaning up environmental oil spills to drug delivery and ensuring that a drug reaches its target organ or tissue.

Other unique properties of ionic compounds are discussed in Section 3.10

Recall from Section 8.2 the various intermolecular forces: dipole–dipole forces, London dispersion forces, and hydrogen bonds.

Section 9.9 explores how anions and cations in solution conduct electric current.

Recall from Section 9.2 that a compound is only soluble when the intermolecular forces between solvent and solute are comparable in strength to the intermolecular forces of the pure solvent or solute.

▲ Oil spills can be a serious environmental problem because oil is insoluble in water.

LOOKING AHEAD The interior of a living cell is largely a water solution that contains many hundreds of different compounds. In Section 23.7, we will see how cells use membranes composed of water-insoluble organic molecules to enclose their watery interiors and to regulate the flow of substances across the cell boundary.

12.2 Families of Organic Molecules: Functional Groups

Learning Objectives:

- Define functional group.
- Identify the functional groups in organic molecules.

More than 18 *million* organic compounds are described in scientific literature, each with unique chemical and physical properties, and many also having unique biological properties (both desired and undesired). How can we ever understand them all?

Chemists have learned through experience that organic compounds can be classified into families according to their structural features, and that the chemical behavior of family members is often predictable based on their specific grouping of atoms. As a result, the millions of compounds can be sorted into just a few general families of organic compounds with simple chemical patterns.

Functional group An atom or group of atoms within a molecule that has a characteristic physical and chemical behavior.

The structural features that allow us to classify organic compounds into distinct chemical families are called **functional groups.** A functional group is an atom or group of atoms that has a characteristic physical and chemical behavior. Each functional group is always part of a larger molecule, and a molecule may have more than one class of functional group present, as we shall soon see. An important property of functional groups is that a given functional group *tends to undergo the same types of reactions in every molecule that contains it.* Once a functional group undergoes a chemical reaction it quite often changes the chemical behavior of the entire molecule. For example, the carbon–carbon double bond is a common functional group. Ethene (C_2H_4), the simplest compound with a carbon–carbon double bond, undergoes many chemical reactions similar to those of oleic acid $(C_{18}H_{34}O_2)$, a much larger and more complex compound that also contains a carbon double bond. Both, for example, react with hydrogen gas in the same manner, as shown in Figure 12.1. We will see in Chapter 13 that the double bond reacts with water and acid to produce alcohols; in doing so a molecule that is completely insoluble in water (such as ethene) is converted to one that shows a substantial increase in its water solubility (ethanol). These identical reactions with hydrogen are typical: *The chemistry of an organic molecule is primarily determined by the functional groups it contains, not by its size or complexity.*

▶ Figure 12.1
The reactions of (a) ethene and (b) oleic acid with hydrogen; reaction of (c) ethene with water in the presence of acid. The carbon–carbon double-bond functional group adds 2 hydrogen atoms in both cases, regardless of the complexity of the rest of the molecule.

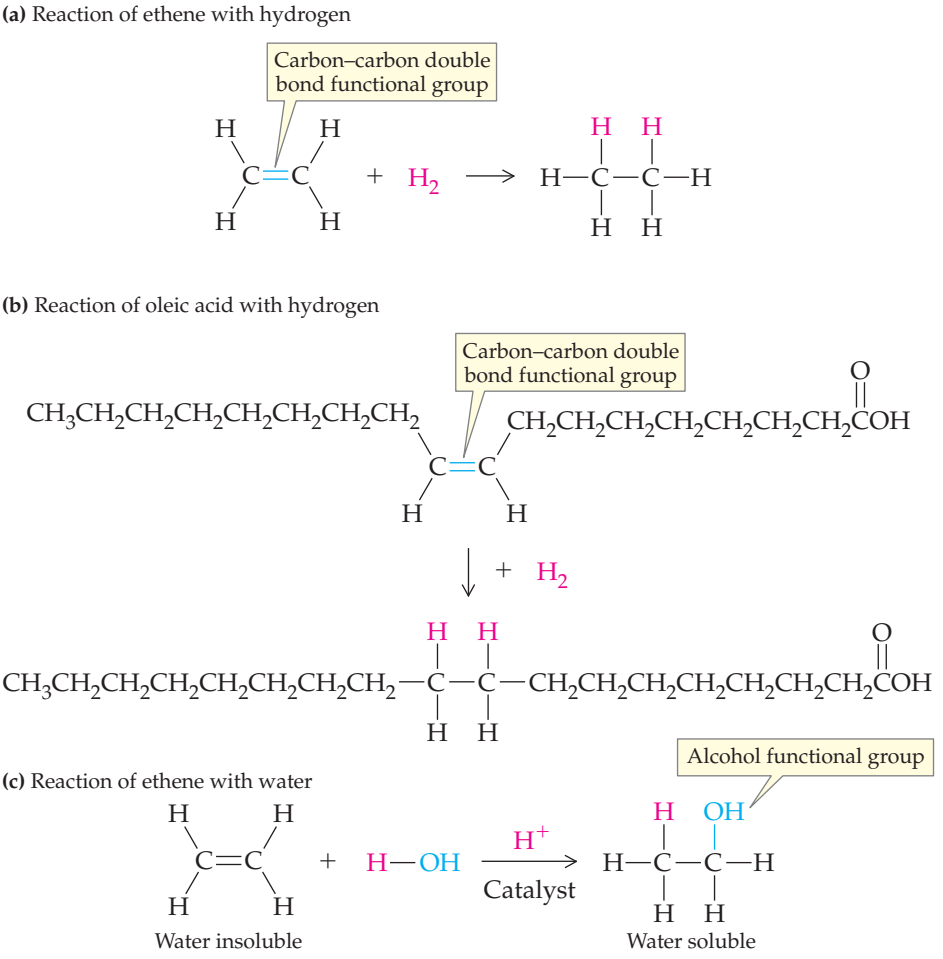
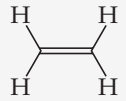
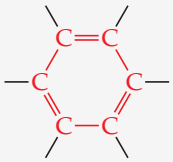
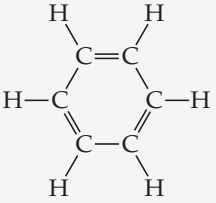
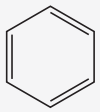
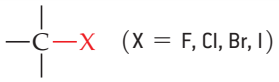
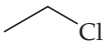
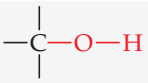
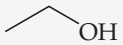
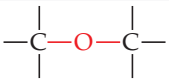
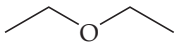
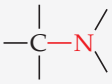
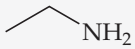
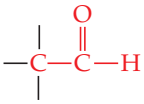
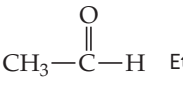
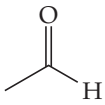
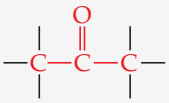
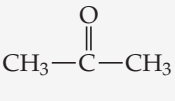
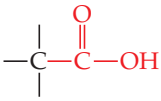
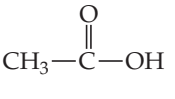
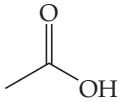
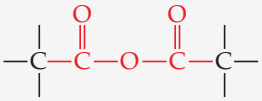
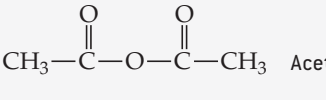
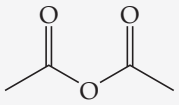
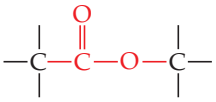
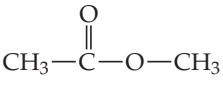
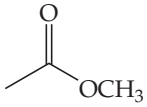
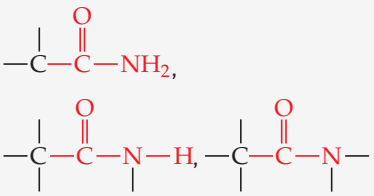
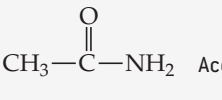
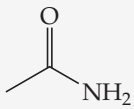
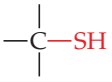
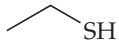
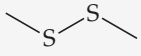
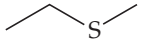


Table 12.1 lists some of the most important families of organic molecules and their distinctive functional groups. Compounds that contain a C═C double bond functional group, for instance, are in the *alkene* family, compounds that have an —OH group bound to a tetravalent carbon are in the *alcohol* family, and so on. To aid in identifying the organic functional groups you will encounter, we have included an Organic Functional Group Concept Map (Figure 12.5) at the end of this chapter; it should be used in

Table 12.1 Some Important Families of Organic Molecules

Family Name	Functional Group Structure*	Simple Example	Line Structure	Name Suffix
Alkane (Chapter 12)	No readily reactive bonds. Contains only C—H and C—C single bonds	$CH_3CH_2CH_3$ Propane		*-ane*
Alkene (Chapter 13)		$H_2C{=}CH_2$ Ethene		*-ene*
Alkyne (Chapter 13)		H—C≡C—H Ethyne		*-yne*
Aromatic (Chapter 13)		 Benzene		None
Alkyl halide (Chapters 12, 14)	 (X = F, Cl, Br, I)	CH_3CH_2Cl Chloroethane		None
Alcohol (Chapter 14)		CH_3CH_2OH Ethanol		*-ol*
Ether (Chapter 14)		$CH_3CH_2{-}O{-}CH_2CH_3$ Diethyl ether		None
Amine (Chapter 16)		$CH_2CH_3NH_2$ Ethanamine		*-amine*
Aldehyde (Chapter 15)		 Ethanal		*-al*
Ketone (Chapter 15)		 Acetone		*-one*
Carboxylic acid (Chapter 17)		 Acetic acid		*-ic acid*
Anhydride (Chapter 17)		 Acetic anhydride		None
Ester (Chapter 17)		 Methyl acetate		*-ate*
Amide (Chapter 17)		 Acetamide		*-amide*
Thiol (Chapter 14)		CH_3CH_2SH Ethanethiol		None
Disulfide (Chapter 14)	C—S—S—C	CH_3SSCH_3 Dimethyl disulfide		None
Sulfide (Chapter 14)	C—S—C	$CH_3CH_2SCH_3$ Ethyl methyl sulfide		None

The bonds shown in RED refer to the functional group of interest and the atoms required.
*The bonds whose connections are not specified are assumed to be attached to carbon or hydrogen atoms in the rest of the molecule.

conjunction with Table 12.1. Also at the end of each organic chemistry chapter you will find a summary of functional group reactions discussed in that chapter. You will find Table 12.1, Figure 12.5, and these Functional Group Summaries helpful as you proceed through the remainder of this text.

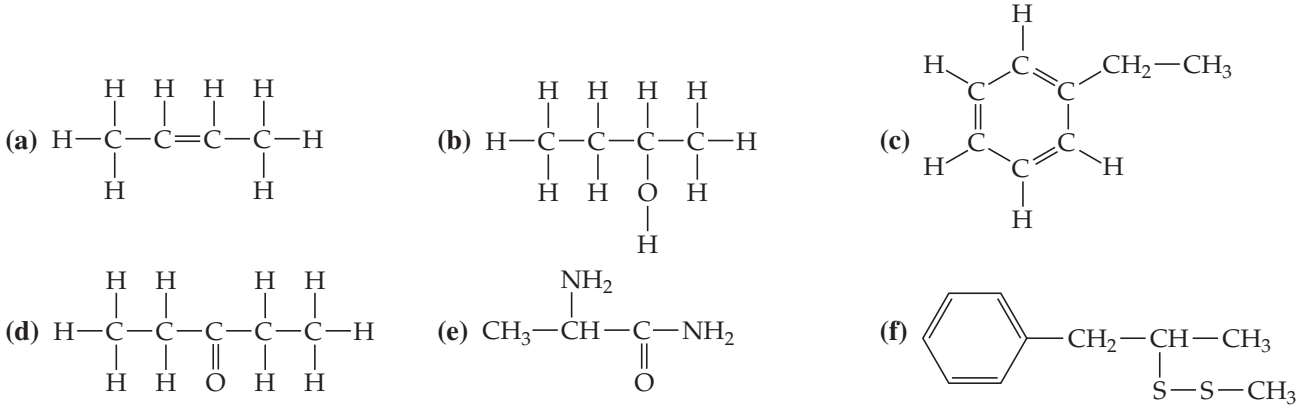
Much of the chemistry discussed in this and the next five chapters is the chemistry of the families listed in Table 12.1, so it is best to learn the names and become familiar with their structures now. Note that they fall into four groups:

Hydrocarbon An organic compound that contains only carbon and hydrogen.

- The first four families in Table 12.1 are **hydrocarbons,** organic compounds that contain only carbon and hydrogen. *Alkanes* have only single bonds and contain no functional groups. As we will see later in this chapter, the absence of functional groups makes alkanes relatively unreactive. *Alkenes* contain a carbon–carbon double-bond functional group; *alkynes* contain a carbon–carbon triple-bond functional group; and *aromatic* compounds contain a six-membered benzene ring of carbon atoms with three alternating double bonds.
- The next four families in Table 12.1 have functional groups that contain only single bonds and have a carbon atom bonded to an electronegative atom. *Alkyl halides* have a carbon–halogen bond; *alcohols* have a carbon–oxygen bond; *ethers* have two carbons bonded to the same oxygen; and *amines* have a carbon–nitrogen bond.
- The next six families in Table 12.1 have functional groups that contain a carbon–oxygen double bond: *aldehydes, ketones, carboxylic acids, anhydrides, esters,* and *amides.*
- The remaining three families in Table 12.1 have functional groups that contain sulfur: *thioalcohols* (known simply as *thiols*), *sulfides,* and *disulfides.* These three families play an important role in protein function (Chapter 18).
- Many of the organic molecules we will come across in later chapters (in particular the biochemistry chapters) will have more than one functional group present in the same molecule (see, e.g., for the amino acids Section 18.3). When this is the case, we will classify the molecule as chemically belonging to multiple functional group families; from a biological and medical standpoint these molecules are quite often classified according their biologically relevant function (e.g., neurotransmitters (Sections 28.5 to 28.7) or nucleic acids (Section 26.2).

Worked Example 12.1 Molecular Structures: Identifying Functional Groups

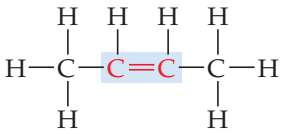
To which family of organic compounds do the following compounds belong? Explain.



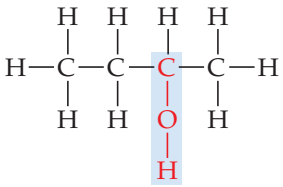
ANALYSIS Use the Organic Functional Group Concept Map (Figure 12.5, see end of chapter) and Table 12.1 to identify each functional group, and name the corresponding family to which the compound belongs. Begin by determining what elements are present and whether multiple bonds are present.

SOLUTION

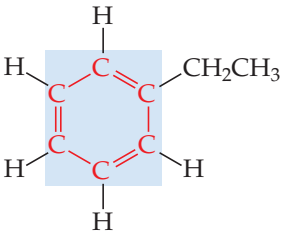
(a) This compound contains only carbon and hydrogen atoms, so it is a *hydrocarbon.* There is only one carbon–carbon double bond, so it is an *alkene.*



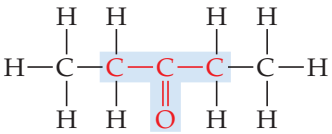
(b) This compound contains an oxygen and has only single bonds. The presence of the O—H group bonded to tetravalent carbon identifies this compound as an *alcohol.*



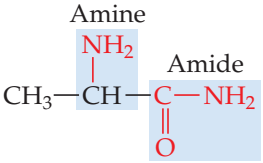
(c) This compound also contains only carbon and hydrogen atoms, which identifies it as a *hydrocarbon.* It has three double bonds in a ring. The six-membered carbon ring with alternating double bonds also identifies this compound as an *aromatic* hydrocarbon compound.



(d) This molecule contains an oxygen that is double bonded to a carbon (a *carbonyl group,* discussed in Chapter 16), and there is no singly bound oxygen or nitrogen also connected to the carbon. The carbon–oxygen double bond is connected to two other carbons (as opposed to a hydrogen) that identifies this compound as a *ketone.*

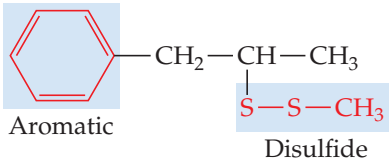


(e) Here, we have an example of a molecule belonging to multiple functional group families. This molecule contains oxygen and nitrogen in addition to carbon and hydrogen, so it is not a hydrocarbon. The presence of the carbonyl group further classifies this molecule, but here we run into a problem: one $-NH_2$ is attached to the carbonyl but the other $-NH_2$ is not. This leads us to conclude that there are two functional groups present: an *amide* and an *amine.*



We will see in Chapter 16 that while the NH_2 of an amine produces a basic molecule, the NH_2 of an amide does not, and that amides, despite having a nitrogen in them, are nonbasic (Chapter 17).

(f) This molecule also contains two functional groups: a ring containing alternating carbon–carbon single and double bonds as well as an S—S group. From our concept map, we trace the double bond to indicate we have an aromatic hydrocarbon, while the sulfurs indicate the presence of a disulfide.



Worked Example 12.2 Molecular Structures: Drawing Functional Groups

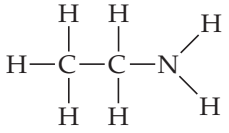
Given the family of organic compounds to which the compound belongs, propose structures for compounds having the following chemical formulas.

(a) An amine having the formula C_2H_7N
(b) An alkyne having the formula C_3H_4
(c) An ether having the formula $C_4H_{10}O$

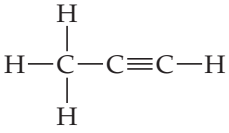
ANALYSIS Identify the functional group for each compound from Table 12.1. Once the atoms in this functional group are eliminated from the chemical formula, the remaining structure can be determined. (Remember that each carbon atom forms four bonds, nitrogen forms three bonds, oxygen forms two bonds, and hydrogen forms only one bond.)

SOLUTION

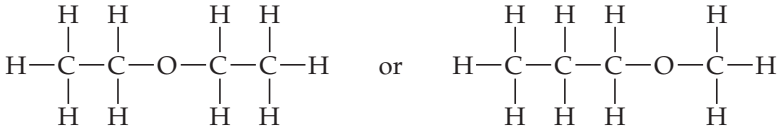
(a) Amines have a C—NH_2 group. Eliminating these atoms from the formula leaves 1 C atom and 5 H atoms. Since only the carbons are capable of forming more than one bond, the 2 C atoms must be bonded together. The remaining H atoms are then bonded to the carbons until each C has 4 bonds.



(b) The alkynes contain a C≡C bond. This leaves 1 C atom and 4 H atoms. Attach this C to one of the carbons in the triple bond, and then distribute the H atoms until each carbon has a full complement of four bonds.



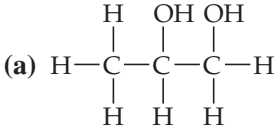
(c) The ethers contain a C—O—C group. Eliminating these atoms leaves 2 C atoms and 10 H atoms. The C atoms can be distributed on either end of the ether group, and the H atoms are then distributed until each carbon atom has a full complement of four bonds.



PROBLEM 12.1

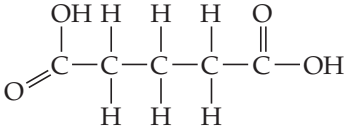
Locate and identify the functional groups in (a) propylene glycol, one of the major ingredients used in electronic cigarettes; (b) glutaric acid, produced in the body during the metabolism of lysine and tryptophan; (c) lactic acid, from sour milk; and (d) phenylalanine, an amino acid found in proteins.

(a)



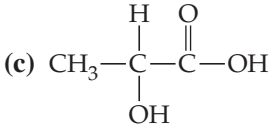
Propylene glycol

(b)

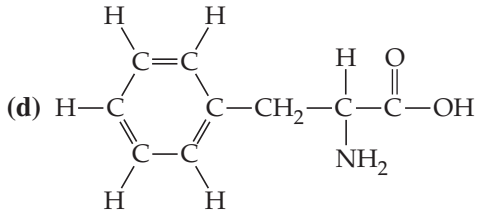


Glutaric acid

(c)



(d)



PROBLEM 12.2

Draw structures for molecules that fit the following descriptions:

(a) C_3H_6O containing an aldehyde functional group
(b) C_3H_6O containing a ketone functional group
(c) $C_3H_6O_2$ containing a carboxylic acid functional group

HANDS-ON CHEMISTRY 12.1

To see how much organic chemistry impacts your daily life, let's take a look at some of the common products that you should have around your home and see what is "organic" in them. You will need to have an internet connection to fully carry out this activity.

a. Let's begin by looking at a simple substance found in almost every pantry: vinegar. Vinegar is simply diluted acetic acid. Look up the structure of acetic acid and draw it. Circle the functional group in it. What other food products can you find that contain vinegar? You may want to look in your refrigerator as well as your pantry.

b. Other common organic compounds found in a home are citric acid, folic acid, dextrose, and thiamine. Look up the structures of each of these and draw them, circling and identifying as many functional groups present as you can. Do any of these four compounds go by a more recognizable name? If so, what? See if you can find at least one food item than contains one or more of these in it. Canned items such as soups are a good place to start. Some of them may be listed as their salt forms (like citrate, folate, thiamine mononitrate, etc). You may have to make a trip to the store to complete this. Provide at least one role the compound plays in the item in which it is present.

c. In the chapter opener, the antibiotic ointment Neosporin was mentioned. What are the three antibiotics found in it? Look up the structures of each of these and draw them, circling and identifying as many functional groups present as you can.

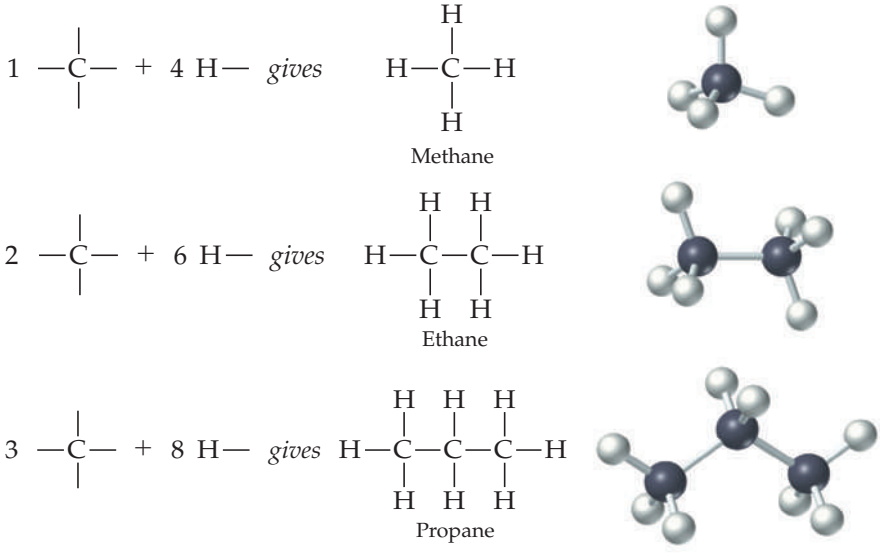
12.3 The Structure of Organic Molecules: Alkanes and Their Isomers

Learning Objective:

- Recognize structural (constitutional) isomers and functional group isomers.

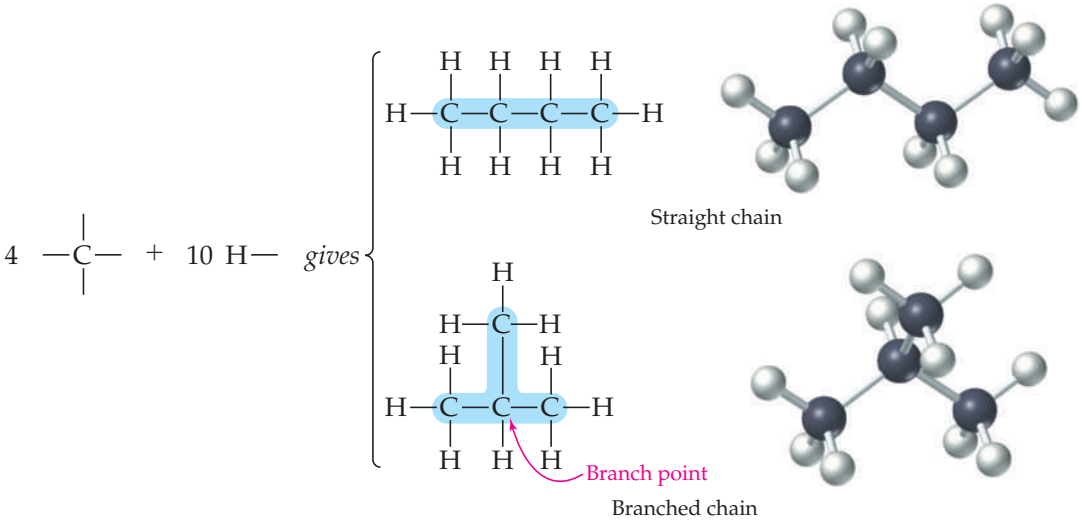
Hydrocarbons that contain only single bonds belong to the family of organic molecules called **alkanes.** Alkanes are most commonly found and used as fuels; the tank of gas found on a backyard barbecue is usually the hydrocarbon propane. Imagine how 1 carbon and 4 hydrogens can combine, and you will realize there is only one possibility: methane, CH_4. Now, imagine how 2 carbons and 6 hydrogens can combine—only ethane, CH_3CH_3, is possible. Likewise, with the combination of 3 carbons with 8 hydrogens—only propane, $CH_3CH_2CH_3$, is possible. The general rule for *all* hydrocarbons except methane is that each carbon *must* be bonded to at least one other carbon. The carbon atoms bond together to form the "backbone" of the compound, with the hydrogens on the periphery. The general formula for alkanes is C_nH_{2n+2}, where n is the number of carbons in the compound.

Alkane A hydrocarbon that has only single bonds.

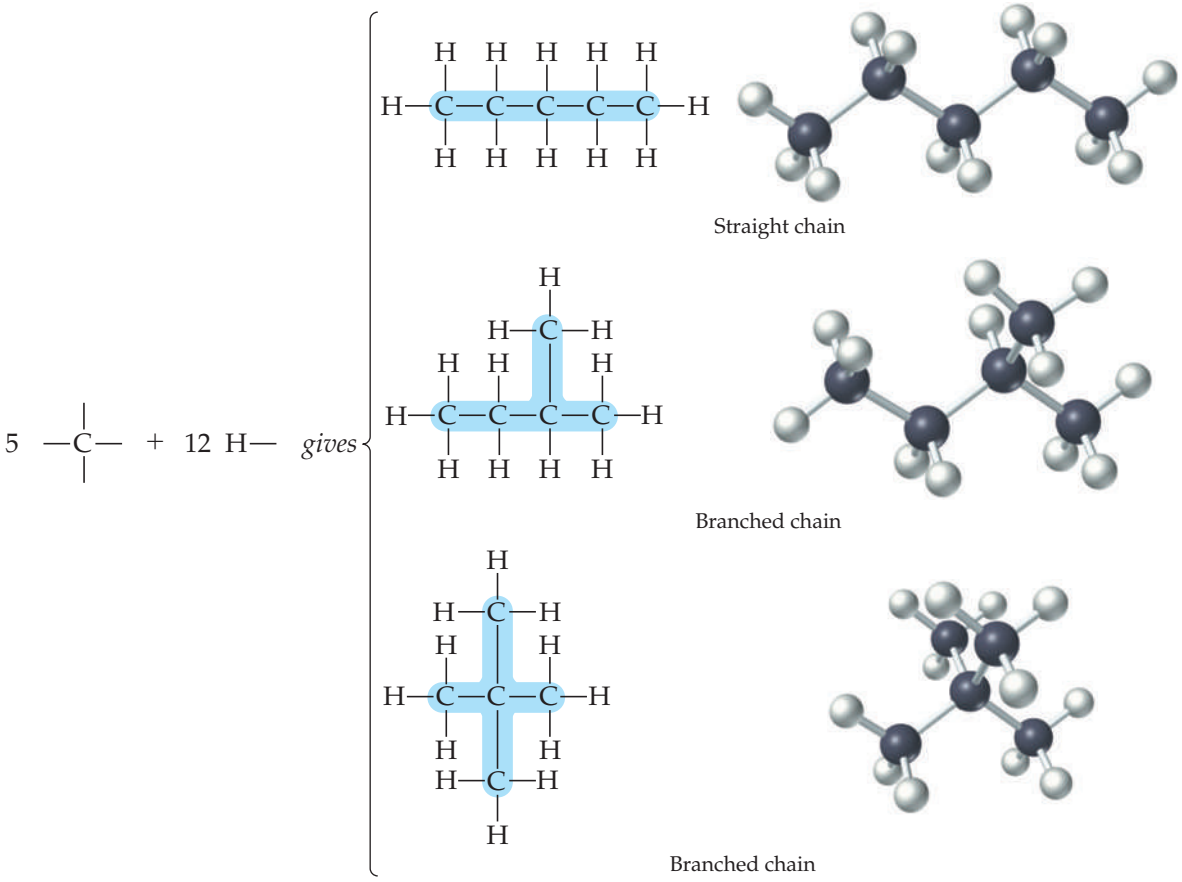


Isomers Compounds with the same molecular formula but different structures.

In alkanes, as the number of carbons becomes greater than three, the ability to form *isomers* arises. Compounds that have the same molecular formula but different structural formulas are called **isomers** of one another. For example, there are two ways in which molecules that have the formula C_4H_{10} can be formed. The 4 carbons can either be joined in a continuous row or have a branched arrangement:



The same is seen with the molecules that have the formula C_5H_{12}, for which three isomers are possible.



Compounds with all their carbons connected in a continuous chain are called **straight-chain alkanes;** those with a branching connection of carbons are called **branched-chain alkanes.** Note that in a straight-chain alkane, you can draw a line through all the carbon atoms without lifting your pencil from the paper. In a branched-chain alkane, however, you must either lift your pencil from the paper or retrace your steps to draw a line through all the carbons.

Straight-chain alkane An alkane that has all its carbons connected in a row.

Branched-chain alkane An alkane that has a branching connection of carbons.

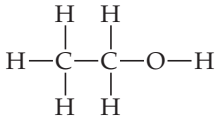
The two isomers of C_4H_{10} and the three isomers of C_5H_{12} shown above are **constitutional (or structural) isomers**—compounds with the same molecular formula but with different connections among their constituent atoms. Needless to say, the number of possible alkane isomers grows rapidly as the number of carbon atoms increases.

Constitutional isomers Compounds with the same molecular formula but different connections among their atoms. Also known as structural isomers.

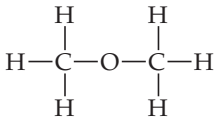
Constitutional isomers of a given molecular formula are chemically distinct from one another. They have different structures, physical properties (such as melting and boiling points), and potentially different physiological properties. When the molecular formula contains atoms other than carbon and hydrogen, the constitutional isomers obtained can also be **functional group isomers:** isomers that differ in both molecular connection and family classification. In these cases, the differences between isomers can be dramatic. For example, ethanol and dimethyl ether both have the formula C_2H_6O, but ethanol is a liquid with a boiling point of 78.5 °C (351.5 K) and dimethyl ether is a gas with a boiling point of 23 °C (296 K). While ethanol is a depressant of the central nervous system, dimethyl ether is a nontoxic compound with anesthetic properties at high concentrations. Clearly, molecular formulas by themselves are not very useful in organic chemistry; knowledge of structures is also necessary.

Functional group isomer Isomers having the same chemical formula but belonging to different chemical families due to differences in bonding; ethanol and dimethyl ether are examples of functional group isomers.

Ethanol
C_2H_6O



Dimethyl ether
C_2H_6O



Worked Example 12.3 Molecular Structures: Drawing Isomers

Draw all isomers that have the formula C_6H_{14}.

ANALYSIS Knowing that all the carbons must be bonded together to form the molecule, find all possible arrangements of the 6 carbon atoms. Begin with the isomer that has all 6 carbons in a straight chain, then draw the isomer that has 5 carbons in a straight chain, using the remaining carbon to form a branch, then repeat for the isomer having 4 carbons in a straight chain and 2 carbons in branches. Once each carbon backbone is drawn, arrange the hydrogens around the carbons to complete the structure. (Remember that each carbon can only have *four* bonds total.)

SOLUTION

The straight-chain isomer contains all 6 carbons bonded to form a chain with no branches. The branched isomers are drawn by starting with either a 5-carbon chain or a 4-carbon chain and by adding the extra carbons as branches in the middle of the chain. Hydrogens are added until each carbon has a full complement of four bonds.

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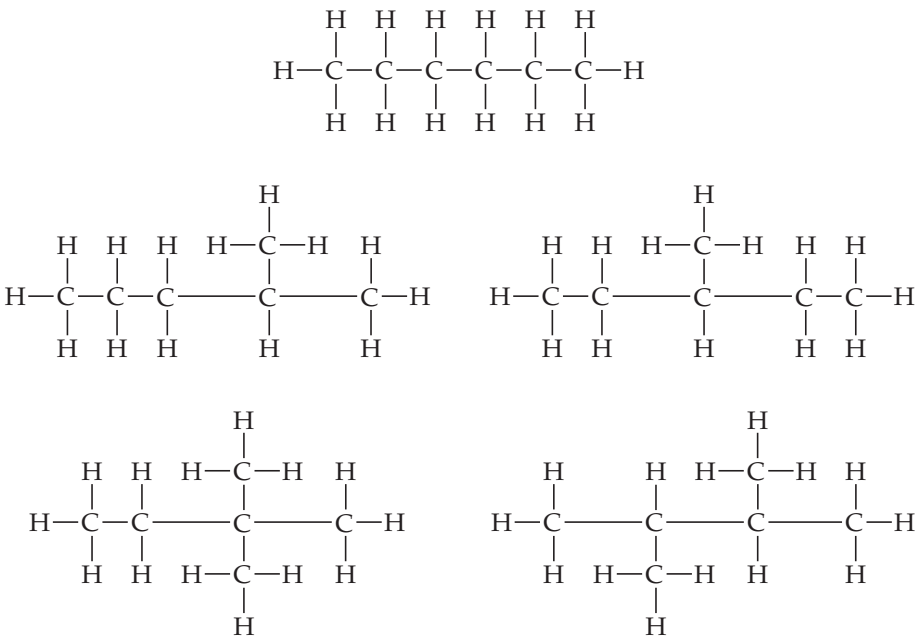


PROBLEM 12.3

Draw the straight-chain isomer with the formula **(a)** C_7H_{16} and **(b)** C_9H_{20}.

PROBLEM 12.4

There are two branched-chain isomers with the formula C_7H_{16}, where the longest chain in the molecule is six carbons long. Draw them.

12.4 Drawing Organic Structures

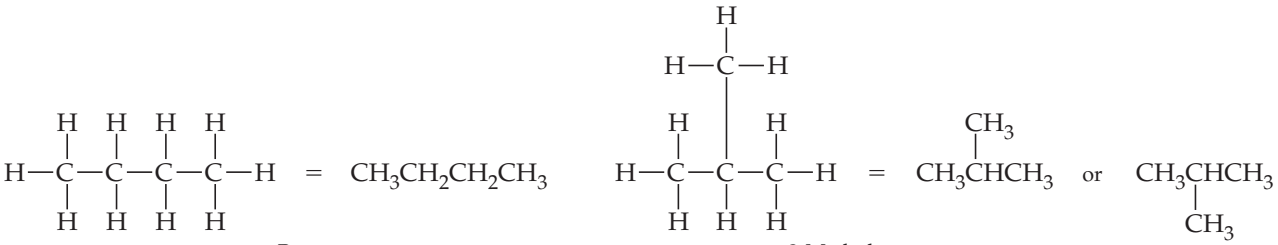
Learning Objectives:

- Draw structural, condensed, and line formulas for simple chemical compounds.
- Convert any given structural, condensed, or line formula into its corresponding alternative.

Condensed structure A shorthand way of drawing structures in which C—C and C—H bonds are understood rather than shown.

Drawing structural formulas that show every atom and every bond in a molecule is both time-consuming and awkward, even for relatively small molecules. Much easier is the use of **condensed structures,** which are simpler but still show the essential information about which functional groups are present and how atoms are connected. In condensed structures, C—C and C—H single bonds are not necessarily shown; rather, they are "understood." If a carbon atom has three hydrogens bonded to it, we write CH_3 (or H_3C if needed; this is only done in special cases); if the carbon has two hydrogens bonded to it, we write CH_2; and so on. For example, the 4-carbon, straight-chain alkane called butane and its branched-chain isomer (2-methylpropane), both of which have the formula C_4H_{10} can be written as the following condensed structures:

Condensed structures were explored in Section 4.7.



Butane — Structural formula — Condensed formula

2-Methylpropane — Structural formula — Condensed formula

Note in these condensed structures for butane and 2-methylpropane that the bonds between carbons are not usually shown—the CH_3 and CH_2 units are simply placed next to one another—but that the branch in the 2-methylpropane isomer *is* shown for clarity. It does not matter whether the branch is drawn above or below the main chain.

Occasionally, as a further simplification, not all the CH_2 groups (called **methylenes**) are shown. Instead, CH_2 is shown once in parentheses, with a subscript indicating the number of methylene units strung together. For example, the 6-carbon straight-chain alkane (hexane) can be written as:

Methylene Another name for a CH_2 unit.

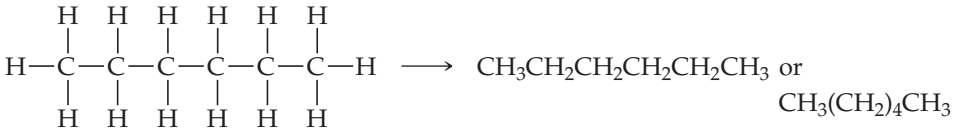
$$CH_3CH_2CH_2CH_2CH_2CH_3 \text{ or } CH_3(CH_2)_4CH_3$$

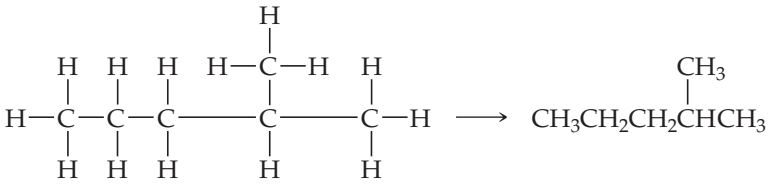
Worked Example 12.4 Molecular Structures: Writing Condensed Structures

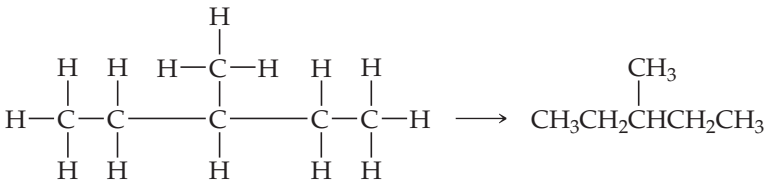
Write condensed structures for the isomers from Worked Example 12.3.

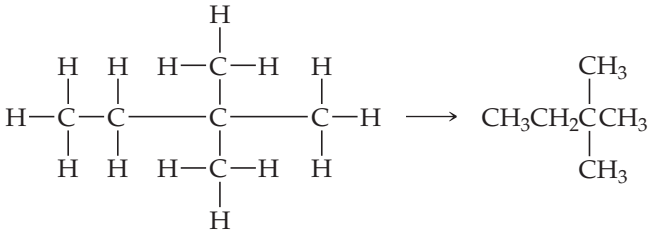
ANALYSIS Eliminate all horizontal bonds, substituting reduced formula components (CH_3, CH_2, and so on) for each carbon in the compound. Show bonds in branched isomers for clarity.

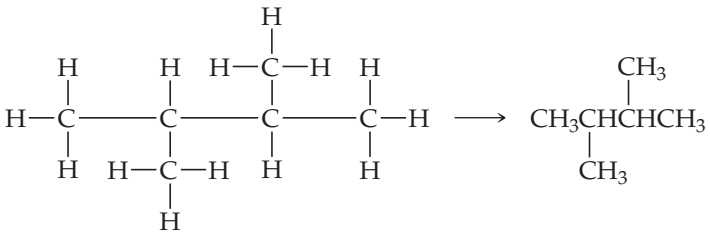
SOLUTION





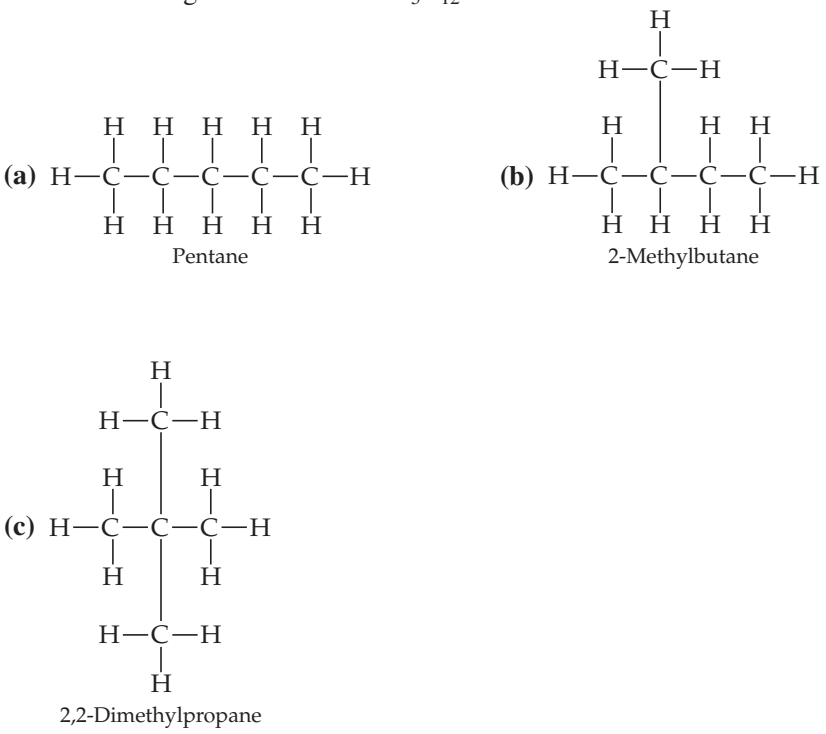






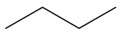
PROBLEM 12.5

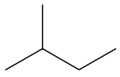
Draw the following three isomers of C_5H_{12} as condensed structures:



Line structure Also known as line-angle structure; a shorthand way of drawing structures in which carbon and hydrogen atoms are not explicitly shown. Instead, a carbon atom is understood to be wherever a line begins or ends and at every intersection of two lines, and hydrogens are understood to be wherever they are needed to have each carbon form four bonds.

Another way of representing organic molecules is to use **line (or line-angle) structures,** which are structures in which the symbols C and H do not appear. Instead, a chain of carbon atoms and their associated hydrogens are represented by a zigzag arrangement of short lines, with any branches off the main chain represented by additional lines. The line structure for butane and its branched-chain isomer 2-methylbutane, for instance, is


same as $CH_3CH_2CH_2CH_3$

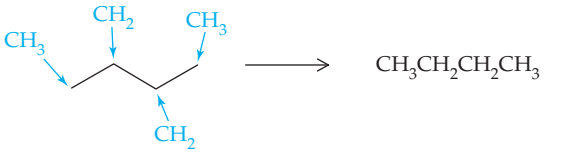

same as $CH_3CHCH_2CH_3$ (CH_3 branch)

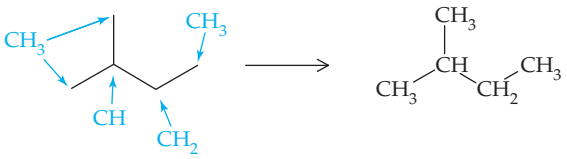
Line structures are a simple and quick way to represent organic molecules without showing all carbons and hydrogens present. Chemists, biologists, pharmacists, doctors, and nurses all use line structures to conveniently convey to one another very complex organic structures. Another advantage is that a line structure gives a more realistic depiction of the angles seen in a carbon chain.

Drawing a molecule in this way is simple, provided one follows these guidelines:

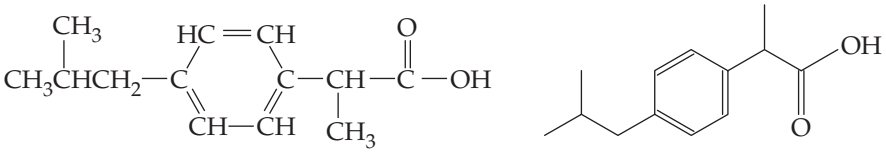
1. Each carbon–carbon bond is represented by a line.
2. Anywhere a line ends or begins, as well as any vertex where two lines meet, represents a carbon atom.
3. Any atom other than another carbon or a hydrogen attached to a carbon must be shown.
4. Since a neutral carbon atom forms four bonds, all bonds not shown for any carbon are understood to be the number of carbon–hydrogen bonds needed to have

the carbon form four bonds. Only bonds between two carbons (or carbon and an element other than hydrogen) are shown.





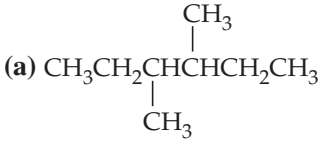
Converting line structures to structural formulas or to condensed structures is simply a matter of correctly interpreting each line ending and each intersection in a line structure. For example, the common pain reliever ibuprofen has the condensed and line structures

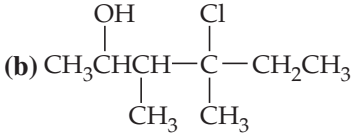


Finally, it is important to note that chemists and biochemists often use a mixture of structural formulas, condensed structures, and line structures to represent the molecules they study. As you progress through this textbook, you will see many complicated molecules represented in this way, so it is a good idea to get used to thinking interchangeably in all three formats.

Worked Example 12.5 Molecular Structures: Converting Condensed Structures to Line Structures

Convert the following condensed structures to line structures:

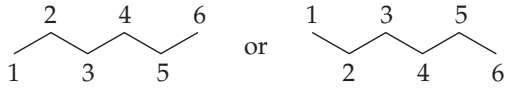




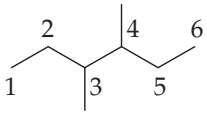
ANALYSIS Find the longest continuous chain of carbon atoms in the condensed structure. Begin the line structure by drawing a zigzag line in which the number of vertices plus line ends equals the number of carbon atoms in the chain. Show branches coming off the main chain by drawing vertical lines at the vertices as needed. Show all atoms that are not carbons or are not hydrogens attached to carbons.

SOLUTION

(a) Begin by drawing a zigzag line in which the total number of ends + vertices equals the number of carbons in the longest chain (here six, with the carbons numbered for clarity):



Looking at the condensed structure, you see CH_3 groups on carbons 3 and 4; these two CH_3 groups (methyl groups) are represented by lines coming off those carbons in the line structure:



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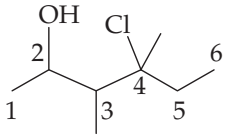
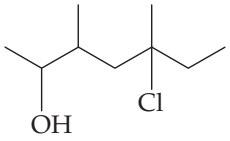
This is the complete line structure. Notice that the hydrogens are not shown but understood. For example, carbon 4 has three bonds shown: one to carbon 3, one to carbon 5, and one to the branch CH_3 group; the fourth bond this carbon must have is understood to be to a hydrogen.

(b) Proceed as in (a), drawing a zigzag line for the longest chain of carbon atoms, which again contains 6 carbons. Next draw a line coming off each carbon bonded to a CH_3 group (carbons 3 and 4). Both the OH and the Cl groups must be shown to give the final structure:



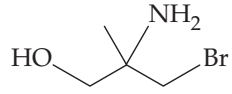
Note from this line structure that it does not matter in such a two-dimensional drawing what direction you show for a group that branches off the main chain, as long as it is attached to the correct carbon. This is true for condensed structures as well. Quite often, the direction that a group is shown coming off a main chain of carbon atoms is chosen simply for aesthetic reasons. The line structure can also be shown this way:



Worked Example 12.6 Molecular Structures: Converting Line Structures to Condensed Structures

Convert the following line structures to condensed structures:

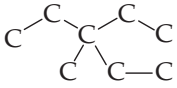
(a) 

(b) 

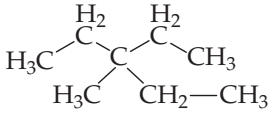
ANALYSIS Convert all vertices and line ends to carbons. Write in any noncarbon atoms and any hydrogens bonded to a noncarbon atom. Add hydrogens as needed so that each carbon has four groups attached. Remove lines connecting carbons except for branches.

SOLUTION

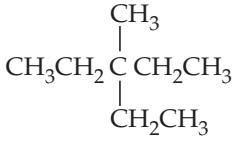
(a) Anywhere a line ends and anywhere two lines meet, write a C:



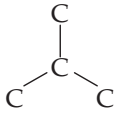
Because there are no atoms other than carbons and hydrogens in this molecule, the next step is to add hydrogens as needed to have four bonds for each carbon:



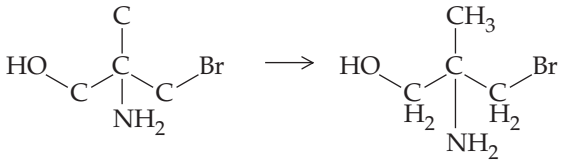
Finally, eliminate all lines except for branches to get the condensed structure:



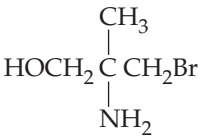
(b) Begin the condensed structure with a drawing showing a carbon at each line end and at each intersection of two lines:



Next, write in all the noncarbon atoms and the hydrogen bonded to the oxygen. Then, add hydrogens so that each carbon forms four bonds:



Eliminate all lines except for branches for the completed condensed structure:



PROBLEM 12.6

Convert the following condensed structures to line structures:

(a) $CH_3CH_2CHCH_2CH_2CH_3$ with CH_2OH branch

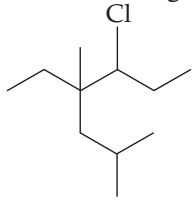
(b) $CH_3CH(CH_3)CH(CH_2CH_3)CH_2CH(CH_3)CH_3$

(c) $CH_3-CH(Br)-CH(CH_3)-CH_2-CH_2-CH(CH_3)-OH$

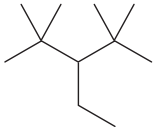
PROBLEM 12.7

Convert the following line structures to condensed structures:

(a)



(b)



PROBLEM 12.8

Draw both condensed and line structures for the chemicals listed in Problem 12.1.

12.5 The Shapes of Organic Molecules

Learning Objective:

- Determine if two given structures are the different conformers of the same molecule, different structural isomers, or different molecules.

Every carbon atom in an alkane has its four bonds pointing toward the four corners of a tetrahedron, but chemists do not usually worry about three-dimensional shapes when writing condensed structures. Condensed structures do not imply any particular three-dimensional shape; they only indicate the connections between atoms without specifying geometry. Line structures do try to give some limited feeling for the shape of a molecule, but even here, the ability to show three-dimensional shape is limited unless dashed and wedged lines are used for the bonds (Sections 4.8 and 14.10).

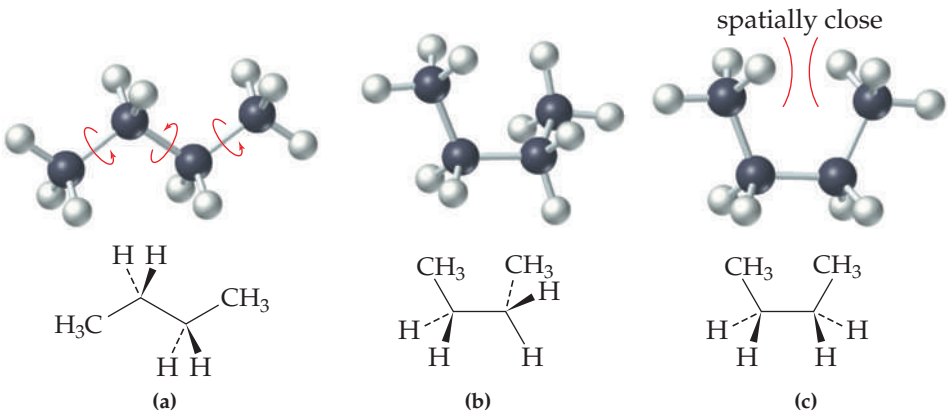
Butane, for example, has no one single shape because *rotation* takes place around carbon–carbon single bonds. The two parts of a molecule joined by a carbon–carbon

Conformation The specific three-dimensional arrangement of atoms in a molecule achieved specifically through rotations around carbon–carbon single bonds.

Conformer Molecular structures having identical connections between atoms where the interconversion of C—C bond rotations results only in a different spatial arrangement of atoms.

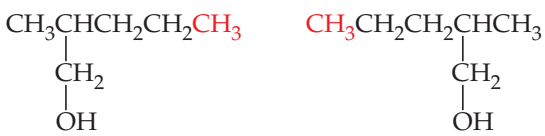
single bond in a noncyclic structure (like butane) are free to spin around the bond, giving rise to an infinite number of possible three-dimensional geometries, or **conformations.** The various conformations of a molecule such as butane are called **conformers** of one another. Conformers differ from one another as a result of rotation around carbon–carbon single bonds. Although the conformers of a given molecule have different three-dimensional shapes (due to the bond angles in the molecule) and different energies (due to how groups are oriented with respect to one another), the conformers cannot be separated from one another. A given butane molecule might be in its fully extended conformation at one instant but in a more twisted conformation an instant later (Figure 12.2). An actual sample of butane contains a great many molecules that are constantly changing conformation. Some of these conformations have the groups staggered with respect to each other (Figure 12.2a and 12.2b), whereas some have all groups eclipsing one another (Figure 12.2c). Because molecules do have a three-dimensional shape and because atoms do occupy space, a more crowded conformer, where groups larger than H are near one another (Figure 12.2b), will have higher energy than the least crowded conformer, where the large groups are as far apart as possible (Figure 12.2a). Those conformers where groups on adjacent atoms are eclipsed will have the highest energy of all due to what is known as steric crowding. At any given instant, however, most of the molecules have the least crowded, lowest-energy extended conformation shown in Figure 12.2a. The same is true for all other alkanes: At any given instant, most molecules are in the least crowded conformation.

In Section 14.10, we will see how the three dimensional structure of some organic molecules can lead to enantiomers (isomers that are nonsuperimposable mirror images of one another), an important property of many biologically active molecules.



▶ **Figure 12.2**
Some conformations of butane (there are many others as well). The least crowded, extended conformation in (a) is the lowest-energy one, whereas the eclipsed conformation shown in (c), where the two CH_3 groups are spatially on top of one another, is the highest-energy one. In this drawing, those bonds shown with a wedge are coming out of the plane of the paper toward the reader, whereas those with a dash are going out of the same plane, away from the reader.

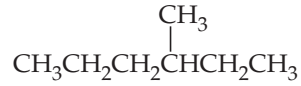
As long as any two structures have identical connections between atoms and are interconvertible either by "flipping" the molecule or by rotating C—C bonds, they are conformers of each other and represent the same compound, no matter how the structures are drawn. It is important to remember that no bonds are broken and reformed when interconverting conformers. Sometimes, you have to mentally rotate structures to see whether they are conformers or actually different molecules. To see that the following two structures represent conformers of the same compound rather than two isomers, picture one of them flipped right to left so that the red CH_3 groups are on the same side.



Another way to determine whether two structures are conformers is to name each one using the International Union of Pure and Applied Chemistry (IUPAC) nomenclature rules (Section 12.6). If two structures have the same name, they are conformers of the same compound.

Worked Example 12.7 Molecular Structures: Identifying Conformers

The following structures all have the formula C_7H_{16}. Which of them represent the same molecule?

(a)  **(b)**  **(c)** 

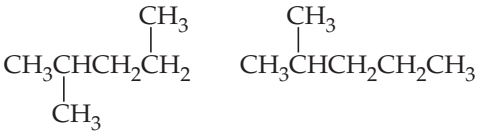
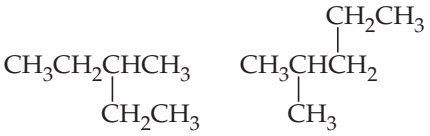
ANALYSIS Pay attention to the *connections* between atoms. Do not get confused by the apparent differences caused by writing a structure right to left versus left to right. Begin by identifying the longest chain of carbon atoms in the molecule.

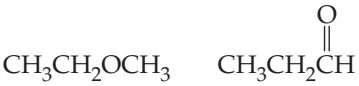
SOLUTION

Molecule (a) has a straight chain of six carbons with a $-CH_3$ branch on the second carbon from the end. Molecule (b) also has a straight chain of six carbons with a $-CH_3$ branch on the second carbon from the end and is therefore identical to (a). That is, (a) and (b) are conformers of the same molecule. The only difference between (a) and (b) is that one is written "forward" and one is written "backward." Molecule (c), by contrast, has a straight chain of 6 carbons with a $-CH_3$ branch on the *third* carbon from the end and is, therefore, an isomer of (a) and (b).

Worked Example 12.8 Molecular Structures: Identifying Conformers and Isomers

Are the following pairs of compounds the same (conformers), isomers, or unrelated?

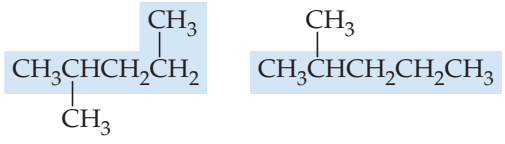
(a)  **(b)** 

(c) 

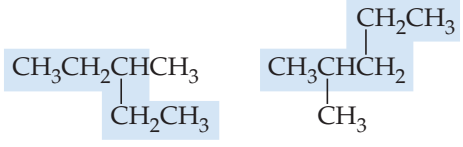
ANALYSIS First compare molecular formulas to see if the compounds are related, and then look at the structures to see if they are the same compound or isomers. Find the longest continuous carbon chain in each, and then compare the locations of the substituents connected to the longest chain.

SOLUTION

(a) Both compounds have the same molecular formula (C_6H_{14}), so they are related. Since the $-CH_3$ group is on the second carbon from the end of a 5-carbon chain in both cases, these structures represent the same compound and are conformers of each other.



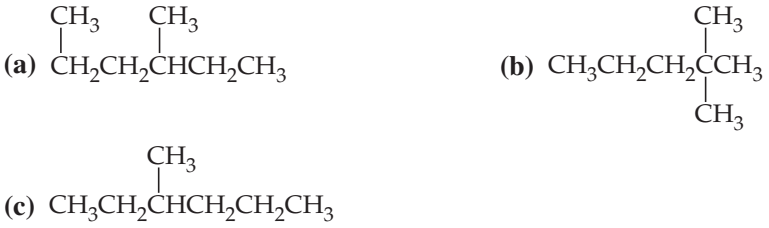
(b) Both compounds have the same molecular formula (C_6H_{14}), and the longest chain in each is 5 carbon atoms. A comparison shows, however, that the $-CH_3$ group is on the middle carbon atom in one structure and on the second carbon atom in the other. These compounds are isomers of each other.



(c) These compounds have different formulas $(C_3H_8O$ and $C_3H_6O)$, so they are unrelated; they are neither conformers nor isomers of each other.

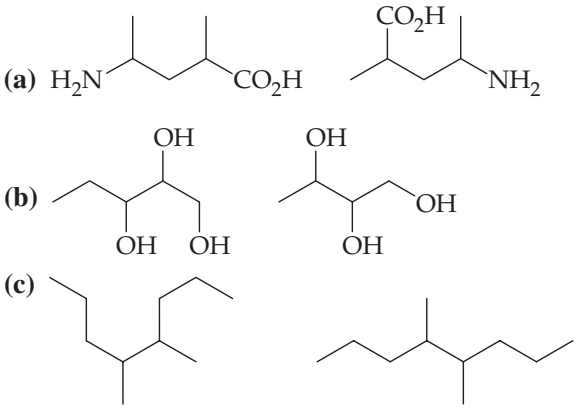
PROBLEM 12.9

Which of the following structures represent the same molecule?



PROBLEM 12.10

Are the pairs of compounds shown below the same molecule, isomers, or different molecules?



12.6 Naming Alkanes

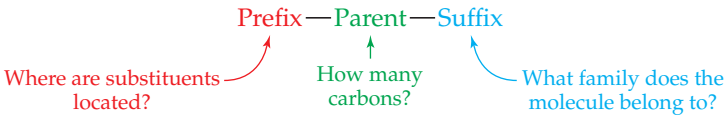
Learning Objective:

- Name an alkane given its structure and draw an alkane given its name.

When relatively few pure organic chemicals were known, new compounds were named at the whim of their discoverer. Thus, urea is a crystalline substance first isolated from urine, and the barbiturates were named by their discoverer in honor of his friend Barbara. As more and more compounds became known, however, the need for a systematic method of naming compounds became apparent.

The system of naming *(nomenclature)* now used is one devised by IUPAC (pronounced *eye*-you-pack). In the IUPAC system for simple organic compounds, a chemical name has three parts: *prefix, parent,* and *suffix*. The prefix specifies the location of functional groups and other **substituents** in the molecule; the parent tells how many carbon atoms are present in the longest continuous chain; and the suffix identifies what family the molecule belongs to.

Substituent An atom or group of atoms attached to a parent compound.



Straight-chain alkanes are named by counting the number of carbon atoms and adding the family suffix *-ane*. With the exception of the first four compounds—*meth*ane, *eth*ane, *prop*ane, and *but*ane—whose parent names have historical origins, the alkanes are named from Greek numbers according to the number of carbons present (Table 12.2). Thus, *pent*ane is the 5-carbon alkane, *hex*ane is the 6-carbon alkane, and so on. Straight-chain alkanes have no substituents, so prefixes are not needed. The first 10 alkane names are so common that they should be memorized.

Alkyl group The part of an alkane that remains when a hydrogen atom is removed.

Substituents, such as $-CH_3$ and $-CH_2CH_3$, that branch off the main chain are called **alkyl groups.** An alkyl group can be thought of as the part of an alkane that

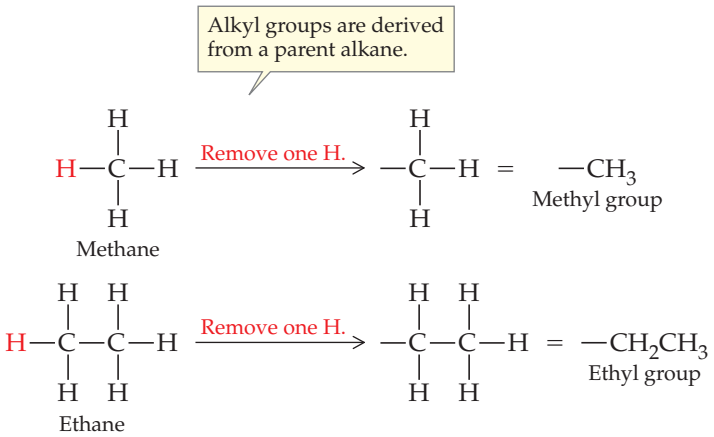
Table 12.2 Names of Straight-Chain Alkanes

Number of Carbons	Structure	Name
1	CH_4	Methane
2	CH_3CH_3	Ethane
3	$CH_3CH_2CH_3$	Propane
4	$CH_3CH_2CH_2CH_3$	Butane
5	$CH_3CH_2CH_2CH_2CH_3$	Pentane
6	$CH_3CH_2CH_2CH_2CH_2CH_3$	Hexane
7	$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$	Heptane
8	$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$	Octane
9	$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$	Nonane
10	$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$	Decane

remains when one hydrogen atom is removed to create an available bonding site. For example, removal of a hydrogen from methane, CH_4, gives the **methyl group, $-CH_3$,** and removal of a hydrogen from ethane, CH_3CH_3, gives the **ethyl group, $-CH_2CH_3$.** Notice that these alkyl groups are named simply by replacing the *-ane* ending of the parent alkane with an *-yl* ending:

Methyl group The $-CH_3$ alkyl group.

Ethyl group The $-CH_2CH_3$ alkyl group.

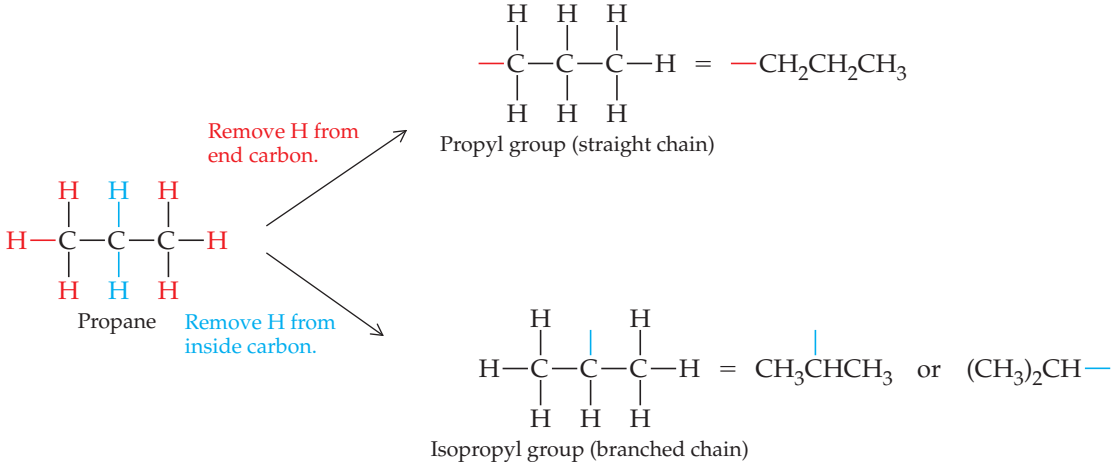


Both methane and ethane have only one "kind" of hydrogen. It does not matter which of the four methane hydrogens is removed, so there is only one possible methyl group. Similarly, it does not matter which of the six equivalent ethane hydrogens is removed, so only one ethyl group is possible.

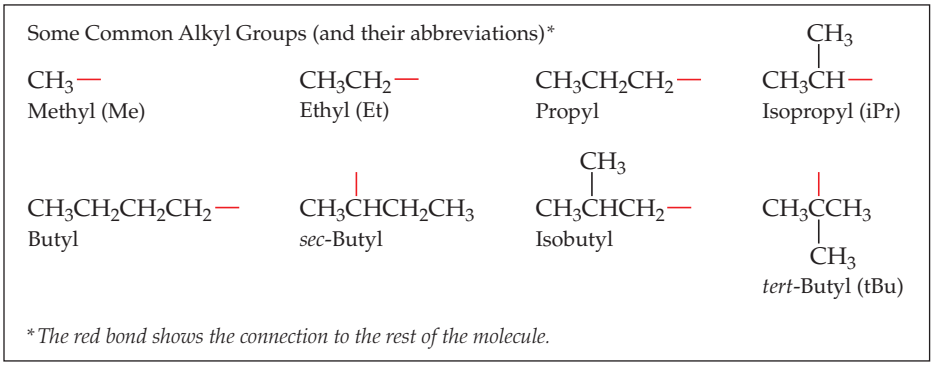
The situation is more complex for larger alkanes, which contain more than one kind of hydrogen. Propane, for example, has two different kinds of hydrogens. Removal of any one of the 6 hydrogens attached to an end carbon yields a straight-chain alkyl group called **propyl,** whereas removal of either one of the two hydrogens attached to the central carbon yields a branched-chain alkyl group called **isopropyl:**

Propyl group The straight-chain alkyl group $-CH_2CH_2CH_3$.

Isopropyl group The branched-chain alkyl group $-CH(CH_3)_2$.



It is important to realize that alkyl groups are not compounds but rather are simply partial structures that help us name compounds. The names of some common alkyl groups are listed in Figure 12.3; you will want to commit them to memory.



▲ **Figure 12.3**
The most common alkyl groups found in organic molecules are shown here; the red bond shows the attachment the group has to the rest of the molecule.*

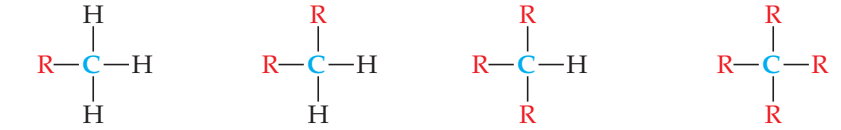
There are four possible substitution patterns for carbons attached to four atoms and these are designated *primary, secondary, tertiary,* and *quaternary. It is important to note that these designations strictly apply to carbons having only single bonds.* Notice that four butyl (4-carbon) groups are listed in Figure 12.3: butyl, *sec*-butyl, isobutyl, and *tert*-butyl. The prefix iso stands for isomer, and was introduced to distinguish an alkyl group that was attached through a primary carbon, but was branched rather than an unbranched chain. The prefix *sec-* stands for *secondary* (since the attachment point of the alkyl group is via a secondary carbon), and the prefix *tert-* stands for *tertiary,* as the attachment point is a tertiary carbon. A **primary (1°) carbon atom** has one other carbon attached to it (typically indicated as an —R group in the molecular structure), a **secondary (2°) carbon atom** has two other carbons attached, a **tertiary (3°) carbon atom** has three other carbons attached, and a **quaternary (4°) carbon atom** has four other carbons attached:

Primary (1°) carbon atom A carbon atom with one other carbon attached to it.

Secondary (2°) carbon atom A carbon atom with two other carbons attached to it.

Tertiary (3°) carbon atom A carbon atom with three other carbons attached to it.

Quaternary (4°) carbon atom A carbon atom with four other carbons attached to it.



Primary carbon (1°) has one other carbon attached.

Secondary carbon (2°) has two other carbons attached.

Tertiary carbon (3°) has three other carbons attached.

Quaternary carbon (4°) has four other carbons attached.

R represents a linkage to another C.

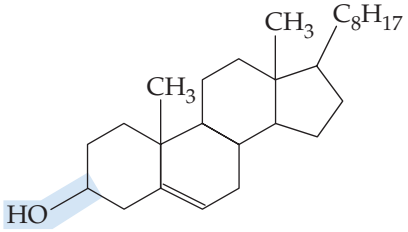
Organic chemists use the abbreviation R to represent an unspecified group where the direct attachment to the atom under discussion is a carbon; it could be as simple as a CH_3, or as complicated as you could ever imagine! It is used so chemists can focus on a particular group of interest (a functional group, or a specific carbon atom) without the clutter of the rest of the molecule, and allows for more general discussions of reactivity. It is common that when abbreviations are used, some qualifier be placed on them (e.g., R = CH_3, C_2H_5).

Table 12.3 contains a list of the most common abbreviations you will see in this text. We will keep the use of these to a minimum; you should only use them yourself if your instructor approves. The use of abbreviations can greatly simplify discussions of reactions; for example, the generalized formula for an alcohol might refer to an

Table 12.3 Common Abbreviations in Organic Chemistry

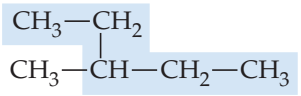
R	**R**esidue or **R**est of the molecule; used to represent the part of the organic molecule *not* under consideration for the current discussion. Does not contain functional groups that can also react under the conditions being examined. Usually means a carbon group but can generally be anything.
R′, R″, R‴	Prime notation; used when different R groups are needed. Read as "R-prime", "R-double prime", etc.
X	A polar group; usually reserved to represent a halogen. Almost always used to represent a "leaving group": An atom or group that can leave in either its anionic or neutral form.
Y or **Z**	Also a polar group; used when different polar groups are present. Usually used to indicate a group attached via an O or S atom. Infrequently used.
M	A metal or metal ion; used primarily when the exact identity of the metal is not crucial to the discussion. Typically a Na or K.
Ar	An aromatic group ("**Ar**yl"); a more specific **R** group. Typically used when its presence imparts special properties on the C to which it is attached. The most common is a phenyl group (Chapter 13).
Ph	A phenyl group (—C_6H_5; Chapter 13); a benzene ring with a single group attached.

alcohol as simple as CH_3OH or CH_3CH_2OH or one as complicated as cholesterol, shown here:



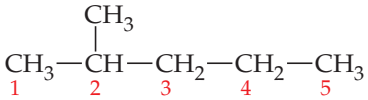
Branched-chain alkanes can be named by following four steps:

STEP 1: Name the main chain. Find the longest continuous chain of carbons, and name the chain according to the number of carbon atoms it contains. The longest chain may not be immediately obvious because it is not always written on one line; you may have to "turn corners" to find it.



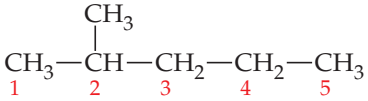
Name as a substituted pentane, not as a substituted butane, because the *longest* chain has five carbons.

STEP 2: Number the carbon atoms in the main chain, beginning at the end nearer the first branch point.



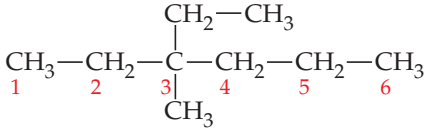
The first (and only) branch occurs at C2 if we start numbering from the left, but would occur at C4 if we started from the right by mistake.

STEP 3: Identify the branching substituents, and number each according to its point of attachment to the main chain.



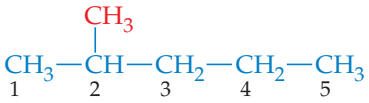
The main chain is a pentane. There is one methyl (—CH_3) substituent group connected to C2 of the chain.

If there are two substituents on the same carbon, assign the same number to both. There must always be as many numbers in the name as there are substituents.

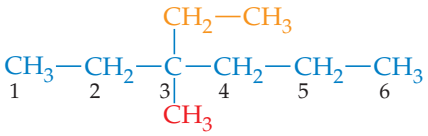


The main chain is a hexane. There are two substituents, a methyl (—CH_3) and an ethyl (—CH_2CH_3), both connected to C3 of the chain.

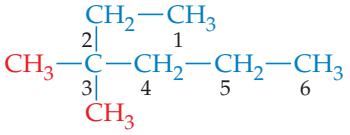
STEP 4: **Write the name as a single word,** using hyphens to separate the numbers from the different prefixes and commas to separate numbers, if necessary. If two or more different substituent groups are present, cite them in alphabetical order. If two or more identical substituents are present, use one of the prefixes *di-*, *tri-*, *tetra-*, and so forth, but do not use these prefixes for alphabetizing purposes.



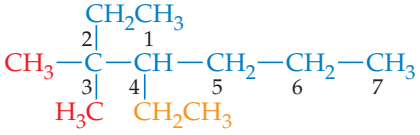
2-Methylpentane (a 5-carbon main chain with a 2-methyl substituent)



3-Ethyl-3-methylhexane (a 6-carbon main chain with 3-ethyl and 3-methyl substituents cited alphabetically)



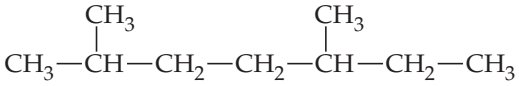
3,3-Dimethylhexane (a 6-carbon main chain with two 3-methyl substituents)

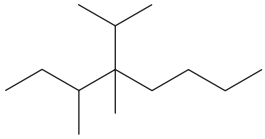


4-Ethyl-3,3-dimethylheptane (a 7-carbon main chain with two 3-methyl substituents and one 4-ethyl substituents, cited alphabetically based on the group, not the prefix (di).

Worked Example 12.9 Naming Organic Compounds: Alkanes

What is the IUPAC name of the following alkanes?

(a) 

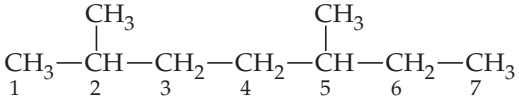
(b) 

ANALYSIS Follow the four steps outlined in the text.

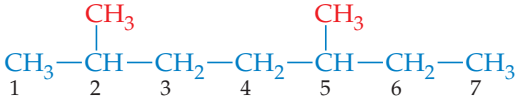
SOLUTION

(a) **STEP 1:** The longest continuous chain of carbon atoms is seven, so the main chain is a *hept*ane.

STEP 2: Number the main chain beginning at the end nearer the first branch.



STEP 3: Identify and number the substituents (a 2-methyl and a 5-methyl in this case):



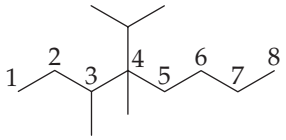
Substituents: 2-Methyl and 5-Methyl

STEP 4: Write the name as one word, using the prefix *di-* because there are two methyl groups. Separate the two numbers by a comma, and use a hyphen between the numbers and the word.

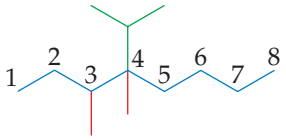
Name: 2, 5-Dimethylheptane

(b) **STEP 1:** The longest continuous chain of carbon atoms is eight, so the main chain is an *oct*ane.

STEP 2: Number the main chain beginning at the end nearer the first branch.



STEP 3: Identify and number the substituents.



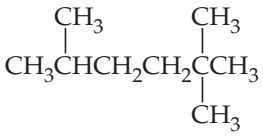
3-Methyl, 4-Methyl, 4-Isopropyl

STEP 4: Write the name as one word, again using the prefix *di-* because there are two methyl groups.

Name: 3, 4-Dimethyl-4-isopropyloctane

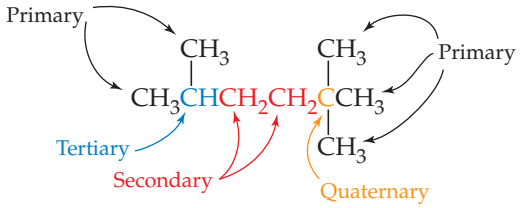
Worked Example 12.10 Molecular Structure: Identifying 1°, 2°, 3°, and 4° Carbons

Identify each carbon atom in the following molecule as primary, secondary, tertiary, or quaternary.



ANALYSIS Look at each carbon atom in the molecule, count the number of other carbon atoms attached, and make the assignment accordingly: primary (1 carbon attached), secondary (2 carbons attached), tertiary (3 carbons attached), and quaternary (4 carbons attached).

SOLUTION



Note: Hydrogens, when attached to a carbon, are given the same primary, secondary, or tertiary designation as the C to which they are attached (and this is why they have been given the same color as their carbons in the figure above).

We will see the primary, secondary, and tertiary classification used again when we study alcohols and alkyl halides in Chapter 14, as well as when we study amines in Chapter 16. For alcohols and alkyl halides, the classification will be identical to that used for hydrogens; this will change slightly when we discuss amines.

Worked Example 12.11 Molecular Structures: Drawing Condensed Structures from Names

Draw condensed and line structures corresponding to the following IUPAC names:

(a) 2,3-Dimethylpentane

(b) 3-Ethylheptane

(c) 4-*tert*-Butylheptane

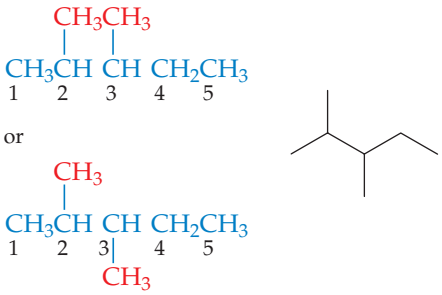
ANALYSIS Starting with the parent chain, add the named alkyl substituent groups to the appropriately numbered carbon atoms.

—*continued on next page*

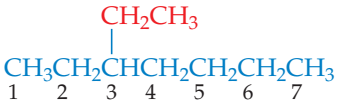
—continued from previous page

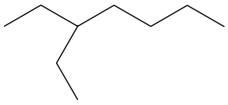
SOLUTION

(a) The parent chain has 5 carbons (*pent*ane), with two methyl groups ($—CH_3$) attached to the second and third carbon in the chain.

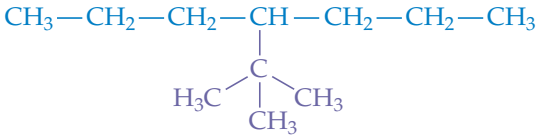


(b) The parent chain has 7 carbons (*hept*ane), with one ethyl group ($—CH_2CH_3$) attached to the third carbon in the chain.

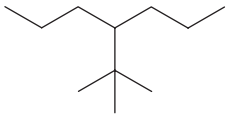




(c) Again, the parent chain has 7 carbons (*hept*ane), with one tert-butyl group ($—C(CH_3)_3$) attached to the fourth carbon in the chain.



4-(*tert*-butyl)heptane

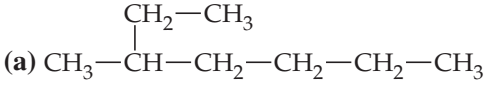


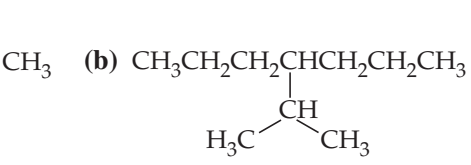
PROBLEM 12.11

Identify each carbon in the molecule shown in Worked Example 12.9b as primary, secondary, tertiary, or quaternary.

PROBLEM 12.12

What are the IUPAC names of the following alkanes?





PROBLEM 12.13

Draw both condensed and line structures corresponding to the following IUPAC names and label each carbon as primary, secondary, tertiary, or quaternary.

(a) 3-Methylhexane **(b)** 3,4-Dimethyloctane **(c)** 2,2,4-Trimethylpentane

PROBLEM 12.14

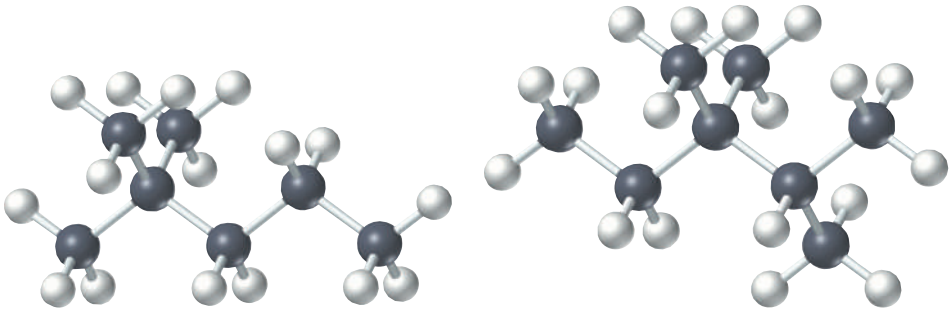
Draw and name alkanes that meet the following descriptions:

(a) A 5-carbon alkane with a tertiary carbon atom

(b) A 7-carbon alkane that has both a tertiary and a quaternary carbon atom

KEY CONCEPT PROBLEM 12.15

What are the IUPAC names of the following alkanes?



(a) (b)

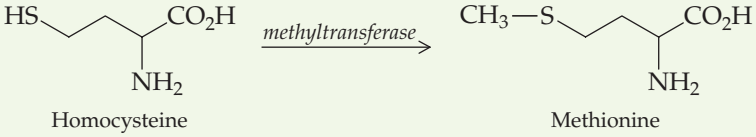
CHEMISTRY IN ACTION

How Important Can a Methyl Group Really Be?

How does a living organism make a molecule as complex and beautiful as DNA (Chapter 26) or the neurotransmitters (Chapter 28) from simple starting points? Most complicated biomolecules are synthesized via an anabolic pathway (a biochemical pathway that creates molecules). Anabolic pathways will take a relatively simple starting material (usually obtained from food digestion) and convert it into the desired end product via a series of biochemical steps. Sometimes, however, this is not enough and what is known as a post synthetic modification must be carried out at the cellular level. Universally, one of the most important of these is methylation, the addition of a lowly $-CH_3$ group to a nitrogen (N-methylation), an oxygen (O-methylation), or a sulfur (S-methylation). Addition of a simple methyl group can greatly change the function of molecules. Biological systems typically need assistance to carry out these molecular conversions, which is accomplished through the use of a class of enzyme known as methyltransferases (Section 19.3), many of which rely on the B vitamins as cofactors (Section 19.2). This highly controlled process is found in every cell in the body and is key to a number of processes, including the regulation of healing, cell energy, and expression of DNA. In fact, the efficiency of the process of biological methylation reduces with time and can cause a number of age-related disorders, including cardiovascular disease and even cancer. Consider homocysteine, a naturally occurring, nonprotein amino acid that is typically found in blood plasma when body chemistry is out of balance. Biologically, it forms from the amino acid methionine (Chapter 18) by loss of the methyl group from sulfur.

Homocysteine is a pro-oxidant and as such is poisonous to cells (cytotoxic). A pro-oxidant is a chemical that interferes with the way cells use or get rid of oxygen and other oxidizing species. One consequence of this is the buildup of the reactive oxygen species (radicals) that cause oxidative damage to the cell (as a note, the over-the-counter pain medication paracetamol (Tylenol) can also act as a pro-oxidant; overdoses of paracetamol can fatally damage the liver, where it is metabolized). High levels of homocysteine result in a number of disorders, including DNA strand breakage and an increase in the risk of heart disease. Normally, homocysteine has low circulating levels due to its rapid re-methylation to methionine. Deficiencies in the B vitamins B-12, B-6, and folic acid, the cofactors necessary for the methyltransferases to work, typically lead to high levels of homocysteine. The simple addition of a $-CH_3$ methyl group to the sulfur of homocysteine can neutralize its cytotoxic behavior.

▲ Blood analysis is an invaluable aid in the diagnosis of disease. For example, abnormal levels of homocysteine can indicate an increased risk of atherosclerosis.



Homocysteine Methionine

CIA Problem 12.1 What is an anabolic pathway?

CIA Problem 12.2 What does "cytotoxic" mean?

CIA Problem 12.3 What cofactors are necessary for methyltransferases to work?

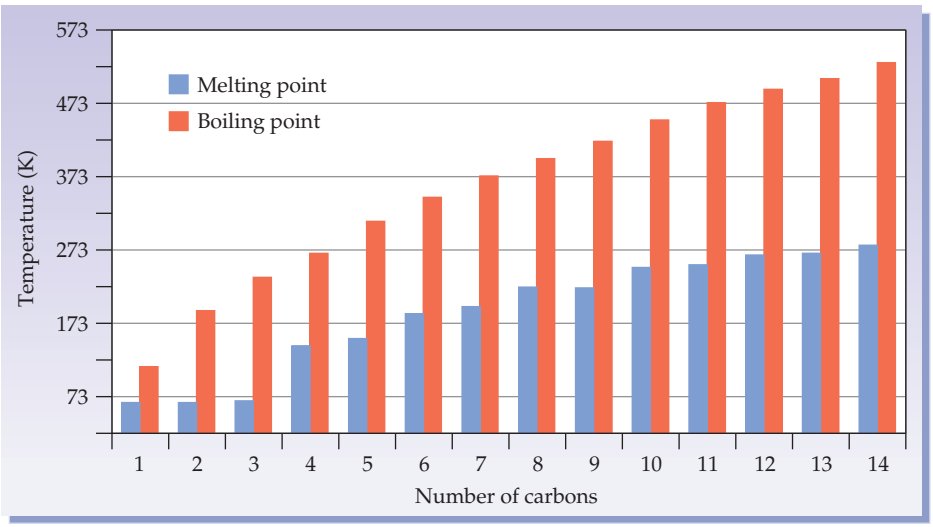
12.7 Properties of Alkanes

Learning Objective:

- Identify the physical properties of alkanes.

There are three major intermolecular forces that need to be considered when discussing the properties of organic molecules: dipole–dipole forces (attractions between the δ^+ and δ^- ends of adjacent polar molecules; Section 8.2), hydrogen bonding (seen in molecules that contain N—H and O—H groups; Section 8.2), and London dispersion forces (due to instantaneous polarizations of a molecule's electron cloud, these are the only intermolecular forces available to nonpolar molecules; Section 8.2). Intermolecular forces are what cause molecules to aggregate or "stick" to one another; hydrogen bonds are the strongest, dipole–dipole forces follow in strength, and London dispersion forces are the weakest. Alkanes contain only nonpolar C—C and C—H bonds, so the only intermolecular forces influencing them are weak London dispersion forces. London dispersion forces increase both as molecules get bigger (due to an increase in the number of electrons within the molecule) and as their surface area increases. The effect of these forces is shown in the regularity with which the melting and boiling points of straight-chain alkanes increase with molecular size (Figure 12.4). The first four alkanes—methane, ethane, propane, and butane—are gases at room temperature and pressure. Alkanes with 5–15 carbon atoms are liquids; those with 16 or more carbon atoms are generally low-melting, waxy solids. Similar results are seen for branched alkanes; however, due to the ability of these to have more compact, spherical shapes, their melting and boiling points can be quite different from their straight-chain counterparts.

Review the effects of London dispersion forces on molecules in Section 8.2.



▶ **Figure 12.4**
The boiling and melting points for the straight-chain alkanes increase with molecular size.

Since they do not possess significant dipole moments, alkanes are nonpolar and as such are insoluble in polar solvents such as water but soluble in nonpolar organic solvents, such as pentane, hexane, and other alkanes ("like dissolves like"). Because of this aversion to water, alkanes are said to be hydrophobic ("water hating"). Because alkanes are generally less dense than water, they float on its surface. Low-molecular-mass alkanes are volatile and must be handled with care because their vapors are flammable. Mixtures of alkane vapors and air can explode when ignited by a single spark.

Recall from Section 9.2 the rule of thumb when predicting solubility: "like dissolves like."

The physiological effects of alkanes are limited. Methane, ethane, and propane gases are nontoxic, but the danger of inhaling them lies in potential suffocation due to lack of oxygen. Breathing the vapor of larger alkanes in large concentrations can

induce loss of consciousness. There is also a danger in breathing droplets of liquid alkanes because they dissolve nonpolar substances in lung tissue and cause pneumonia-like symptoms.

Mineral oil, petroleum jelly, and paraffin wax are mixtures of higher alkanes. All are harmless to body tissue and are used in numerous food and medical applications. Mineral oil passes through the body unchanged and is sometimes used as a laxative. Petroleum jelly (sold as Vaseline) softens, lubricates, and protects the skin. Paraffin wax is used in candle making, on surfboards, and in home canning. See the Chemistry in Action on page 428 for more surprising uses of alkanes.

Properties of Alkanes:

- Odorless or mild odor; colorless; tasteless; nontoxic
- Nonpolar; insoluble in water but soluble in nonpolar organic solvents; less dense than water
- Flammable; otherwise not very reactive

12.8 Reactions of Alkanes

Learning Objectives:

- Determine the basic reactions of alkanes.
- Draw the isomeric products formed during the halogenation of simple alkanes.

Alkanes do not react with acids, bases, or most other common laboratory *reagents* (a substance that causes a reaction to occur). Their only major reactions are with oxygen (combustion) and with halogens (halogenation). Both of these reaction types have complicated mechanisms and occur through the intermediacy of free radicals (see "Halogenation" later in the chapter).

Another important radical reaction is found in the formation of the polymers that make up such things as plastics; this is a radical reaction seen primarily with organic molecules that contain double bonds (Section 13.7).

Combustion

Most of you probably get to school every day using some sort of transportation that uses gasoline, which is a mixture of alkanes, or use a mixture of alkanes when cooking on your gas stove or grilling on your backyard gas barbecue. To power a vehicle or use a gas grill, that mixture of alkanes must be converted into energy. The reaction of an alkane with oxygen is called **combustion,** an oxidation reaction that commonly takes place in a controlled manner in an engine or furnace. Carbon dioxide and water are always the products of complete combustion of any hydrocarbon, and a large amount of heat is released (ΔH is a negative number). Some examples were given in Table 7.1.

Combustion A chemical reaction that produces a flame, usually because of burning with oxygen.

Combustion reactions are exothermic, as we learned in Section 7.3.

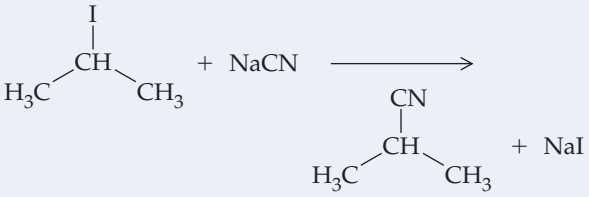
$$CH_4(g) + 2\,O_2(g) \longrightarrow CO_2(g) + 2\,H_2O(g) \quad \Delta H = -891\ \text{kJ/mol}$$

When hydrocarbon combustion is incomplete because of faulty engine or furnace performance, carbon monoxide and carbon-containing soot are among the products. Carbon monoxide is a highly toxic and dangerous substance, especially so because it has no odor and can easily go undetected (see the Chemistry in Action "CO and NO: Pollutants or Miracle Molecules?" in Chapter 4). Breathing air that contains as little as 2% CO for only one hour can cause respiratory and nervous system damage or death. The supply of oxygen to the brain is cut off by carbon monoxide because it binds strongly to blood hemoglobin at the site where oxygen is normally bound. By contrast with CO, CO_2 is nontoxic and causes no harm, except by suffocation when present in high concentration.

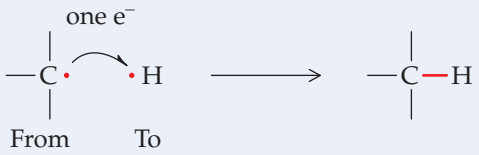
MASTERING REACTIONS

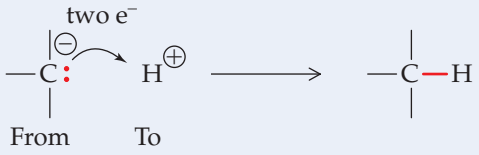
Organic Chemistry and the Curved Arrow Formalism

Starting with this chapter and continuing on through the remainder of this text, you will be exploring the world of organic chemistry and its close relative, biochemistry. Both of these areas of chemistry are much more "visual" than those you have been studying; organic chemists, for example, look at how and why reactions occur by examining the flow of electrons. For example, consider the following reaction of 2-iodopropane with sodium cyanide:



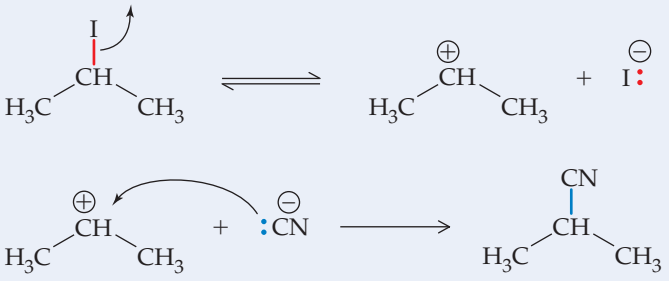
This seemingly simple process (known as a *substitution reaction,* discussed in Chapter 13) is not adequately described by the equation. To help to understand what may really be going on, organic chemists use what is loosely described as "electron pushing" and have adopted what is known as *curved arrow formalism* to represent it. The movement of electrons is depicted using curved arrows, where the number of electrons corresponds to the head of the arrow. Single-headed arrows represent movement of one electron, whereas a double-headed arrow indicates the movement of two.



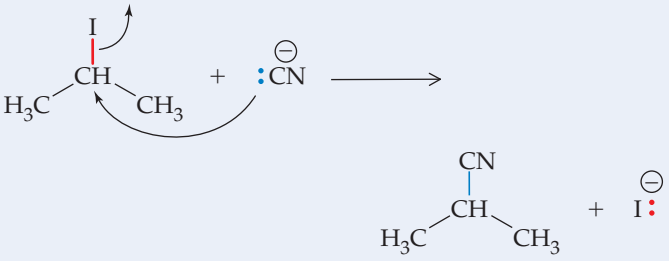


The convention is to show the movement *from* an area of high electron density (the start of the arrow) *to* one of lower electron density (the head of the arrow). Using curved arrow formalism, we can examine the reaction of 2-iodopropane with sodium cyanide in more detail. There are two distinct paths by which this reaction can occur.

Path 1

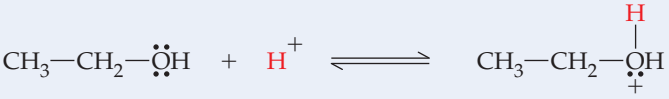


Path 2



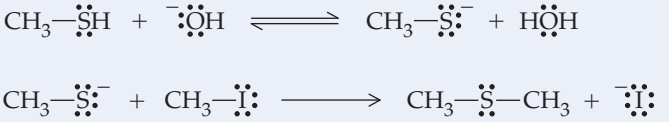
Notice that while both pathways lead ultimately to the same product, the curved arrow formalism shows us that they have significantly different ways of occurring. Although it is not important right now to understand which of the two paths is actually operative (it turns out to be a function of solvent, concentrations, catalysts, temperature, and other conditions), it is important that you get used to thinking of reactions as an "electron flow" of sorts. Throughout the next several chapters, you will see more of these "Mastering Reactions" boxes; they are intended to give you a little more insight into the otherwise seemingly random reactions that organic molecules undergo.

MR Problem 12.1 When ethanol is treated with acid, the initially formed intermediate is known as an oxonium ion.



Using the curved arrow formalism, show how this process most likely occurs.

MR Problem 12.2 Consider the following two-step process:



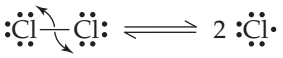
Using the curved arrow formalism, show how each step of this process is most likely to occur.

PROBLEM 12.16

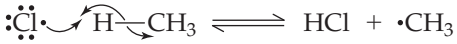
Write a balanced equation for the complete combustion of methane with oxygen (see Worked Example 5.3 for guidance).

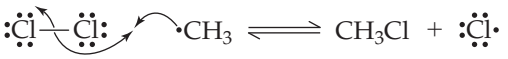
Halogenation

The second notable reaction of alkanes is *halogenation,* the replacement of an alkane hydrogen by a chlorine or bromine in a process initiated by heat or light. This process is known as "free radical halogenation" and occurs in a step-wise manner (a "free radical", or a "radical", is a molecule or atom containing a single, unpaired electron; since a radical does not have an octet of electrons around all of its atoms, it is highly reactive). Following is the reaction of methane with chlorine gas; the process is identical for bromine.

Step 1  Initiation

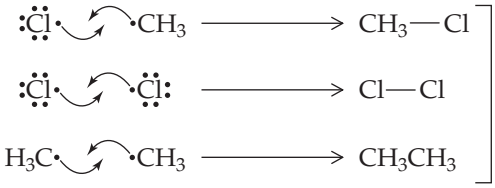
(Note: It is common practice to show only the single electron for radicals with lone pairs—Cl•)

Step 2  Propagation-1

Step 3  Propagation-2

The reaction starts by the formation of chlorine radicals (Cl•); this occurs because the Cl–Cl bond is extremely weak and therefore reactive, in this case being easily broken upon exposure to sunlight or heat. Radicals contain seven electrons (one short of the desired octet) and are extremely reactive, so much so they can remove a hydrogen from a carbon (Step 2). The newly formed carbon radical (here, H_3C•) reacts with another Cl_2 to give chloromethane and regenerate the chlorine radical (Step 3), which is then free to react with another C–H bond (Step 2). Step 1 is called the initiation step, as a radical is initially formed where none were before. Steps 2 and 3 are called propagation steps, since one radical is used and another generated; this is known as a chain reaction, as the chlorine radical generated in Step 3 reenters the reaction to cause Step 2 to occur again. This process will occur over and over until either (i) the reaction is intentionally stopped, (ii) all C–H bonds have been replaced by Cl, or (iii) a termination step occurs (a step in which two radicals combine, thus eliminating radicals from the reaction).

Termination Steps



Any step where radicals are used and not regenerated can be a termination step.

Halogenation is important because it is used to prepare both a number of molecules that are key industrial solvents (such as dichloromethane, chloroform, and carbon tetrachloride) as well as others (such as bromoethane) that are used for the preparation of other larger organic molecules. As shown above, only one H at a time is replaced; however, if allowed to react for a long enough time, all Hs will be replaced with halogens. Complete chlorination of methane, for example, yields carbon tetrachloride:

$$CH_4 + 4\,Cl_2 \xrightarrow{\text{Heat or light}} CCl_4 + 4\,HCl$$

Although the above equation for the reaction of methane with chlorine is balanced, it does not fully represent what actually happens. In fact, this reaction, like many organic reactions, yields a mixture of products.

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$
$$CH_3Cl \xrightarrow{Cl_2} CH_2Cl_2 + HCl$$
$$CH_2Cl_2 \xrightarrow{Cl_2} CHCl_3 + HCl$$
$$CHCl_3 \xrightarrow{Cl_2} CCl_4 + HCl$$

CH_3Cl, chloromethane (singly)
CH_2Cl_2, dichloromethane (doubly)
$CHCl_3$, chloroform
CCl_4, carbon tetrachloride

When we write the equation for an organic reaction, our attention is usually focused on converting a particular reactant into a desired product; any minor by-products and inorganic compounds (such as the HCl formed in the chlorination of methane) are often of little interest and are ignored. Thus, it is not always necessary to balance the equation for an organic reaction as long as the reactant, the major product, and any necessary reagents and conditions are shown. A chemist who plans to convert methane into bromomethane might therefore, write the equation as

$$CH_4 \xrightarrow[\text{Light, heat}]{Br_2} CH_3Br$$

Like many equations for organic reactions, this equation is not balanced.

In using this convention, it is customary to put reactants and reagents above the arrow and conditions, solvents, and catalysts below the arrow.

Worked Example 12.12 Drawing Isomers of Singly Chlorinated or Brominated Alkanes

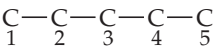
(a) Draw all singly chlorinated isomers obtained upon the reaction of pentane with Cl_2.

$$CH_3CH_2CH_2CH_2CH_3 + Cl_2 \longrightarrow ?$$

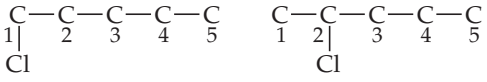
ANALYSIS First, identify the parent alkane and then add chlorine systematically to each carbon to create new structures. Compare structures to determine whether they are unique or identical to others you have drawn.

SOLUTION

STEP 1: Begin by drawing the structure of the alkane starting material. Remove all hydrogens to get a skeletal structure; number the carbons.

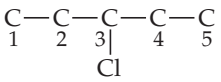
$CH_3CH_2CH_2CH_2CH_3$ becomes 

STEP 2: One at a time, place a Cl on each carbon that is connected to three or less carbon atoms and draw that skeletal structure.

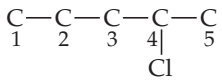


A

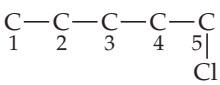
B



C



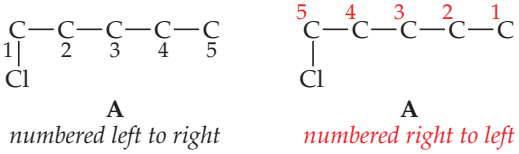
D



E

In this example, there are only carbons attached to one or two other carbons.

STEP 3: Now compare the structures you drew in Step 2, eliminating all that are the same. The simplest way to do this is to designate each structure you drew as a "C#" isomer. Be sure to check numbering in both directions.

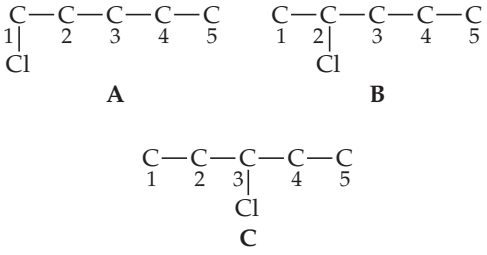


Structure A is the C1 isomer if numbered from left to right or the C5 isomer if numbered from right to left. Doing this for all structures obtained, we get the following correlations:

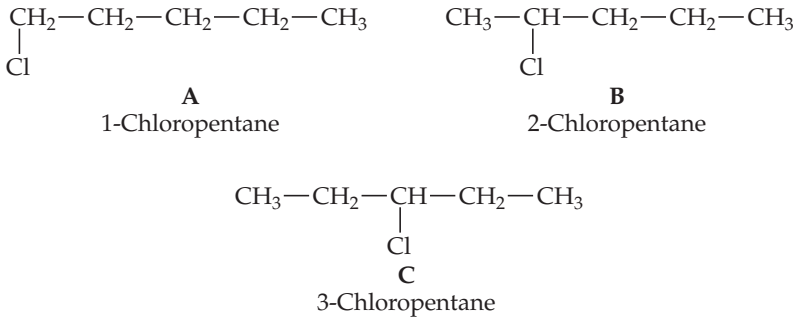
Structure **A** = C1 or C5 Structure **B** = C2 or C4 Structure **C** = C3 in either direction

Structure **D** = C4 or C2 Structure **E** = C5 or C1

Based on this, structures A and E are the same, as are B and D. Structure C is unique. Keep all unique structures, as well as one of each identical pair (here, we will keep A and B, since they have the lowest index numbers). From this, we get:

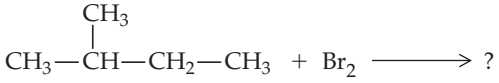


STEP 4: Finish by putting in hydrogens so that each C has four bonded atoms.



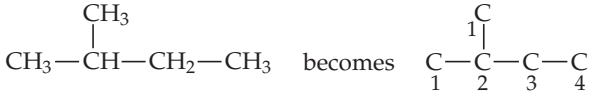
Note: One trick to use if you are not sure if two compounds are the same or different is to name them. Identical compounds will have the same name; if the compounds have different names, they are different compounds.

(b) Repeat for monobromination of the branched alkane 2-methylbutane.



SOLUTION

STEP 1: Draw and number the skeletal structure:



With branched isomers, you need only number in the direction that gives the branch point the lowest number possible. Number in both directions only if you get the same number for the branch point either way.

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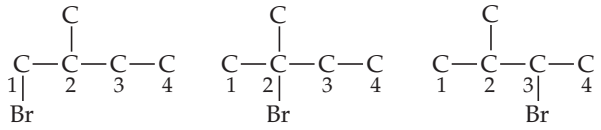
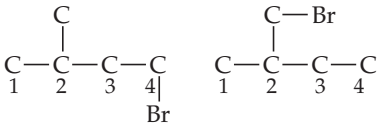
STEP 2: The possible monobromo isomers are as follows:



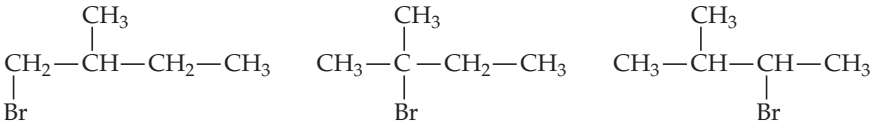
A **B** **C**



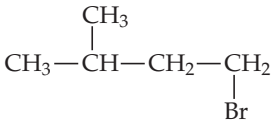
D **E**

STEP 3: Here, only A and E are identical; all others are unique.

STEP 4: The isomers are, therefore:



A **B** **C**



D

Note: This method can be used to draw isomers of almost any combination of carbons and functional groups (such as —OH, —NH_2, etc.)

PROBLEM 12.17

Write the structures of all singly chlorinated products that form when 2,4-dimethylpentane is reacted with Cl_2.

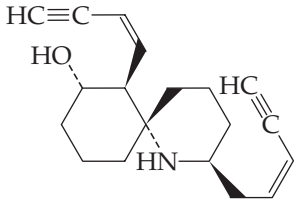
12.9 Cycloalkanes

Learning Objective:

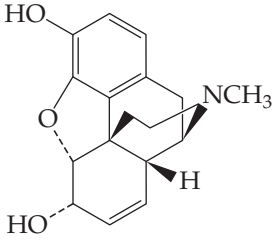
- Identify a cycloalkane from its structure.

Cycloalkane An alkane that contains a ring of carbon atoms.

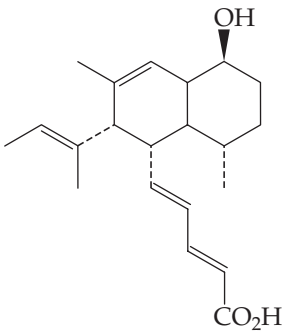
The organic compounds described thus far have all been open-chain, or *acyclic,* alkanes. **Cycloalkanes,** which contain rings of carbon atoms, are also well known and are widespread throughout nature, with many of them having unique biological properties:



Histrionicotoxin 283A
Toxin isolated from poison dart frog

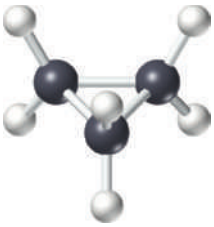


Morphine
Pain killer



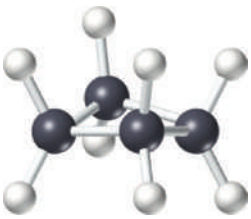
Phomopsidin
Inhibitor of microtubule assembly;
isolated from a marine-derived fungi

To form a closed ring requires an additional C—C bond and the loss of 2 H atoms. Compounds of all ring sizes from 3 through 30 and beyond have been prepared in the laboratory. The two simplest cycloalkanes—cyclopropane and cyclobutane—contain 3 and 4 carbon atoms, respectively.



CH_2
$H_2C—CH_2$

Cyclopropane
(mp –128 °C/145 K, bp –33 °C/240 K)



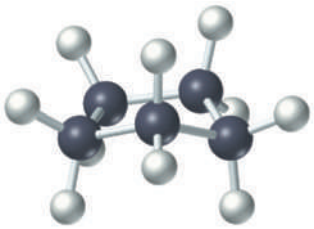
$H_2C—CH_2$
$H_2C—CH_2$

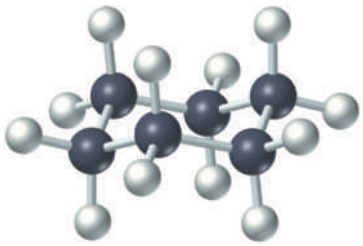
Cyclobutane
(mp –50 °C/223 K, bp –12 °C/261 K)

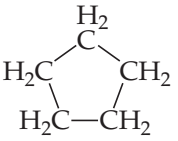
Note that if we flatten the rings in cyclopropane and cyclobutane, the C—C—C bond angles are 60° *and* 90°, respectively—values that are considerably compressed from the normal tetrahedral value of 109.5°. As a result, these compounds are less stable and more reactive than other cycloalkanes. The five-membered (cyclopentane) ring has nearly ideal bond angles, and so does the six-membered (cyclohexane) ring. Both cyclopentane and cyclohexane accomplish this nearly ideal state by adopting a puckered, nonplanar shape, further discussion of which, while important, is beyond the scope of this textbook. Both cyclopentane and cyclohexane rings are therefore stable, and many naturally occurring and biochemically active molecules, such as the steroids (Chapter 28), contain such rings. These rings, and the shape they impart on the molecules that contain them, are an important component of what is known as structure–activity relationships in rational drug design.

Cyclic and acyclic alkanes are similar in many of their properties. Cyclopropane and cyclobutane are gases at room temperature (like propane and butane), whereas larger cycloalkanes, like larger alkanes, are liquids or solids. Like alkanes, cycloalkanes are nonpolar, insoluble in water, and flammable. Because of their cyclic structures, however, cycloalkane molecules are more rigid and less flexible than their open-chain counterparts. Rotation is not possible around the carbon–carbon bonds in cycloalkanes without breaking open the ring. This property is known as **restricted rotation** and can lead to isomer formation (see Group Problem 12.76).

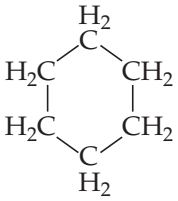
Restricted Rotation The limited ability of a molecule to rotate around a given bond.







Cyclopentane—all bond angles are near 109°.



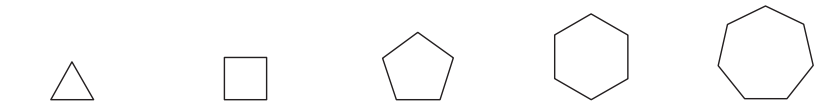
Cyclohexane—all bond angles are near 109.5°.

12.10 Drawing and Naming Cycloalkanes

Learning Objective:

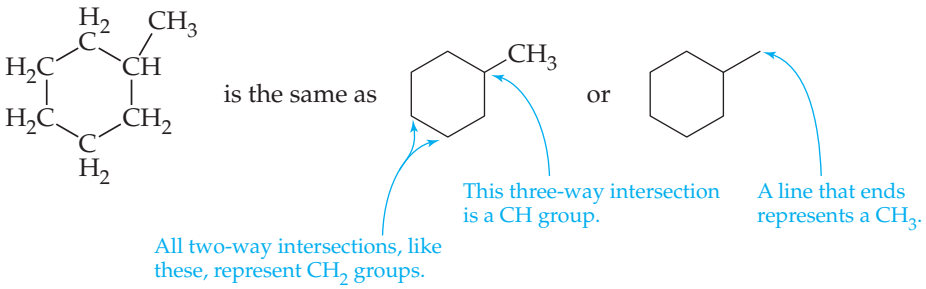
- Name a cycloalkane given its structure and draw a cycloalkane given its name.

Even condensed structures become awkward when we work with large molecules that contain rings. Thus, line structures are used almost exclusively in drawing cycloalkanes, with *polygons* used for the cyclic parts of the molecules. A triangle represents cyclopropane, a square represents cyclobutane, a pentagon represents cyclopentane, and so on, where, just like alkanes, a carbon is found at every point two or more lines meet, or wherever a line ends.



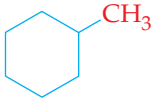
Cyclopropane Cyclobutane Cyclopentane Cyclohexane Cycloheptane

Methylcyclohexane, for example, looks like this in a line structure.



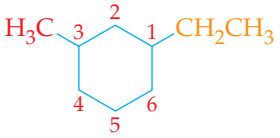
Cycloalkanes are named by a straightforward extension of the rules for naming open-chain alkanes. In most cases, only two steps are needed.

STEP 1: **Use the cycloalkane name as the parent.** That is, compounds are named as alkyl-substituted cycloalkanes rather than as cycloalkyl-substituted alkanes. If there is only one substituent on the ring, it is not even necessary to assign a number because all ring positions are identical.



Parent compound: Cyclohexane
Name: Methylcyclohexane
(not cyclohexylmethane)

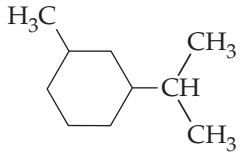
STEP 2: Identify and number the substituents. Start numbering at the group that has alphabetical priority, and proceed around the ring in the direction that gives the second substituent the lowest possible number.



1-Ethyl-3-methylcyclohexane
(not 1-ethyl-5-methylcyclohexane or
1-methyl-3-ethylcyclohexane or
1-methyl-5-ethylcyclohexane)

Worked Example 12.13 Naming Organic Compounds: Cycloalkanes

What is the IUPAC name of the following cycloalkane?

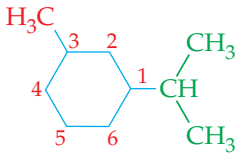


ANALYSIS First, identify the parent cycloalkane and then add the positions and identity of any substituents.

SOLUTION

STEP 1: The parent cycloalkane contains six carbons (*hex*ane), hence, *cyclohexane.*

STEP 2: There are two substituents; a methyl ($-CH_3$) and an isopropyl ($-CH(CH_3)_2$). Alphabetically, the isopropyl group is given priority (number 1); the methyl group is then found on the third carbon in the ring.



1-Isopropyl-3-methylcyclohexane

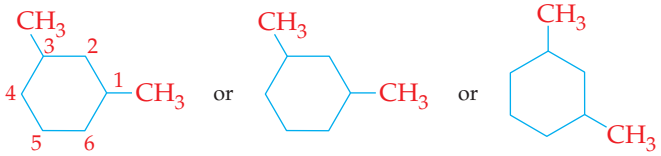
Worked Example 12.14 Molecular Structures: Drawing Line Structures for Cycloalkanes

Draw a line structure for 1,3-dimethylcyclohexane.

ANALYSIS This structure consists of a 6-carbon ring (cyclo*hex*ane) with two methyl groups (*di*methyl) attached at positions 1 and 3. Draw a hexagon to represent a cyclohexane ring, and attach a $-CH_3$ group at an arbitrary position that becomes the first carbon in the chain, designated as C1. Then count around the ring to the third carbon (C3), and attach another $-CH_3$ group.

SOLUTION

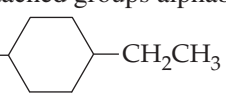
Note that the C3 methyl group could have been written as H_3C- to emphasize that attachment to the ring is through the carbon. This is a common practice for methyl groups that are attached on the left side of a cycloalkane ring. Note also that as long as the methyl groups are 1, 3 to one another, it does not matter how we orient the ring.

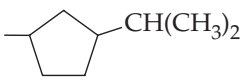


1,3-Dimethylcyclohexane

PROBLEM 12.18

What are the IUPAC names of the following cycloalkanes? Remember to assign priority to the attached groups alphabetically.

(a) H_3C-  $-CH_2CH_3$

(b) CH_3CH_2-  $-CH(CH_3)_2$

PROBLEM 12.19

Draw line structures that represent the following IUPAC names:

(a) 1,1-Diethylcyclohexane **(b)** 1,3,5-Trimethylcycloheptane

PROBLEM 12.20

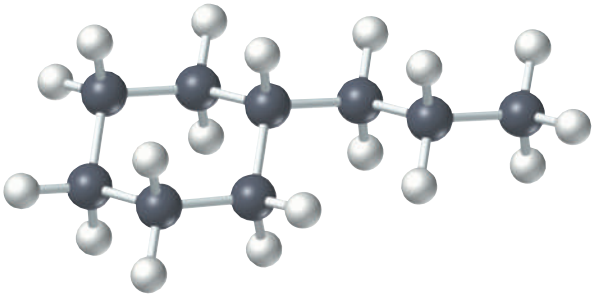
What is wrong with the following names? It will be helpful to draw the structures as named before making your decision.

(a) 1,4,5-Trimethylcyclohexane **(b)** Cyclohexylcyclopentane

(c) 1-Ethyl-2-methyl-3-ethylcyclopentane

KEY CONCEPT PROBLEM 12.21

Redraw the following cycloalkane in both condensed and line formula format. What is its IUPAC name?



CHEMISTRY IN ACTION

Surprising Uses of Petroleum

Petroleum, arising from the decay of ancient plants and animals, is found deep below the earth's crust; it is a mixture of hydrocarbons of varying sizes. Petroleum's worth as both a portable, energy-dense fuel and as the starting point of many industrial chemicals makes it one of the world's most important commodities. About 90% of vehicular fuel needs worldwide are met by oil. In addition, 40% of total energy consumption in the United States is petroleum-based. In an effort to create a "greener" environment and more sustainable energy, a great fervor has developed to find alternative energy sources, but a question arises: Can we completely eliminate the need for petroleum from our lives, even if we could find an alternative energy for transportation purposes?

Petrochemicals, which we first mentioned in the chapter opener, are chemical products derived specifically from petroleum and generally refer to those products that are not used for fuels. When crude oil is refined and cracked (the process during which complex organic molecules found in oil are converted into simpler molecules by breaking carbon–carbon bonds), a number of fractions having different boiling ranges are obtained. The primary petrochemicals obtained can be broken down into three categories:

1. Alkenes (or olefins; Chapter 13): Primarily ethene, propene, and butadiene. Ethene and propene are important sources of industrial chemicals and plastics products.
2. Aromatics (Chapter 13): Most important among these are benzene, toluene, and the xylenes. These raw materials are used for making a variety of compounds, from dyes and synthetic detergents, to plastics and synthetic fibers, to pharmaceutical starting materials.
3. Synthesis gas: A mixture of carbon monoxide and hydrogen used to make methanol (which is used as both a solvent and starting point for other products).

▲ Petroleum jelly, originally an unwanted by-product of drilling, has found many uses in today's average household.

What specific types of products are made from these petrochemicals? Let's look at a few:

Lubricants such as light machine oils, motor oils, and greases are products used to keep almost all mechanical devices running smoothly and to prevent them from seizing up under high-use conditions. Wax is another raw petroleum product. Paraffin waxes are used to make candles and polishes as well as food packaging such as milk cartons. The shine you see on the fruit in your local supermarket is also a result of the use of wax.

Most of the rubber soles found on today's shoes are derived from butadiene. Natural rubber becomes sticky when hot and stiff when cold, but man-made rubber stays much more flexible. Car tires are also made from synthetic rubber, which makes them much safer to drive on. Today, the demand for synthetic rubber is four-times greater than for natural rubber.

One very interesting petroleum-derived material was once considered a nuisance by-product of oil drilling. "Black rod wax" is a paraffin-like substance that forms on oil-drilling rigs, causing the drills to malfunction. Workers had to scrape the thick, viscous material off to keep the drills running. However, they found that when applied to cuts and burns it would cause these injuries to heal faster. A young chemist named Robert Chesebrough, after purifying the material, obtained a light-colored gel he named vaseline, or petroleum jelly. Chesebrough demonstrated his miracle product by burning his skin, then spreading the healing ointment on his injuries. Its use in promoting the healing of minor cuts, abrasions, and dry skin and lips soon followed, as we saw in the opening of this chapter. While the use of Vaseline® for burns has fallen out of favor (due to its ability to seal in heat as well as moisture), it is still important as a base for a number of antibacterial ointments. Today, we know that the primary effect that petroleum jelly has on the healing process is that of sealing wounds from moisture loss, allowing the skin to heal from the bottom up more effectively.

As you can see, petroleum has many uses that are key in our everyday lives. Although lessening its use as a fuel for transportation can help to conserve what reserves we have, its complete elimination from our lives is, at this point in time, nearly impossible.

CIA Problem 12.4 (a) Why is the demand for synthetic rubber greater than that of natural rubber? (b) Butadiene is used in the manufacture of synthetic rubber. Why is this more desirable than natural rubber?

CIA Problem 12.5 (a) What common produce items might you see paraffin waxes being used on? (b) What consumer products are manufactured with ethene and propene?

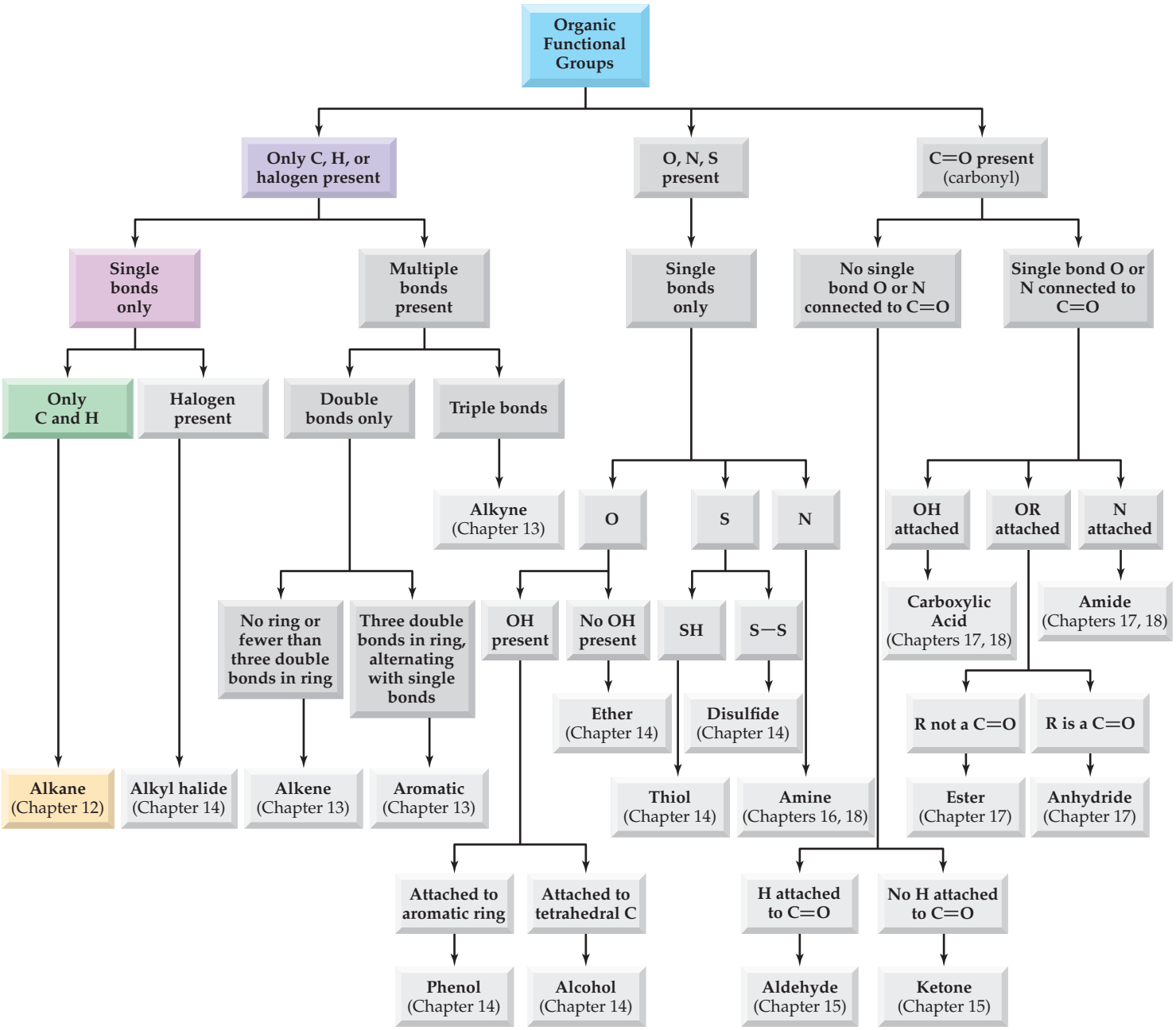
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Identify the general structural characteristics of organic molecules, in particular, the tetravalent nature of carbon and the different ways in which it can be expressed.** Compounds made up primarily of carbon and hydrogen atoms are classified as organic. Each carbon atom in an organic molecule is tetravalent, meaning it can form a total of four bonds. Many organic compounds contain carbon atoms that are joined in chains by a combination of single (C—C), double (C=C), or triple (C≡C) bonds. We focused here primarily on *alkanes and cycloalkanes,* hydrocarbon compounds that contain only single bonds between all C atoms *(see Problems 27, 29, 30, 68, 70, and 74).*
- **Define functional group.** Organic compounds can be classified into various families according to the functional groups they contain (Table 12.1). A *functional group* is a part of a larger molecule and is composed of a group of atoms that has characteristic structure and chemical reactivity *(see Problem 28).*
- **Identify the functional groups in organic molecules.** Being able to identify the functional group family to which an organic molecule belongs is important, as a given functional group undergoes nearly the same chemical reactions in every molecule where it occurs *(see Problems 23, 31–35, 64, and 71).*
- **Recognize structural (constitutional) isomers and functional group isomers.** Structural or constitutional isomers are compounds that have the same formula but different structural connections of atoms. When atoms other than carbon and hydrogen are present, the ability to have *functional group isomers* arises; these are molecules that, due to the differences in their connections, have not only different structures but also belong to different families of organic molecules *(see Problems 26, 36–47, 58, 73, and 76).*
- **Draw structural, condensed, and line formulas for simple chemical compounds.** Organic compounds can be represented by *structural formulas* in which all atoms and bonds are shown, by *condensed structures* in which not all bonds are drawn, or by *line structures* in which the carbon skeleton is represented by lines and the locations of C and H atoms are understood *(see Problems 22, 23, 73, and 75).*
- **Convert any given structural, condensed, or line formula into its corresponding alternative.** Chemists and biochemists often use a mixture of structural, condensed, and line formula to represent the complicated molecules they study. Since organic molecules are drawn using all three of these motifs, being able to think interchangeably in all three formats is important in the study of organic and biological molecules *(see Problems 49, 52, and 53).*
- **Determine if two given structures are the different conformers of the same molecule, different structural isomers, or different molecules.** Structural isomers have the same chemical formula but different connections of atoms; different molecules have different chemical formulas; and conformers have the same chemical formula and connections of atoms with different spatial arrangements of those atoms. Free rotation around C—C single bonds allows a given organic compound the ability to adopt a number of different spatial arrangements. These are called *conformations* or *conformers.* Different conformations of a molecule have different energies depending on whether large groups of atoms are close to one another or not *(see Problems 46, 47, 49, 72, and 76).*
- **Name an alkane given its structure and draw an alkane given its name.** A *straight-chain alkane* has all its carbons connected in a row, and a *branched-chain alkane* has a branching connection of atoms somewhere along its chain. Straight-chain alkanes are named by adding the family ending *-ane* to a parent; this tells how many carbon atoms are present. Branched-chain alkanes are named by using the longest continuous chain of carbon atoms for the parent and then identifying the *alkyl groups* present as branches off the main chain. The positions of the substituent groups on the main chain are identified by numbering the carbons in the chain so that the substituents have the lowest index numbers *(see Problems 24, 25, and 50–53).*
- **Identify the physical properties of alkanes.** Alkanes are generally nonpolar, insoluble in water (hydrophobic), and unreactive. They possess low melting and/or boiling points due to their weak intermolecular forces. Alkanes are generally nontoxic and therefore have limited physiological effects *(see Problems 68 and 78).*
- **Determine the basic reactions of alkanes.** Alkanes possess low reactivity; their principal chemical reactions are *combustion,* a reaction with oxygen that gives carbon dioxide and water, and *halogenation,* a reaction in which hydrogen atoms are replaced by chlorine or bromine *(see Problems 60 and 71).*
- **Draw the isomeric products formed during the halogenation of simple alkanes.** Drawing the isomeric products obtained on halogenation of an alkane can be accomplished by systematically and methodically replacing hydrogens one carbon at a time and then comparing each structure obtained with one another to determine if the

molecules are the same or different structurally. One way to tell if the compounds are the same or different is to name them; identical compounds have the same name. This procedure for drawing isomeric products can be used to draw isomers of almost any combination of carbons and functional groups *(see Problems 62, 63, and 69)*.

- **Identify a cycloalkane from its structure.** Hydrocarbons that have only single bonds arraigned in a ring of carbon atoms are called *cycloalkanes.* Due to their cyclic nature, they have what is known as restricted rotation, meaning they cannot adopt as wide a range of conformations as the corresponding alkanes can. Cycloalkanes possess almost identical physical and chemical properties as alkanes *(see Problems 25 and 54–56)*.
- **Name a cycloalkane given its structure and draw a cycloalkane given its name.** Cycloalkanes are named by adding *cyclo-* as a prefix to the name of the alkane corresponding to the number of carbons in the ring. Cycloalkanes-containing groups attached to the main ring are named the same way as branches in an alkane are. The positions of the substituent groups on the ring are identified by numbering the carbons in the chain so that the substituents have the lowest possible set of position numbers *(see Problems 25, 41, 53, and 59)*.

CONCEPT MAP: INTRODUCTION TO ORGANIC CHEMISTRY FAMILIES



▲ **Figure 12.5 Functional Group Concept Map.** Learning to classify organic molecules by the families they belong to is a crucial skill you need to develop, since the chemistry that both organic and biological molecules undergo is directly related to their functional groups. This concept map will aid you in this classification. First introduced in Section 12.2, it will be a key reference as you proceed through the rest of the chapters in this book. As we discuss each family in later chapters, sections of it will be reproduced and expanded to help also tie in the chemistry that those functional groups undergo. Functional groups will be grayed out until they are discussed; as each functional group is discussed, it will become colorized.

KEY WORDS

Alkane, *p. 399*
Alkyl group, *p. 410*
Branched-chain alkane, *p. 401*
Combustion, *p. 419*
Condensed structure, *p. 402*
Conformation, *p. 408*
Conformer, *p. 408*
Constitutional isomers, *p. 401*
Cycloalkane, *p. 424*
Ethyl group, *p. 411*
Functional group, *p. 394*
Functional group isomer, *p. 401*
Hydrocarbon, *p. 396*
Isomers, *p. 400*
Isopropyl group, *p. 411*
Line structure, *p. 404*
Methyl group, *p. 411*
Methylene group, *p. 403*
Organic chemistry, *p. 391*
Primary (1°) carbon atom, *p. 412*
Propyl group, *p. 411*
Quaternary (4°) carbon atom, *p. 412*
Restricted rotation, *p. 425*
Secondary (2°) carbon atom, *p. 412*
Straight-chain alkane, *p. 401*
Substituent, *p. 410*
Tertiary (3°) carbon atom, *p. 412*

SUMMARY OF KEY REACTIONS

Beginning with this chapter, and continuing through Chapter 17, you will find a "Summary of Key Reactions" section located right before the end of chapter problems. In this section, we will summarize all the key reactions discussed in that chapter, along with references to those previously discussed as needed. It is intended as an aid in your study of organic and biochemistry and will be a useful reference guide.

1. Combustion of an alkane with oxygen to yield carbon dioxide and water (Section 12.8):

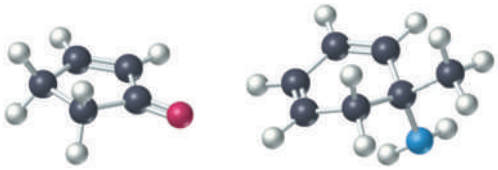
$$CH_4 + 2\,O_2 \longrightarrow CO_2 + 2\,H_2O$$

2. Halogenation of an alkane to yield an alkyl halide (Section 12.8):

$$CH_4 + Cl_2 \xrightarrow{light} CH_3Cl + HCl$$

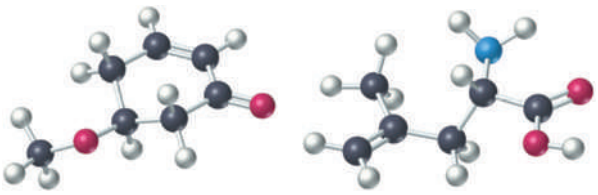
UNDERSTANDING KEY CONCEPTS

12.22 Convert the following models into line drawings (black = C; white = H; red = O; blue = N):



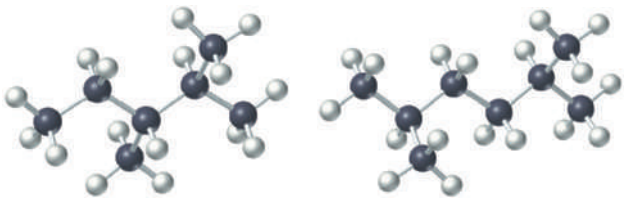
(a) **(b)**

12.23 Convert the following models into line drawings and identify the functional groups in each:



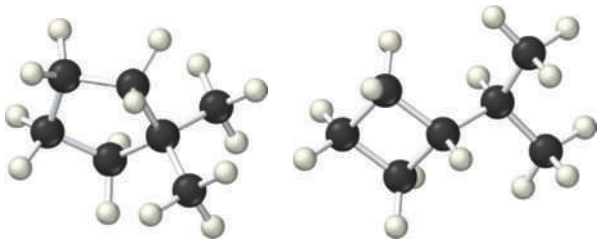
(a) **(b)**

12.24 Give the IUPAC names for the following alkanes:



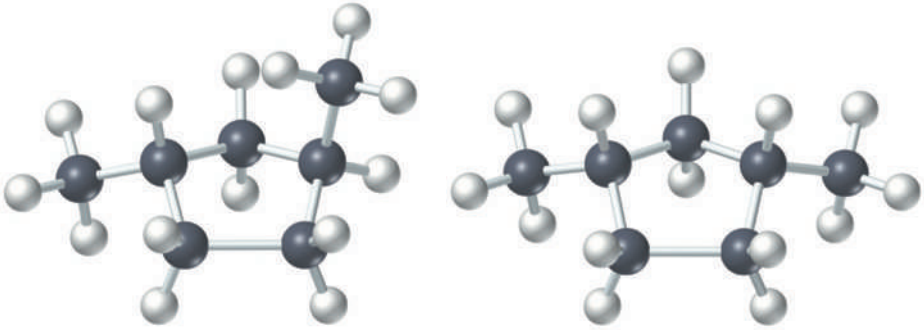
(a) **(b)**

12.25 Give the IUPAC names for the following cycloalkanes:



(a) **(b)**

12.26 The following two compounds are isomers, even though both can be named 1,3-dimethylcyclopentane. What is the difference between them?



(a) **(b)**

ADDITIONAL PROBLEMS

ORGANIC MOLECULES AND FUNCTIONAL GROUPS (SECTIONS 12.1, 12.2)

12.27 What characteristics of carbon make possible the existence of so many different organic compounds?

12.28 What are functional groups, and why are they important?

12.29 Why are most organic compounds nonconducting and insoluble in water?

12.30 What is meant by the term *polar covalent bond*? Give an example of such a bond.

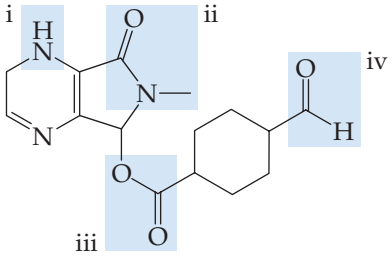
12.31 For each of the following, give an example of a member compound containing 5 carbons total:

(a) Alcohol **(b)** Amine

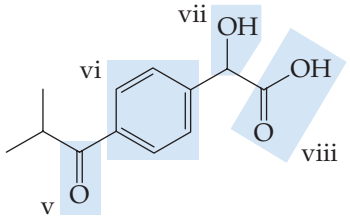
(c) Carboxylic acid **(d)** Ether

12.32 Identify the highlighted functional groups in the following molecules:

(a) i ii iii iv

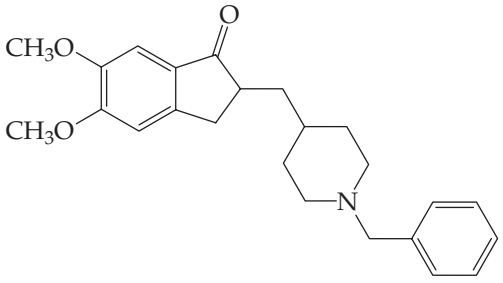


(b) v vi vii viii



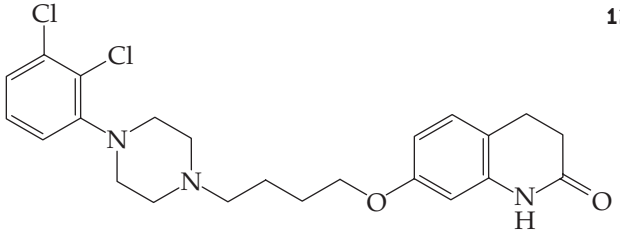
12.33 Identify the functional groups in the following molecules:

(a)



Donepezil
(used in Alzheimers treatment)

(b)



Aripiprazole
(Abilify)

12.34 Propose structures for molecules that fit the following descriptions:

(a) An aldehyde with the formula $C_5H_{10}O$

(b) An ester with the formula $C_6H_{12}O_2$

(c) A compound with the formula C_3H_7NOS that is both an amide and a thiol

12.35 Propose structures for molecules that fit the following descriptions:

(a) An amide with the formula C_4H_9NO

(b) An aldehyde that has a ring of carbons, $C_6H_{10}O$

(c) An aromatic compound that is also an ether, $C_8H_{10}O$

ALKANES AND ISOMERS (SECTIONS 12.3, 12.4, 12.9)

12.36 What requirement must be met for two compounds to be isomers?

12.37 If one compound has the formula C_5H_{10} and another has the formula C_4H_{10}, are the two compounds isomers? Explain.

12.38 **(a)** What is the difference between a secondary carbon and a tertiary carbon? **(b)** What about the difference between a primary carbon and a quaternary carbon? **(c)** How many secondary carbons does the structure shown in Additional Problem 12.33b have? Redraw the structure and highlight them all. (Ignore all double-bonded carbons.)

12.39 Why is it not possible for a compound to have a *quintary* carbon (five groups attached to C)?

12.40 Give examples of compounds that meet the following descriptions:

(a) A six carbon alkane with 2 tertiary carbons

(b) Three different cyclohexanes with having two methyl groups attached.

12.41 Give an example of a compound that meets the following descriptions:

(a) A 5-carbon alkane with only primary and quaternary carbons

(b) A cycloalkane with three substituents

12.42 **(a)** There are two isomers with the formula C_4H_{10}. Draw both the condensed and line structure for each isomer. **(b)** Using the structures you drew in (a) as a starting point, draw both the condensed and line structures for the four isomeric chlorides having the chemical formula C_4H_9Cl.

12.43 Write condensed structures for the following molecular formulas. More than one isomer will be required for each.

(a) Isomers of C_8H_{18} that contain three methyl groups and a longest chain of 5 carbons

(b) Cyclohexanes with a chemical formula of C_8H_{16}

(c) C_2H_4O

(d) Ketones and aldehydes with C_4H_8O

(e) Write the line structures for (b) and (d).

12.44 How many straight-chain isomers can you write that fit the following descriptions? See Worked Example 12.12 for guidance.

(a) Alcohols (—OH) with a longest chain of 6 carbons

(b) Amines ($—NH_2$) with a longest chain of 7 carbons

12.45 How many isomers can you write that fit the following descriptions? See Worked Example 12.12 for guidance.

(a) Monobromides formed from 2-methylpentane

(b) Monochlorides formed from 3-methylpentane

(c) Alcohols (—OH) formed from 2-methylhexane

12.46 Which of the following pairs of structures are identical, which are isomers, and which are unrelated?

(a) $CH_3CH_2CH_3$ and $CH_3CH_2CH_3$ (CH₃ branch)

(b) $CH_3—NH—CH_3$ and $CH_3CH_2—NH—H$

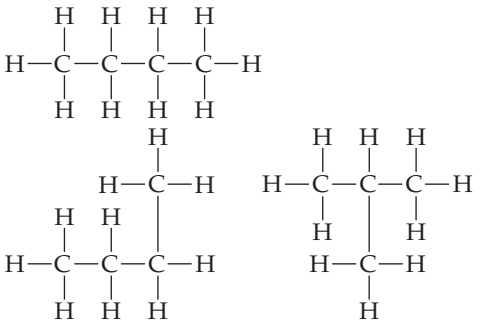
(c) $CH_3CH_2CH_2—O—CH_3$ and $CH_3CH_2CH_2—C(=O)—CH_3$

(d) $CH_3—C(=O)—CH_2CH_2CH(CH_3)_2$ and $CH_3CH_2—C(=O)—CH_2CH_2CH_2CH_3$

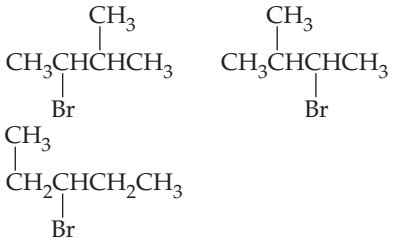
(e) $CH_3CH=CHCH_2CH_2—O—H$ and $CH_3CH_2CH(CH_3)—C(=O)—H$

12.47 Which structures in each group represent the same compound and which represent isomers?

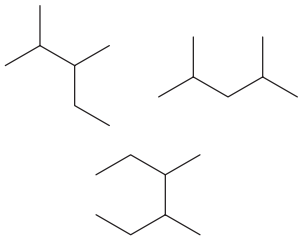
(a)



(b)



(c)



(d) See if you can find some caraway seeds and some mint leaves. Crush each separately and compare their smells. Now look up the structures primarily responsible for the smell of each and carefully compare them. How are they related? These are what are known as *stereoisomers;* this advanced topic is one that will be discussed in Chapter 14.

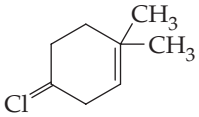
12.48 What is wrong with the following structures?

(a) $CH_3=CHCH_2CH_2OH$

(b) $CH_3CH_2CH=C(=O)—CH_3$

(c) $CH_2CH_2CH_2C\equiv C(CH_3)CH_3$

12.49 There are two things wrong with the following structure. What are they?



ALKANE NOMENCLATURE (SECTIONS 12.6, 12.10)

12.50 What are the IUPAC names of the following alkanes?

(a) $CH_3CH_2CH_2CH_2CH(CH_2CH_3)CH(CH_3)CH_2CH_3$

(b) $CH_3CH_2CH_2CH(CH_3)CH_2CH(CH_2CH_3)CH_3$

(c) $CH_3C(CH_3)CH_2CH_2CH_2CH(CH_3)CH_3$

(d) $CH_3CH_2CH_2C(CH_2CH_2CH_2CH_3)(CH_3)CH(CH_3)CH_3$

(e) $CH_3C(CH_3)CH_2C(CH_3)CH_3$

(f) $CH_3CH_2C(CH_3)CH_2CH(CH_3)CH_2CH_3$

(g) $CH_3(CH_2)_7C(CH_3)_3$

12.51 Give IUPAC names for the five isomers with the formula C_6H_{14}.

12.52 Write condensed structures for the following compounds:

(a) 4-*tert*-Butyl-2-methylheptane

(b) 2,4-Dimethylpentane

(c) 4,4-Diethyl-3-methyloctane

(d) 3-Ethyl-1-isopropyl-5-methylcycloheptane

(e) 1,1,3-Trimethylcyclopentane

12.53 Draw line structures for the following cycloalkanes:

(a) 1,1-Dimethylcyclopropane

(b) 1,3-Dimethylcyclopentane

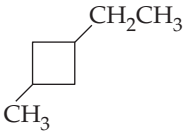
(c) Ethylcyclohexane

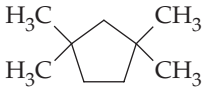
(d) Cycloheptane

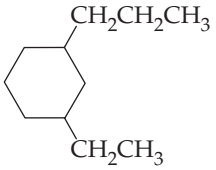
(e) 1-Methyl-3-propylcyclohexane

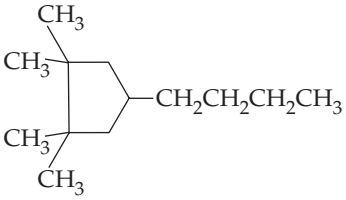
(f) 1-Ethyl-4-isopropylcyclooctane

12.54 Name the following cycloalkanes:

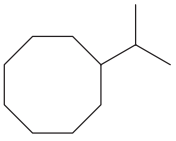
(a) 

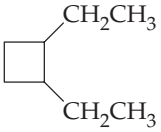
(b) 

(c) 

(d) 

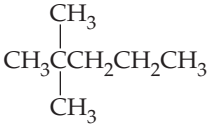
12.55 Name the following cycloalkanes:

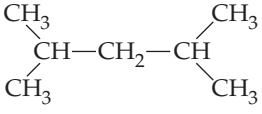
(a) 

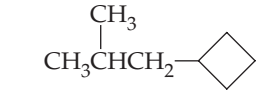
(b) 

(c) 

12.56 The following names are incorrect. Tell what is wrong with each, and provide the correct names.

(a) 
2,2-Methylpentane

(b) 
1,1-Diisopropylmethane

(c) 
1-Cyclobutyl-2-methylpropane

12.57 The following names are incorrect. Write the structural formula that agrees with the apparent name, and then write the correct name of the compound.

(a) 2-Ethylbutane

(b) 2-Isopropyl-2-methylpentane

(c) 5-Ethyl-1,1-methylcyclopentane

(d) 3-Ethyl-3,5,5-trimethylhexane

(e) 1,2-Dimethyl-4-ethylcyclohexane

(f) 2,4-Diethylpentane

(g) 5,5,6,6-Methyl-7,7-ethyldecane

12.58 Draw structures and give IUPAC names for the nine isomers of C_7H_{16}.

12.59 Draw the structural formulas and name all cyclic isomers with the formula C_5H_{10}.

REACTIONS OF ALKANES (SECTION 12.8)

12.60 Propane, commonly known as liquid petroleum (LP) gas, burns in air to yield CO_2 and H_2O. Write a balanced equation for the reaction.

12.61 Write a balanced equation for the combustion of isooctane, C_8H_{18}, a component of gasoline.

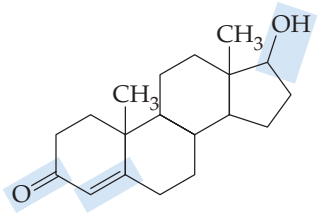
12.62 Write the formulas of the four singly chlorinated isomers formed when 2-methylbutane reacts with Cl_2 in the presence of light.

12.63 Write the formulas of the three doubly brominated isomers formed when 2-methylpropane reacts with Br_2 in the presence of light.

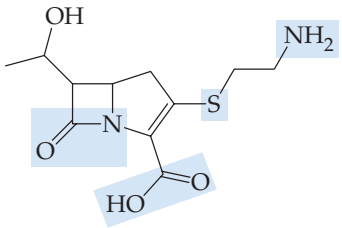
CONCEPTUAL PROBLEMS

12.64 Identify the indicated functional groups in the following molecules:

(a) Testosterone, a male sex hormone

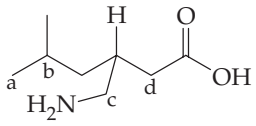


(b) Thienamycin, an antibiotic



(c) Look up the structure of lisdexamfetamine (Vyvanse), a drug used in the treatment of attention deficit hyperactivity disorder (ADHD). Redraw it and identify all the functional groups present. What is known about its therapeutic properties?

12.65 The line structure for pregabalin (Lyrica) is shown as follows:



Identify carbons a–d as primary, secondary, tertiary, or quaternary.

12.66 Consider the compound shown in Problem 12.65; how many tertiary carbons does it have?

12.67 If someone reported the preparation of a compound with the formula C_3H_9, most chemists would be skeptical. Why?

12.68 Most lipsticks are about 70% castor oil and wax. Why is lipstick more easily removed with petroleum jelly than with water?

12.69 When pentane is exposed to Br_2 in the presence of light, a halogenation reaction occurs. Write the formulas of:

(a) All possible products containing only one bromine

(b) All possible products containing two bromines that are *not* on the same carbon

12.70 Which do you think has a higher boiling point, pentane or neopentane (2,2-dimethylpropane)? Why?

12.71 Propose structures for the following:

(a) A carboxylic acid, $C_4H_8O_2$

(b) An iodo-substituted alkene, C_5H_9I

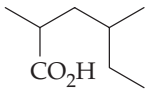
(c) A cyclopentane having a chemical formula C_7H_{14}

(d) An alkene containing only two methyl groups and a chemical formula C_4H_8

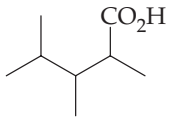
GROUP PROBLEMS

12.72 Which of the following structures represent the same molecule?

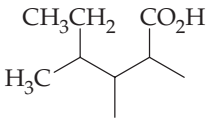
(a)



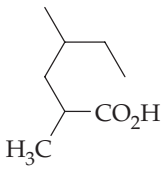
(b)



(c)



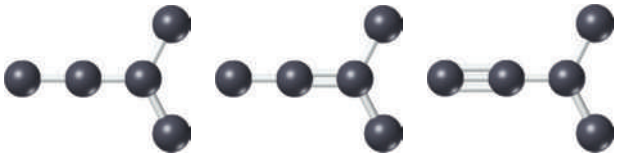
(d)



12.73 In Problem 12.4, you drew the two branched-chain isomers with the formula C_7H_{16}, where the longest chain in the molecule is 6 carbons long. Now see how many other isomers with this chemical formula you can draw.

12.74 Since its discovery, petroleum jelly has been shown to be a household product with many practical uses. Search the internet and see if you can come up with 10 different uses for this "wonder" product.

12.75 How many hydrogen atoms are needed to complete the hydrocarbon formulas for the following carbon backbones?



(a) **(b)** **(c)**

12.76 Refer to the structures shown in Problem 12.26. Using a model kit or the "gum drops and toothpicks" method presented in Hands-On Chemistry 4.1, build models of both structures (a) and (b). These two isomers demonstrate how restricted rotation comes into play for organic molecules (Section 12.9). Can you convert (a) into (b) without breaking any bonds?

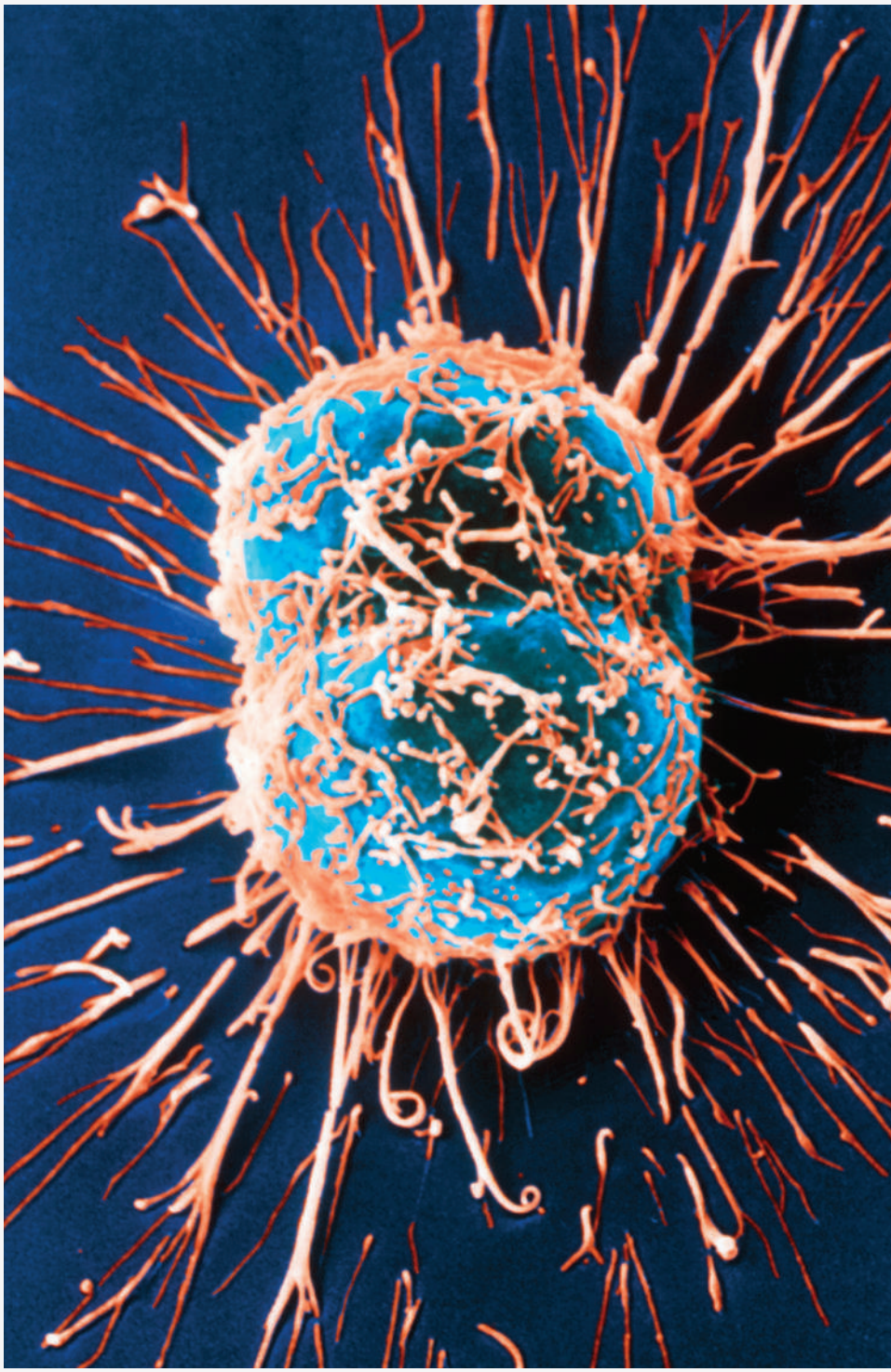
13

Alkenes, Alkynes, and Aromatic Compounds

CONTENTS

CONCEPTS TO REVIEW

A. VSEPR and Molecular Shapes (Section 4.8)
B. Families of Organic Molecules: Functional Groups (Section 12.2)
C. Drawing Organic Structures (Section 12.4)
D. The Shapes of Organic Molecules (Section 12.5)
E. Naming Alkanes (Section 12.6)



▲ In the war on cancer, potent new drugs containing carbon–carbon triple bonds are providing hope for the treatment of diseases such as cervical cancer.

Functional groups give organic molecules their characteristic physical, chemical, and biological properties. In Chapter 12, we examined the simplest hydrocarbons, alkanes, which provide the scaffolding upon which the complicated molecules responsible for life are built. Now we will look at the chemistry of molecules that contain carbon–carbon multiple bonds, or *unsaturated* hydrocarbons. While alkenes and aromatic systems are found in many naturally occurring biomolecules, alkynes are not as commonly observed. However, when

alkynes are found in biological systems, they show surprising physiological activity. Chemists quite often take biologically active molecules that nature provides and use them as starting points in the laboratory to design new drugs to treat disease. Using this strategy, complex alkynes have been isolated from a number of natural sources such as bacterial cultures; these have subsequently shown promise as antitumor agents. Out of this work, the discovery of an extremely interesting class of molecules known as the *enediyne* antibiotics has arisen, a family of naturally occurring compounds that are proving to be among the most potent antitumor agents known. Discussed in more detail in the Chemistry in Action "Enediyne Antibiotics: A Newly Emerging Class of Antitumor Agents" later in the chapter, these toxic molecules, isolated from the bacteria *Micromonospora,* cut deoxyribonucleic acid (DNA) strands, which keeps a cell from reproducing, and could lead to the development of new drugs in the treatment of cancer as well as other diseases.

The last group of unsaturated hydrocarbons we will discuss are known as the aromatic hydrocarbons. *Aromatic compounds* contain a six-membered ring of carbon atoms, have alternating single and double bonds, and possess resonance, which gives aromatic compounds their unique reactivity. If one or more of the carbons in an aromatic ring is replaced by an atom other than C, we obtain what are known as *aromatic heterocyclic* molecules, many of which have unique biological properties. While only alkenes and aromatic compounds are widespread in nature, all of these unsaturated functional groups (including alkynes) are found in many biologically important molecules.

13.1 Alkenes and Alkynes

Learning Objectives:

- Identify the functional groups present in alkenes and alkynes.
- Differentiate between saturated and unsaturated molecules.

Alkanes, introduced in Chapter 12, are **saturated** because each carbon atom has four single bonds. Because this is the maximum number of single bonds a carbon can have, no more atoms can be added to any of the carbons in an alkane—in other words, the molecule is saturated. Alkenes and alkynes, however, are **unsaturated** because they contain carbon–carbon multiple bonds. Atoms can be added to an alkene or alkyne by converting these multiple bonds to single bonds. **Alkenes** are hydrocarbons that contain carbon–carbon double bonds, **cycloalkenes** are hydrocarbons that contain a double bond in a ring system, and **alkynes** are hydrocarbons that contain carbon–carbon triple bonds (cycloalkynes are rare and unknown for rings containing less than eight carbons). As you continue your study of organic and biochemistry, the term *unsaturated* will generically be used to indicate the presence of double bonds; for example, the unsaturated fatty acids (discussed in Chapter 23).

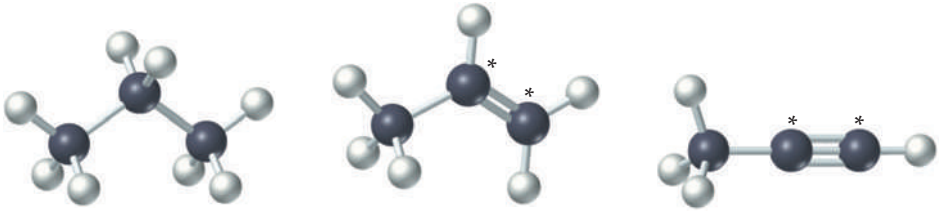
Saturated A molecule in which each carbon atom has the maximum number of single bonds possible (four).

Unsaturated A molecule that contains one or more carbon–carbon multiple bonds.

Alkene A hydrocarbon that contains a carbon–carbon double bond.

Cycloalkene A cyclic hydrocarbon that contains a double bond.

Alkyne A hydrocarbon that contains a carbon–carbon triple bond.



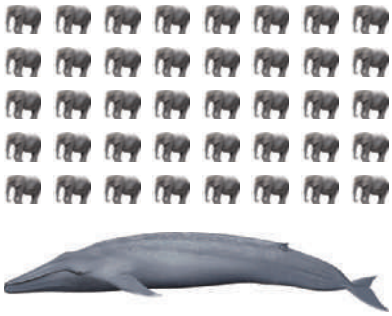
$CH_3CH_2CH_3$
Propane—an alkane
(*saturated*)

$CH_3CH{=}CH_2$
Propene—an alkene
(*unsaturated*)

$CH_3C{\equiv}CH$
Propyne—an alkyne
(*unsaturated*)

Unsaturated carbons are marked with an *

Most of the organic chemicals used in making drugs, explosives, paints, plastics, and pesticides are synthesized by routes that begin with alkenes. Ethene is one of these alkene building blocks that is in tremendous demand, with much of it used for making polyethene, the most common type of plastic in the world. In fact, ethene



▲ An elephant weighs five metric tons, while a blue whale weighs 200 metric tons. That means that the amount of ethene produced worldwide is equal to the weight of 40 million elephants, or 1 million blue whales!

production worldwide is expected to be at a staggering 175 million tons by the end of 2015 and 200 million metric tons by 2020, demonstrating just how important an industrial starting material it is.

Ethene is also formed in the leaves, flowers, and roots of plants, where it acts as a hormone to control seedling growth, stimulate root formation, and regulate fruit ripening; it is thought of as the aging hormone in plants. In its role as a hormone, ethene causes death by signaling the plant to rapidly drop its leaves, effectively shutting down photosynthesis.

13.2 Naming Alkenes and Alkynes

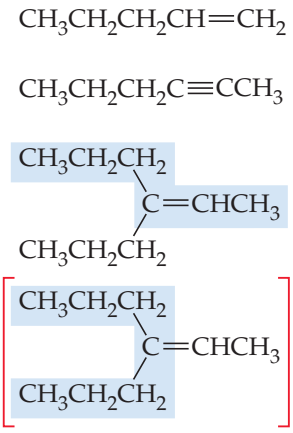
Learning Objectives:

- Name a simple alkene or alkyne given its condensed or line structure.
- Draw the condensed or line structure of an alkene or alkyne given its name.

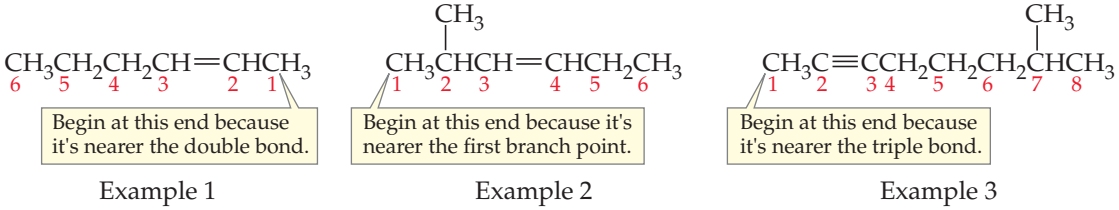
CONCEPTS TO REVIEW Review the IUPAC naming system introduced in Section 12.6.

In the International Union of Pure and Applied Chemistry (IUPAC) system, alkenes and alkynes are named by a series of rules identical to those used for alkanes, with one major addition: the main chain must include all the atoms that are part of the multiple bonds. The parent names indicating the number of carbon atoms in the main chain are the same as those for alkanes, with the *-ene* suffix used in place of *-ane* for alkenes and the *-yne* suffix used for alkynes. The names of alkenes and alkynes also contain a number, called an *index number,* indicating the position of the multiple bond. The main chain in any unsaturated molecule is numbered so that the molecule's name has the lowest index number possible for that multiple bond. This indexing rule for functional groups will be used again and again throughout the remaining chapters of this text.

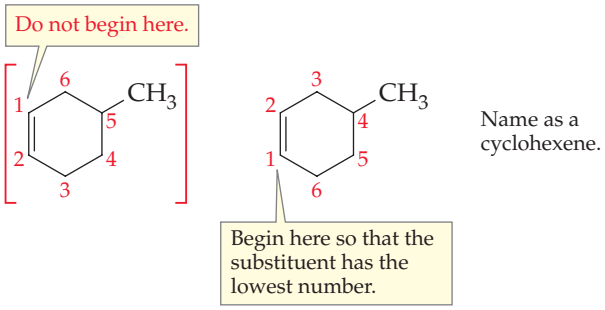
STEP 1: **Name the parent compound.** Find the longest chain containing the double or triple bond, and name the parent compound by adding the suffix *-ene* or *-yne* to the name for the main chain. If there is more than one double or triple bond, the number of multiple bonds is indicated using a numerical prefix (*di*ene = two double bonds, *tri*ene = three double bonds, and so forth).



STEP 2: **Number the carbon atoms in the main chain so that those with multiple bonds have the lowest index numbers possible.** Thus, begin numbering at the end nearer the multiple bond (Examples 1 and 3). If the multiple bond is an equal distance from both ends, begin numbering at the end nearer the first branch point (Example 2).

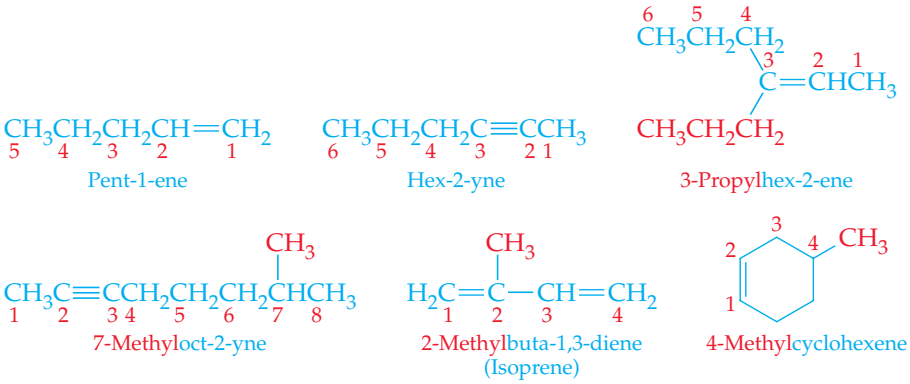


Cycloalkenes are quite common. The double-bonded carbon atoms in substituted cycloalkenes are assigned index numbers of 1 and 2 so as to give the first substituent the next lowest possible index number.



(Cyclic alkynes are rare, and even those that are known are far too reactive to be readily available. For these reasons, we will spend no time discussing them.)

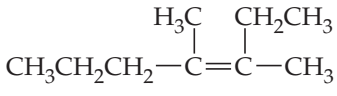
STEP 3: Write the full name. Assign numbers to the branching substituents, and list the substituents alphabetically. Use commas to separate numbers and hyphens to separate words from numbers. Indicate the position of the multiple bond in the chain by giving the number of the *first* multiple-bonded carbon. If more than one double bond is present, identify the position of each and use the appropriate name ending (e.g., 1,3-buta*diene* and 1,3,6-hepta*triene*).



Common Names. For historical reasons, there are a few alkenes and alkynes whose names do not conform to the IUPAC rules. For instance, the 2-carbon alkene $H_2C{=}CH_2$ should properly be called *ethene,* but the name *ethylene* has been used for so long that it is now accepted by the IUPAC. Similarly, the 3-carbon alkene *propene* ($CH_3CH{=}CH_2$) is commonly called *propylene,* and the 4-carbon diene 2-methylbuta-1,3-diene (see above) is more commonly known as *isoprene*. The simplest alkyne, $HC{\equiv}CH$, should be known as *ethyne* but is almost always called *acetylene.*

Worked Example 13.1 Naming Organic Compounds: Alkenes

What is the IUPAC name of the following alkene?



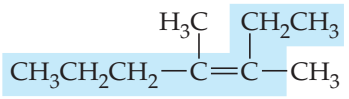
ANALYSIS Identify the parent compound as the longest continuous chain that contains the double bond. The location of the double bond and any substituents are identified by numbering the carbon chain from the end nearer the double bond.

—*continued on next page*

—continued from previous page

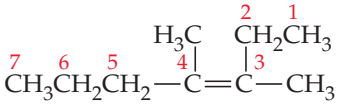
SOLUTION

STEP 1: The longest continuous chain containing the double bond has seven carbons—*heptene*. In this case, we have to turn a corner to find the longest chain.



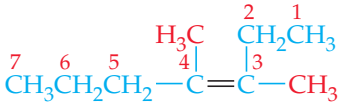
Name as a *heptene*.

STEP 2: Number the chain from the end nearer the double bond. The first double-bond carbon is C4 starting from the left end but C3 starting from the right.



Name as a substituted *hept-3-ene*.

STEP 3: Two methyl groups are attached at C3 and C4.



Substituents: 3-Methyl, 4-Methyl

Name: 3,4-Dimethylhept-3-ene

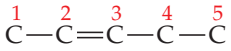
Worked Example 13.2 Molecular Structures: Alkenes

Draw the structure of 3-ethyl-4-methylpent-2-ene using both condensed and line structure.

ANALYSIS Identify the parent name *(pent)* and the location of the double bond and other substituents by numbering the carbons in the parent chain.

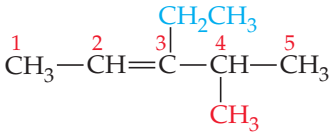
SOLUTION

STEP 1: The parent compound is a five-carbon chain with the double bond between C2 and C3.



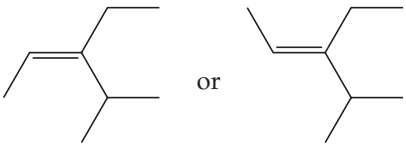
Pent-2-ene

STEP 2: Add the ethyl and methyl substituents on C3 and C4, and write in the additional hydrogen atoms so that each carbon atom has four bonds.



3-Ethyl-4-methylpent-2-ene

Using line structures we can draw it in the following ways:



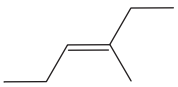
In this particular case either is correct. The two structures differ in the position of the CH_3 with respect to the CH_2CH_3; they are examples of cis–trans isomers (Section 13.3).

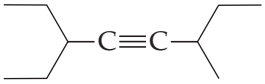
PROBLEM 13.1

What are the IUPAC names of the following compounds?

(a) $CH_3CH_2CH_2CH{=}CHCH(CH_3)CH_3$

(b) $H_2C{=}CHCH_2CH_2C(CH_3){=}CH_2$

(c) 

(d) 

PROBLEM 13.2

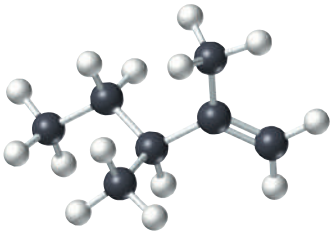
Draw both condensed and line structures corresponding to the following IUPAC names:

(a) 3-Methylhept-1-ene

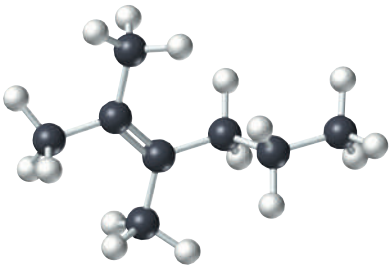
(b) 4,4-Dimethylpent-2-yne

(c) 2-Methylhex-3-ene

(d) 1,3,3-Trimethylcyclohexene



(a)



(b)

KEY CONCEPT PROBLEM 13.3

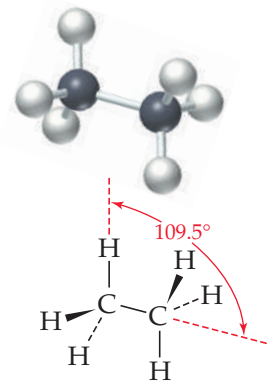
What are the IUPAC names of the two alkenes shown in the margin? Redraw each in line structure format.

13.3 The Structure of Alkenes: Cis–Trans Isomerism

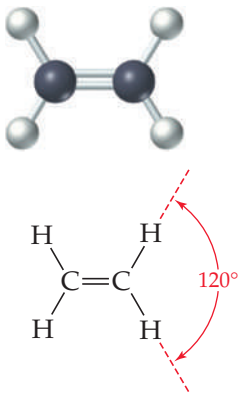
Learning Objective:

- Identify cis–trans isomers of alkenes.

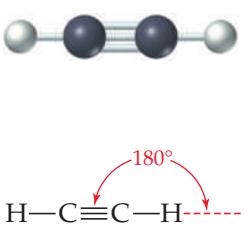
Alkenes and alkynes differ from alkanes in shape because of their multiple bonds. Methane is tetrahedral, but ethene is flat (planar), and ethyne is linear (straight), as predicted by the valence-shell electron-pair repulsion (VSEPR) model discussed in Section 4.8.



Ethane—a tetrahedral molecule with bond angles of 109.5°

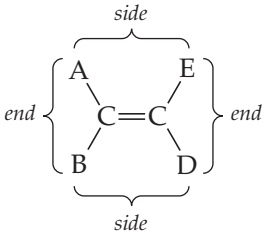


Ethene—a flat molecule with bond angles of 120°



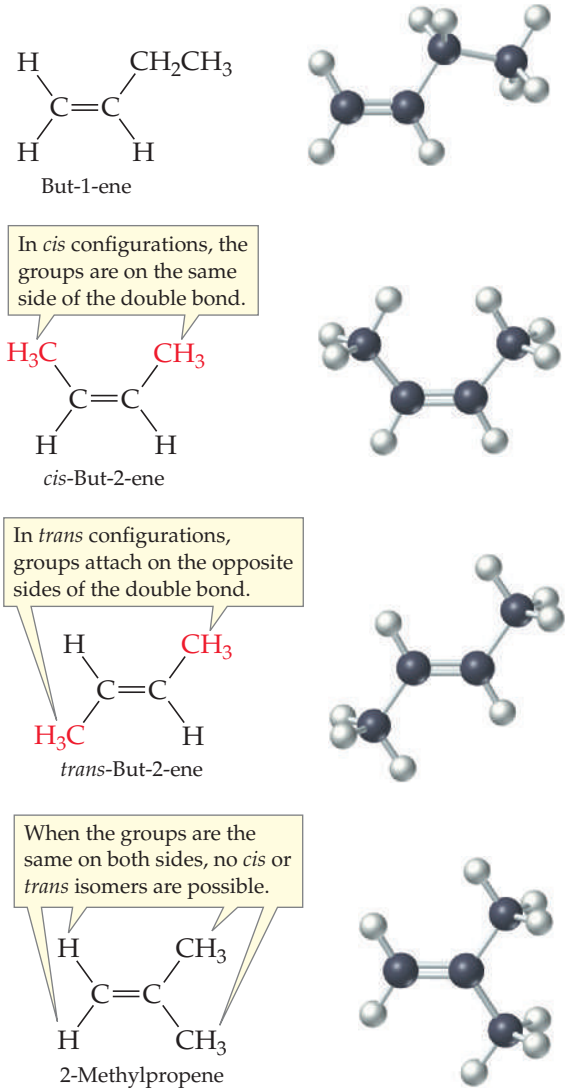
Ethyne—a linear molecule with bond angles of 180°

In ethene, the two carbons and four attached atoms that make up the double-bond functional group lie in a plane. Unlike in alkanes, where free rotation around the C—C single bond occurs, there is no rotation around a double bond, and the molecules are more rigid. However, their restricted freedom of rotation makes a new kind of isomerism possible for alkenes. As a consequence of their rigid nature, alkenes possess *ends* and *sides*.



To see this new kind of isomerism, look at the four C_4H_8 compounds shown on the next page. When written as condensed structures, there appear to be only three alkene isomers of formula C_4H_8: but-1-ene ($CH_2{=}CHCH_2CH_3$), but-2-ene ($CH_3CH{=}CHCH_3$), and 2-methylpropene ($(CH_3)_2C{=}CH_2$). The compounds but-1-ene and but-2-ene are constitutional isomers of each other because their double bonds occur at different positions

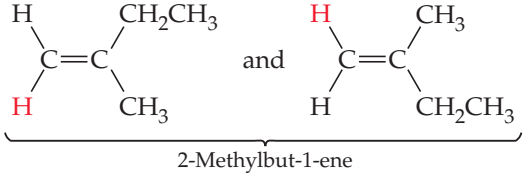
along the chain, and 2-methylpropene is a constitutional isomer of both but-1-ene and but-2-ene because it has the same molecular formula but a different connection of carbon atoms (see Section 12.3). In fact, though, there are *four* isomers of C_4H_8. Because rotation cannot occur around carbon–carbon double bonds, *there are two different but-2-enes*. In one isomer, the two $-CH_3$ groups are on the same side of the double bond; in the other isomer, they are on opposite sides of the double bond.



Cis–trans isomer Alkenes that have the same connections between atoms but differ in their three-dimensional structures because of the way those groups attach to different sides of the double bond.

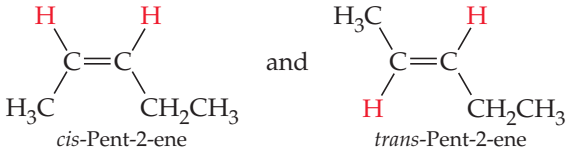
The two but-2-enes are called **cis–trans isomers.** They have the same formula and connections between atoms but have different three-dimensional structures because of the way those groups attach to different sides of the double bond. In this case, the isomer with its methyl groups on the same side of the double bond is named *cis*-but-2-ene, and the isomer with its methyl groups on opposite sides of the double bond is named *trans*-but-2-ene.

Cis–trans isomerism is possible whenever an alkene has two *different* s ubstituent groups on each of its ends. (This means that in the earlier drawing illustrating the sides and ends of an alkene molecule, A $\neq$ B and D $\neq$ E.) If one of the carbons composing the double bond is attached to two identical groups, cis–trans isomerism cannot exist. In 2-methylbut-1-ene, for example, cis–trans isomerism is not possible because C1 is bonded to two identical groups (hydrogen atoms). To convince yourself of this, mentally flip either one of these two structures top to bottom; note that it becomes identical to the other structure.



These compounds are identical. Because the carbon left of the double bond has two H atoms attached, cis–trans isomerism is impossible.

In pent-2-ene, however, the structures do not become identical when one of them is flipped, so cis–trans isomerism does occur.



cis-Pent-2-ene *trans*-Pent-2-ene

These compounds are not identical. Neither carbon of the double bond has two identical groups attached to it.

It is important to note that the molecule must remain intact when you perform this analysis; you cannot break and reform any bonds when flipping and comparing the two structures.

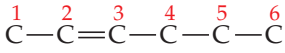
The two substituents that are on the same side of the double bond in an alkene are said to be cis to each other, and those on opposite sides of the double bond are said to be trans to each other. In our generic molecule on the previous page showing ends and sides, for example, A and E are cis to each other, B and D are cis to each other, B and E are trans to each other, and A and D are trans to each other. Thus, in alkenes, the terms cis and trans are used in two ways: (1) as a *relative* term to indicate how various groups are attached to the double-bond carbons (e.g., "groups A and E are cis") and (2) in nomenclature as a way to indicate how the longest chain in the molecule goes in, through, and out of the double bond (e.g., *cis*-but-2-ene and *trans*-but-2-ene). Alkynes, because of their linear structure, cannot have cis–trans isomerism; while the triple bond does have ends, it does not have sides, a necessary requirement of this type of isomer.

Recall from Section 12.5 that rotation around C—C single bonds allows a molecule to exist in multiple conformations.

Worked Example 13.3 Molecular Structure: Cis and Trans Isomers

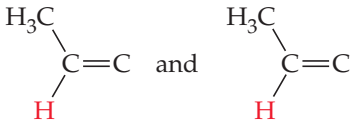
Draw structures for both the cis and trans isomers of hex-2-ene.

ANALYSIS First, draw a condensed structure of hex-2-ene to see which groups are attached to the double-bond carbons.



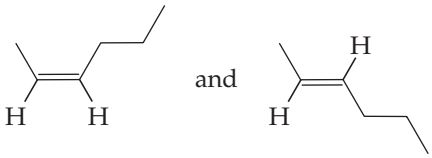
Hex-2-ene

Next, begin to draw the two isomers. Choose one end of the double bond, and attach its groups in the *same way* to generate two identical partial structures.



Finally, attach groups to the other end in the two possible *different ways*.

SOLUTION



Trace the longest chain in each structure. In the structure on the left, the longest chain comes in on one side of the double bond and exits on the same side; thus, the two hydrogens are on the same side of the double bond and this is the cis isomer. The structure on the left is the trans isomer because the longest chain comes in on one side of the double bond and exits on the opposite side, and the two hydrogens are on opposite sides of the double bond. It is common in line structures to show the hydrogens attached to the double bond, but not necessary.

PROBLEM 13.4

Which of the following substances exist as can cis–trans isomers? Draw both isomers for those that do.

(a) 2,3-Dimethylpent-2-ene (condensed structures only)
(b) 2-Methylhex-2-ene (both condensed and line structures)
(c) Hex-2-ene (line structures only)

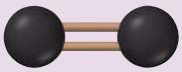
HANDS-ON CHEMISTRY 13.1

Models are an invaluable tool in organic chemistry when discussing structure. In this exercise, you are going to look at double bonds and how they restrict rotation when present in an organic molecule. You will also look at how they can crucially change the shape of a molecule. To accomplish all of this you are going to use models, *but you do not need a model kit to carry out this exercise.* If you have a model kit, follow the instructions included with it to make the "building blocks" described next. If you do not have access to a model kit, follow the instructions next to make "gumdrop building blocks." You will need a box of toothpicks and a bag of multicolored gumdrops (preferred), gummy bears, or mini marshmallows; it does not matter as long as you can insert a toothpick in it and it will stay in place. Throughout this exercise, remember that carbon is tetravalent (forms four bonds) and that hydrogen and chlorine are monovalent (form one bond).

Building Blocks—for this exercise, you will need the following (use the color coding of atoms listed in Table 4.2 as your guide if possible):

Six tetrahedral carbon units—make these by placing four toothpicks into a gumdrop in a tetrahedral array. Use gumdrops of whatever color you have assigned to being carbon (black or some other dark color). Note: There will be times you will have to remove toothpicks to make connections to other units; when you do, make the new connection in the same location as the toothpick you removed.

Three carbon alkene units—to make these, connect two carbon-colored gumdrops to one another using two toothpicks. Be sure that there is some space between them so that they look like an alkene model.



Six "one group" units—simply stick a toothpick into a gumdrop. The gumdrops should all be the same color, although the color should vary from what you've already used.

Note: You may want to take pictures of each model you make with your phone for review later. Once finished with a question, you can disassemble your models for use in the next question.

a. Start by assembling butane by connecting four of your tetrahedral units (you will have to remove toothpicks as necessary to make connections). Add gumdrops at the end of the toothpicks to represent Hs if you wish. By rotating around the single bonds, write down all the conformations possible. Is any one higher in energy than the others? See Section 12.5 for help.

b. Now, using your alkene units, build models of 2-methylpropene, *cis*-but-2-ene, and *trans*-but-2-ene (see Section 13.3). Confirm that these three are all different molecules. Notice that you cannot rotate around the double bond to convert the cis molecule into the trans without breaking the double bond. The cis isomer is slightly higher in energy than the trans; can you come up with a possible reason why?

c. Repeat part b for 2-chlorobut-1-ene, showing that there is only one possible isomer for this compound.

$$CH_3CH_2CCl{=}CH_2$$

d. Cis double bonds are found in many biological molecules, such as the unsaturated fatty acids (see Section 23.2), despite them being of slightly higher energy than the trans. Build two molecules with the following structure, one where all the double bonds are cis and one where they are all trans. Can you come up with a reasonable explanation as to why the all-*cis* molecule might be more advantageous to have in an aqueous environment over the all-trans molecule?

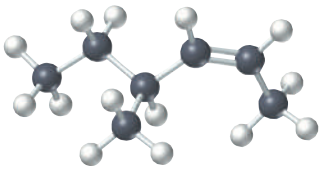
$$CH_2{=}CH{-}CH{=}CH{-}CH{=}CH_2$$

PROBLEM 13.5

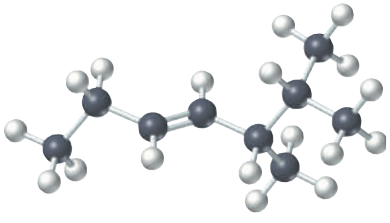
Draw both the condensed and line structures for the cis and trans isomers of 3,4-dimethylhex-3-ene.

KEY CONCEPT PROBLEM 13.6

Name the compounds shown below, including the appropriate *cis*- or *trans*- prefix. Redraw each in line structure format.



(a)



(b)

13.4 Properties of Alkenes and Alkynes

Learning Objective:

- Identify the physical properties of alkenes and alkynes.

The properties of alkenes and alkynes resemble those of alkanes in many respects (Section 12.7). The bonds in alkenes and alkynes are nonpolar, and the physical properties of these compounds are influenced mainly by weak London dispersion forces. Alkenes and alkynes with 1–4 carbon atoms are gases at room temperature, and boiling points increase with the size of the molecules.

Intermolecular forces were described in Section 8.2.

Like alkanes, alkenes and alkynes are insoluble in water, soluble in nonpolar solvents, and less dense than water. They are flammable; those that are gases present explosion hazards when mixed with air. Unlike alkanes, alkenes are more reactive because of their double bonds. As we will see in the next section, alkenes undergo addition of various reagents to their double bonds to yield saturated products. Alkynes, as you might expect, are more reactive since they have two double bonds to react.

Properties of Alkenes and Alkynes

- Nonpolar; insoluble in water; soluble in nonpolar organic solvents; less dense than water
- Flammable; nontoxic
- Alkenes display cis–trans isomerism when each double-bond carbon atom has different substituents
- Cis-trans isomers can have different physical and biological properties.
- Multiple bonds are chemically reactive.

13.5 Types of Organic Reactions

Learning Objective:

- Identify the different types of organic reactions.

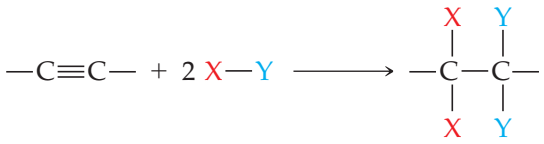
Before looking at the chemistry of alkenes and alkynes, we should first discuss some general reactivity patterns that make the task of organizing and categorizing organic reactions much simpler. Four particularly important kinds of organic reactions are discussed in this section: *additions, eliminations, substitutions,* and *rearrangements.*

- **Addition Reactions** Additions occur when two reactants add together to form a single product with no atoms "left over." We can generalize the process as

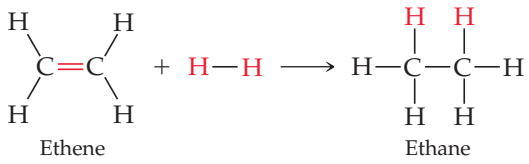
These two reactants add together … $A + B \longrightarrow C$ … to give this single product.

Addition reaction A general reaction type in which a substance X—Y adds to the multiple bond of an unsaturated reactant to yield a saturated product that has only single bonds.

The most common addition reactions encountered in organic chemistry are those in which a reagent adds across a carbon–carbon multiple bond (an unsaturated molecule) to give a product that contains two (for alkenes) or four (for alkynes) new single bonds (a saturated system). This process can be generalized as

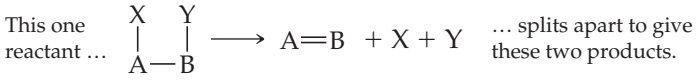


We'll explore the mechanism of addition reactions further in the Mastering Reactions: How Addition Reactions Occur feature on page 456. An example of an addition reaction is the reaction of an alkene, such as ethene, with H_2 to yield an alkane.

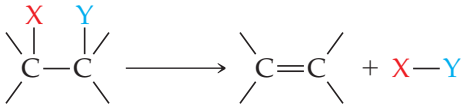


Elimination reaction A general reaction type in which a saturated reactant yields an unsaturated product by losing groups from two adjacent atoms.

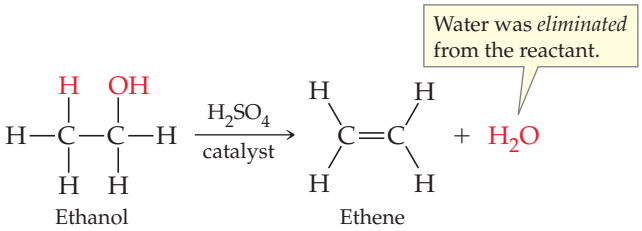
- **Elimination Reactions** Eliminations are the opposite of addition reactions. Eliminations occur when a single reactant splits into two or more products, a process we can generalize as



In almost all cases, an elimination reaction converts the starting material to a product that has two fewer single bonds and a carbon–carbon multiple bond in their place.

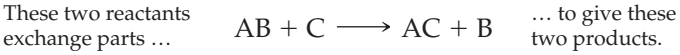


As an example of an elimination reaction, we will see in the next chapter that an alcohol, such as ethanol, eliminates to give water and an alkene when treated with an acid catalyst. This specific process is known as a *dehydration reaction* and can be seen in further detail in the Mastering Reactions: How Eliminations Occur feature on page 483.

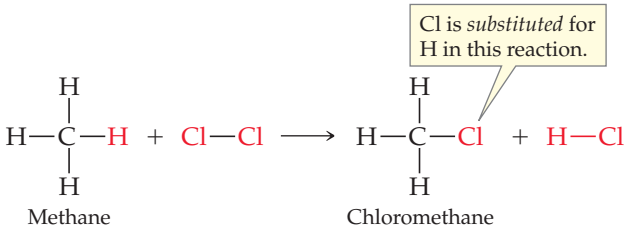


Substitution reaction A general reaction type in which an atom or group of atoms in a molecule is replaced by another atom or group of atoms.

- **Substitution Reactions** Substitutions occur when two reactants exchange parts to give two new products, a process we can generalize as



As an example of a substitution reaction, we saw in Section 12.8 that alkanes, such as methane, react with Cl_2 in the presence of ultraviolet (UV) light to yield alkyl chlorides (the UV light is needed due to the low reactivity of alkanes). Here, a —Cl group substitutes for the —H group of the alkane, and two new products result:



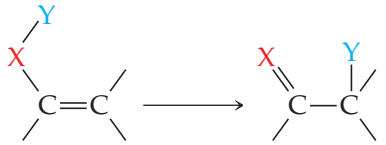
A much more common type of substitution reaction is one that involves alkyl halides and Lewis bases, such as the reaction shown here:

$$CH_3CH_2CH_2Cl + CH_3O^- Na^+ \longrightarrow CH_3CH_2CH_2OCH_3 + Na^+Cl^-$$

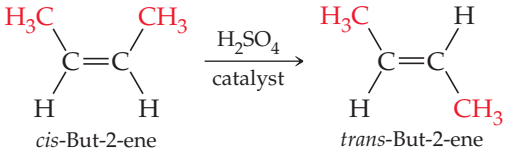
We previously saw another example of this type of substitution reaction in Chapter 12 in Mastering Reactions: Organic Chemistry and the Curved Arrow Formalism on page 420. We'll learn more about alkyl halides and Lewis bases in Chapters 14 and 16.

- **Rearrangement Reactions** Rearrangement occurs when bonds and atoms in the reactant are reorganized to yield a single product that is an isomer of the reactant. A generalized example of one type of rearrangement seen in organic chemistry is

Rearrangement reaction A general reaction type in which a molecule undergoes bond reorganization to yield an isomer.



Rearrangement reactions are important in organic chemistry as well as biochemistry. Because of their complex nature, however, we will not discuss them in detail in this book. An example of a rearrangement is the conversion of *cis*-but-2-ene into its isomer *trans*-but-2-ene by treatment with an acid catalyst:



cis-But-2-ene *trans*-But-2-ene

This simple-looking interconversion involves the breaking of the C═C bond followed by rotation and reformation of the double bond; this is a key process in vision (see the Chemistry in Action "The Chemistry of Vision and Color" p. 448).

LOOKING AHEAD The conversion of glucose to fructose (Chapter 22) is an example of tautomerization, converting one carbohydrate into another.

Worked Example 13.4 Identifying Reactions of Alkenes

Classify the following alkene reactions as addition, elimination, or substitution reactions:

(a) $CH_3CH{=}CH_2 + H_2 \longrightarrow CH_3CH_2CH_3$

(b) $CH_3CH_2CH_2OH \xrightarrow[\text{catalyst}]{H_2SO_4} CH_3CH{=}CH_2 + H_2O$

(c) $CH_3CH_2Cl + KOH \longrightarrow CH_3CH_2OH + KCl$

ANALYSIS Determine whether atoms have been added to the starting compound (addition), removed from the starting compound (elimination), or switched with another reactant (substitution).

SOLUTION

(a) Two H atoms have been *added* in place of the double bond, so this is an *addition* reaction.

(b) A water molecule (H_2O) has been formed by *removing* an H atom and an —OH group from adjacent C atoms, forming a double bond in the process, so this is an *elimination* reaction.

(c) The reactants (CH_3CH_2Cl and KOH) have *traded* the —OH and the —Cl substituent groups, so this is a *substitution* reaction.

PROBLEM 13.7

Classify the following reactions as an addition, elimination, or substitution:

(a) $CH_3Br + NaOH \longrightarrow CH_3OH + NaBr$

(b) $H_2C{=}CH_2 + HCl \longrightarrow CH_3CH_2Cl$

(c) $CH_3CH_2Br \longrightarrow H_2C{=}CH_2 + HBr$

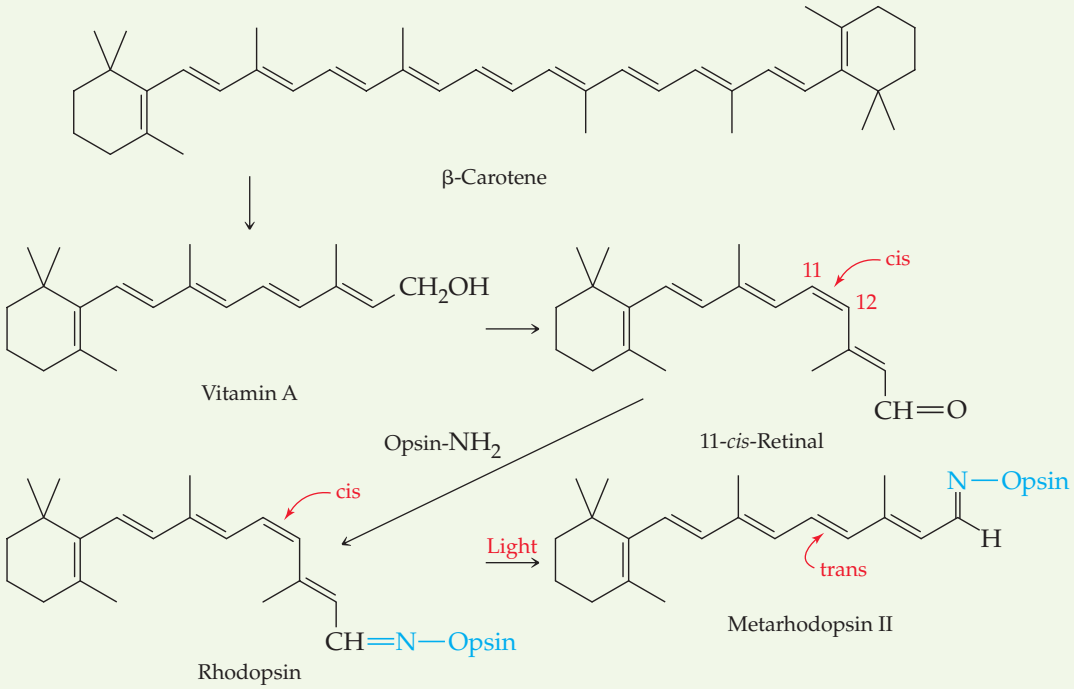
CHEMISTRY IN ACTION

The Chemistry of Vision and Color

Our vision, from the vibrant colors we see to the ability of our eyes to adapt to both bright sunlight and pitch darkness, is one of our key sensory systems, but what is the role of chemistry in this system? A critical player in the ability to see is vitamin A, an important biological alkene.

A vitamin is an organic molecule required by the body in trace amounts and usually obtained through diet (Section 19.9). Beta-carotene, a purple-orange alkene, found in carrots and other yellow vegetables provides our main dietary source of vitamin A (also known as *retinol*). The enzymatic conversion of beta-carotene to vitamin A takes place in the mucosal cells of the small intestine; vitamin A is then stored in the liver, from which it can be transported to the eye. In the eye, vitamin A is oxidized to *retinal,* which undergoes cis–trans isomerization of its C11–C12 double bond to produce 11-*cis*-retinal. Reaction with the protein *opsin* then produces the light-sensitive substance *rhodopsin.*

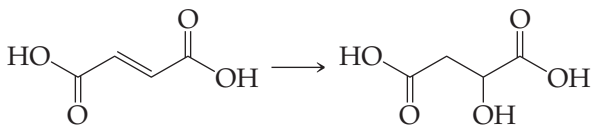
The human eye has two kinds of light-sensitive cells, *rod cells* and *cone cells.* The 3 million rod cells are primarily responsible for seeing in dim light, whereas the 100 million cone cells are responsible for seeing in bright light and for the perception of bright colors. When light strikes the rod cells, cis–trans isomerization of the C11 — C12 double bond occurs



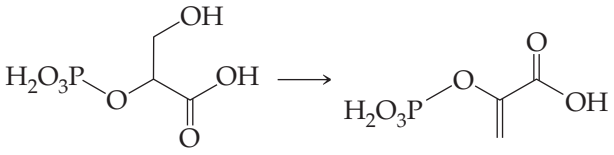
PROBLEM 13.8

Many biological transformations can be simply classified as additions, eliminations, or substitutions. How would you classify the following reactions?

(a) Fumaric acid to malic acid (found in the citric acid cycle, Section 21.8)



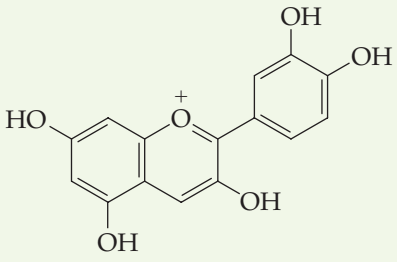
(b) 2-Phosphoglyceric acid to phosphoenolpyruvic acid (found in glycolysis, Section 22.3)



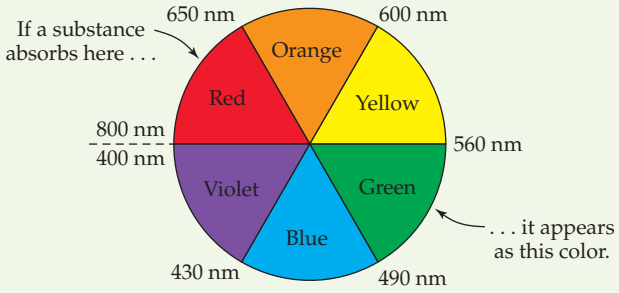
via a rearrangement reaction, and 11-*trans*-rhodopsin, also called *meta*rhodopsin II, is produced. This cis–trans isomerization is accompanied by a change in molecular geometry, which in turn causes a nerve impulse to be sent to the brain, where it is perceived as vision. Metarhodopsin II is then changed back to 11-*cis*-retinal for use in another vision cycle.

While this explains how we see, it does not tell us what causes the actual colors themselves. Other organic compounds such as the plant pigment cyanidin are also brightly colored. This is due to the fact that they are extended conjugated systems.

Conjugated systems are molecules that contain arrays of alternating double and single bonds, and the electrons within the double bonds are spread out, or *delocalized,* over the whole molecule. Whenever there is conjugation in a molecule, a delocalized region of electron density is formed that is in turn capable of absorbing light. Compounds with extended stretches of alternating double and single bonds (10 or more) absorb in the visible region. The presence of a charged atom in the conjugated system, such as the oxygen in cyanidin, allows absorption in the visible range to occur with fewer conjugated double bonds.



Cyanidin
(reddish-blue color in flowers and cranberries)



▲ Using an artist's color wheel, it is possible to determine the observed color of a substance by knowing the color of the light absorbed. Observed and absorbed colors are complementary. Thus, if a substance absorbs red light, it has a green color.

The color that we see is complementary to the color that is absorbed; that is, we see what is left of the white light after certain colors have been absorbed. For example, the plant pigment cyanidin absorbs greenish-yellow light and thus appears reddish-blue. It is speculated that this is also the reason that red-colored mulch seems to promote plant growth: the reflected red color is absorbed by the green plant, creating the effect of additional incoming sunlight for photosynthesis.

CIA Problem 13.1 (a) After the reaction of 11-*cis*-retinal with opsin, classify the reaction rhodopsin undergoes in the presence of light to produce 11-*trans*-rhodopsin. (b) How many hydrogens are present in 11-*cis*-retinal? (c) What are the functional groups present in this molecule?

CIA Problem 13.2 What is the difference in the purpose of the rod cells and the cone cells in the eye?

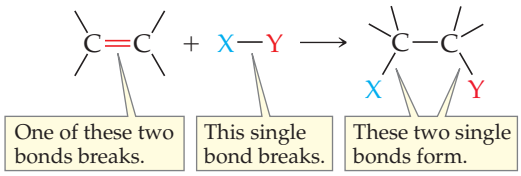
CIA Problem 13.3 Tetrabromofluorescein is a purple dye often used in lipsticks. If the dye is purple, what color does it absorb?

13.6 Addition Reactions of Alkenes

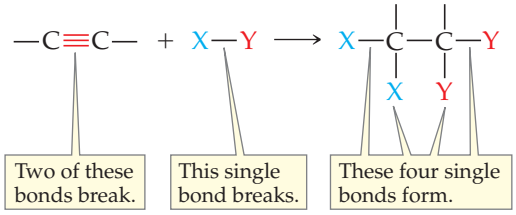
Learning Objectives:

- Predict the addition products obtained when alkenes react with H_2, Cl_2, HCl, or H_2O.
- Identify "unsymmetrically substituted" and "symmetrically substituted" alkenes.
- Utilize Markovnikov's rule when addition reactions to unsymmetrically substituted alkenes occur.

Most of the reactions of alkenes and alkynes are *addition reactions,* where reagent X—Y adds to the multiple bond in the unsaturated reactant to yield a saturated product that has only single bonds.



Addition reactions

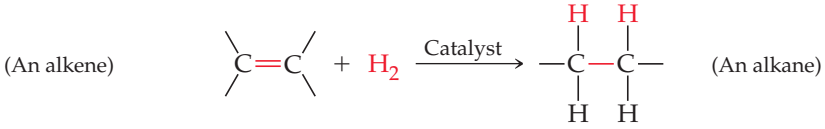


Addition reactions of alkenes are often used to prepare large quantities of industrially important compounds (such as ethanol). Addition reactions of alkenes and alkynes are similar in many ways. Since alkynes are rarely found in nature, and because addition to an alkyne can generally be thought of as a "double addition" of an alkene, we will limit our discussion in this section to the reactions of alkenes, even though alkynes will do the exact same reactions.

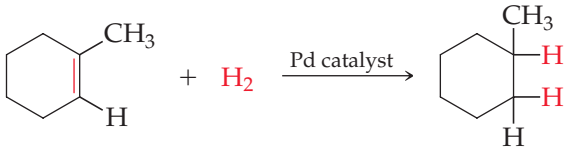
Addition of H_2 to Alkenes: Hydrogenation

Hydrogenation The addition of H_2 to a multiple bond to give a saturated product.

Alkenes and alkynes react with hydrogen, a process called **hydrogenation,** in the presence of a metal catalyst such as palladium to yield the corresponding alkane product.



For example,



1-Methylcyclohexene — Methylcyclohexane (85% yield)

The addition of hydrogen to an alkene is used commercially to convert unsaturated vegetable oils, which contain numerous double bonds, to the saturated fats used in margarine and cooking fats. This process has come under intense scrutiny in recent years because it also creates *trans*-fatty acids in the product (which, in the diet, has been associated with increased risk of heart disease). We will see the structures of these fats and oils in Chapter 23.

Worked Example 13.5 Organic Reactions: Addition

What product would you obtain from the following reaction? Draw both the condensed structure and the line structure of the product.

$$CH_3CH_2CH_2CH{=}CHCH_3 + H_2 \xrightarrow{Pd} ?$$

ANALYSIS Rewrite the reactant, showing a single bond and two partial bonds in place of the double bond.

$$CH_3CH_2CH_2CH{-}CHCH_3$$

Then, add a hydrogen to each carbon atom of the double bond, and rewrite the product in condensed form.

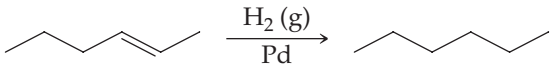
$$CH_3CH_2CH_2\underset{H}{CH}{-}\underset{H}{CHCH_3} \quad \text{is the same as} \quad \underset{\text{Hexane}}{CH_3CH_2CH_2CH_2CH_2CH_3}$$

SOLUTION

The reaction is

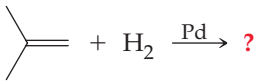
$$CH_3CH_2CH_2CH{=}CHCH_3 + H_2 \xrightarrow{Pd} CH_3CH_2CH_2CH_2CH_2CH_3$$

In line structure format, this reaction would look as follows:



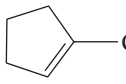
PROBLEM 13.9

Write the structures of the products from the following hydrogenation reactions:

(a)  + H_2 $\xrightarrow{Pd}$?

(b) *cis*-But-2-ene + H_2 $\xrightarrow{Pd}$

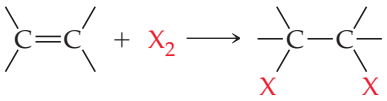
(c) *trans*-Hept-3-ene + H_2 $\xrightarrow{Pd}$?

(d)  + H_2 $\xrightarrow{Pd}$?

Addition of Cl_2 and Br_2 to Alkenes: Halogenation

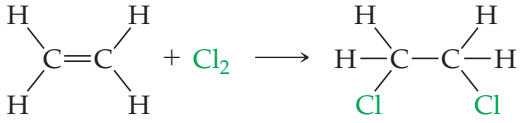
Alkenes react with the halogens Br_2 and Cl_2 to give 1,2-dihaloalkane addition products in a **halogenation (alkene)** reaction.

Halogenation (alkene) The addition of Cl_2 or Br_2 to a multiple bond to give a dihalide product.



(A 1,2-dihaloalkane where X = Br or Cl)

For example,



Ethene 1, 2-Dichloroethane

The addition of Br_2 and Cl_2 to an alkene occurs in an analogous way to that shown in Worked Example 13.5. This reaction is used to manufacture nearly 8 million tons of 1,2-dichloroethane each year in the United States. It is the first step in making the widely used poly(vinyl chloride) plastics (PVC).

Another halogen, Br_2, provides a convenient test for the presence of a carbon–carbon double or triple bond in a molecule (Figure 13.1). A few drops of a reddish-brown solution of Br_2 are added to a sample of an unknown compound; the immediate disappearance of the color reveals the presence of a carbon–carbon multiple bond, because the bromine reacts with the compound to form a colorless dibromide. This test can also be used to determine the level of unsaturation of fats (Chapter 23).

(a)

(b)

▲ **Figure 13.1**
Testing for unsaturation with bromine.
(a) No color change results when the bromine solution is added to hexane (C_6H_{14}). (b) Disappearance of the bromine color when it is added to 1-hexene (C_6H_{12}) indicates the presence of a double bond.

Hydrohalogenation The addition of HCl or HBr to a multiple bond to give an alkyl halide product.

PROBLEM 13.10

What products would you expect from the following halogenation reactions?

(a) 2-Methylpropene + Br_2 ⟶ ?

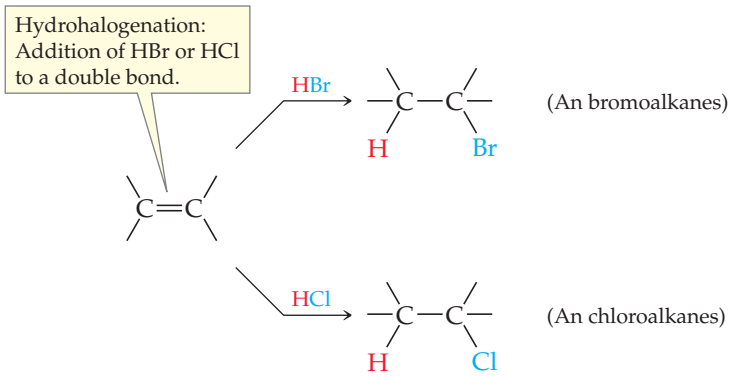
(b) Pent-1-ene + Cl_2 ⟶ ?

(c) $CH_3CH_2CH{=}C(CH_3)CH_2CH(CH_3)_2$ + Cl_2 ⟶ ?

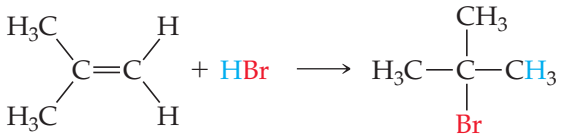
(d)  + Br_2 ⟶ ?

Addition of HBr and HCl to Alkenes

Alkenes react with hydrogen bromide (HBr) to yield *bromoalkanes* (R—Br) and with hydrogen chloride (HCl) to yield *chloroalkanes* (R—Cl), in what are called **hydrohalogenation** reactions.

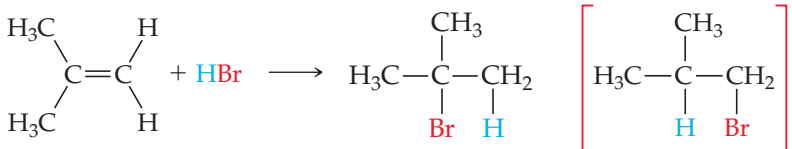


The addition of HBr to 2-methylpropene is an example.



2-Methylpropene 2-Bromo-2-methylpropane

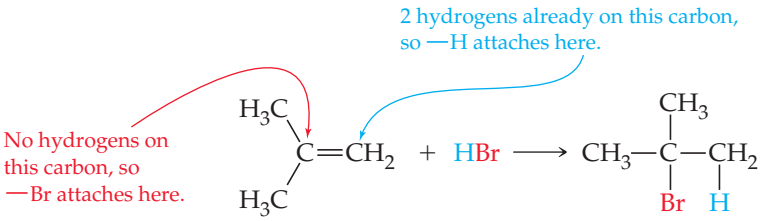
Look carefully at the above example. Only one of the two possible addition products is obtained. 2-Methylpropene *could* add HBr to give 1-bromo-2-methylpropane, but it does not; it gives only 2-bromo-2-methylpropane as the major product.



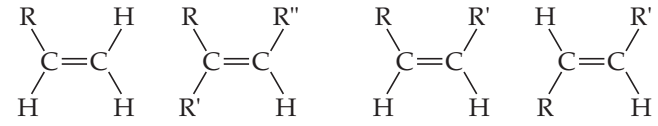
2-Methylpropene 2-Bromo-2-methylpropane (Major product) 1-Bromo-2-methylpropane (Trace)

This result is typical of what happens when HBr and HCl add to an alkene in which one of the double-bond carbons has more hydrogens than the other (an unsymmetrically substituted alkene). The results of such additions can be predicted using **Markovnikov's rule,** formulated in 1869 by the Russian chemist Vladimir Markovnikov.

Markovnikov's rule In the addition of HX to an alkene, the major product arises from the H attaching to the double-bond carbon that has the larger number of H atoms *directly* attached to it and the X attaching to the carbon that has the smaller number of H atoms attached.



Note that the terms "unsymmetrically substituted" and "symmetrically substituted" here refer only to the *number* of hydrogens and carbons attached to each carbon engaged in the double bond and not to the *identity* of the carbon groups attached.

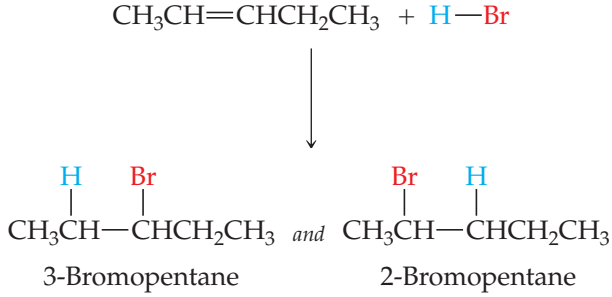


"Unsymmetrically substituted" "Symmetrically substituted"

In the examples above, R, R', and R" can be any group except H and do not have to be different in this context.

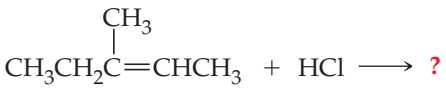
The scientific reason behind Markovnikov's rule is a powerful and important principle in organic chemistry. The Mastering Reactions: How Addition Reactions Occur feature on page 456 discusses Markovnikov's rule in further detail, including the stability of intermediates known as *carbocations* that form during the reaction.

Both possible products form in equal amounts if an alkene has equal numbers of H atoms attached to the double-bond carbons (a symmetrically substituted double bond).



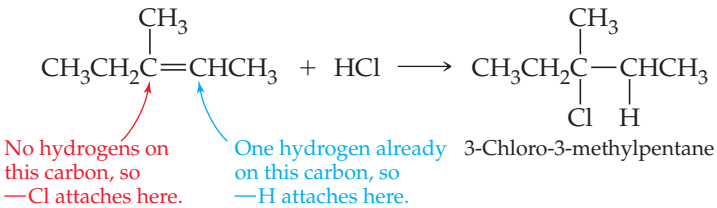
Worked Example 13.6 Organic Reactions: Markovnikov's Rule

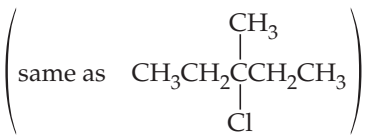
What major product do you expect from the following reaction?



ANALYSIS The reaction of an alkene with HCl leads to the formation of an alkyl chloride addition product according to Markovnikov's rule. To make a prediction, look at the starting alkene and count the number of hydrogens attached to each double-bond carbon. Then write the product by attaching H to the carbon with more hydrogens and attaching Cl to the carbon with fewer hydrogens.

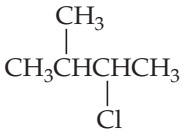
SOLUTION





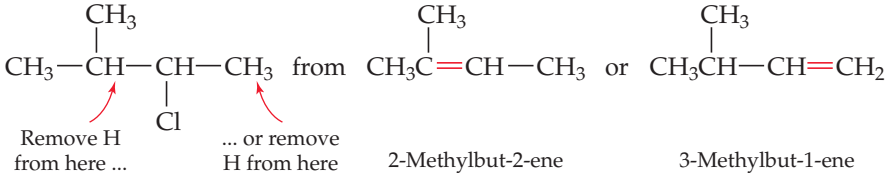
Worked Example 13.7 Organic Reactions: Markovnikov's Rule

From what two different alkenes can 2-chloro-3-methylbutane be made?



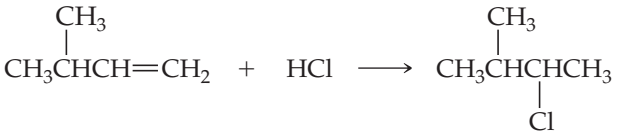
2-Chloro-3-methylbutane

ANALYSIS 2-Chloro-3-methylbutane is an alkyl chloride that might be made by addition of HCl to an alkene. To generate the possible alkene precursors, remove the —Cl group and an —H atom from adjacent carbons and replace with a double bond.



Look at the possible alkene addition reactions to see which is compatible with Markovnikov's rule. In this case, addition to 3-Methylbut-1-ene is compatible. Note that if HCl is added to 2-Methylbut-2-ene, the major product will have the Cl attached to the wrong carbon (the carbon with the methyl group on it).

SOLUTION



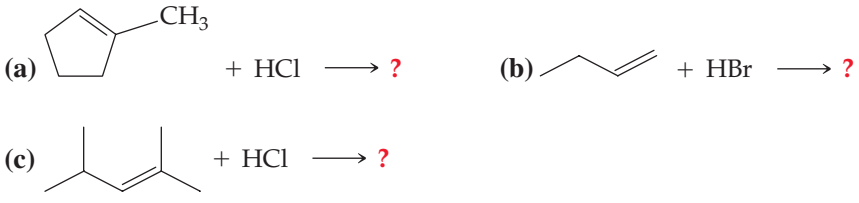
3-Methylbut-1-ene 2-Chloro-3-methylbutane

PROBLEM 13.11

Draw all possible products formed when 2-methylbut-2-ene undergoes addition with HCl. Label them as being either the major or the minor product.

PROBLEM 13.12

What major products do you expect from the following reactions?

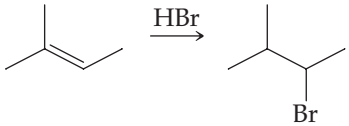


PROBLEM 13.13

In the following addition reactions, are the given alkyl halides obtained as the major products? Give a reason for your answer.

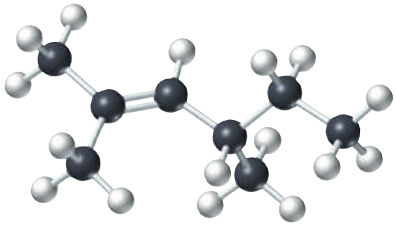
(a) 3-Chloro-3-ethylpentane from addition of HCl to 3-ethylpent-2-ene

(b)



KEY CONCEPT PROBLEM 13.14

What product do you expect from the following reaction? Draw your answer in both condensed and line structure formats.

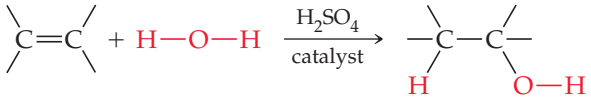


+ HBr ⟶ ?

Addition of Water to Alkenes: Hydration

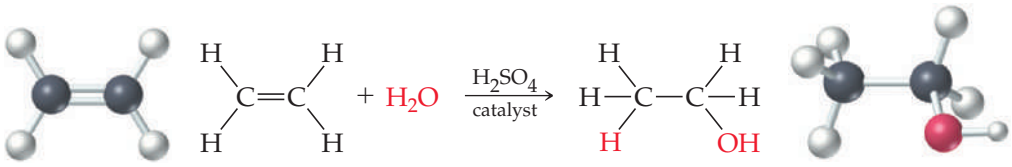
Although a water molecule (H—OH) could be considered as another type of H—X, an alkene will not react with pure water alone. If, however, a small amount of a strong acid catalyst such as H_2SO_4 is added, an addition reaction takes place to yield an *alcohol* (R—OH); a reaction known as a **hydration** reaction. In fact, the United States produces nearly 100 million gallons of ethanol each year by this method.

Hydration The addition of water to a multiple bond to give an alcohol product.



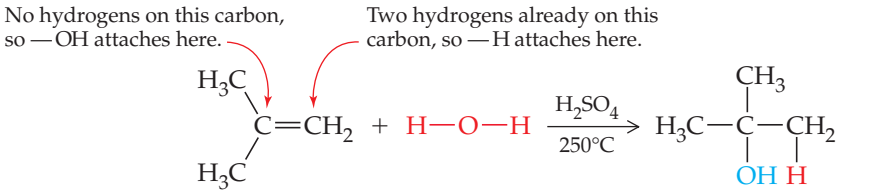
An alcohol

For example,



Ethene Ethanol

As with the addition of HBr and HCl, we can use Markovnikov's rule to predict the product when water adds to an unsymmetrically substituted alkene. Hydration of 2-methylpropene, for example, gives 2-methylpropan-2-ol as the major product:



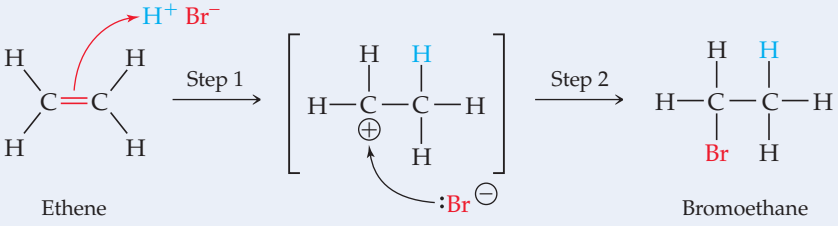
2-Methylpropan-2-ol

(same as CH_3CCH_3, with OH)

MASTERING REACTIONS

How Addition Reactions Occur

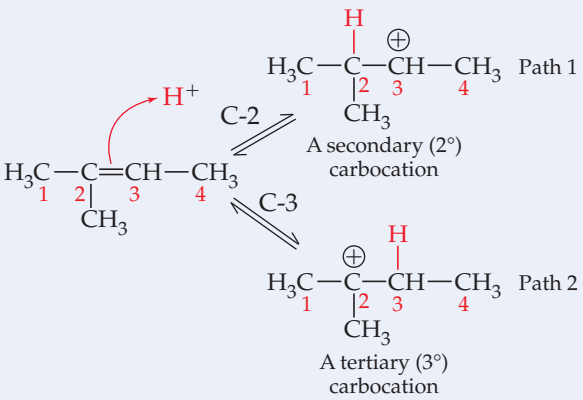
How do alkene addition reactions take place? Do two molecules, say ethene and HBr, simply collide and immediately form a product molecule of bromoethane, or is the process more complex? In Chapter 12, we presented a useful and convenient way for organic chemists to visualize reactions (see Mastering Reactions: Organic Chemistry and the Curved Arrow Formalism on p. 420). Here, we apply this to the study of addition reactions, specifically those involving H^+. Detailed studies show that alkene addition reactions take place in two distinct steps, as illustrated in the following figure for the addition of HBr to ethene.



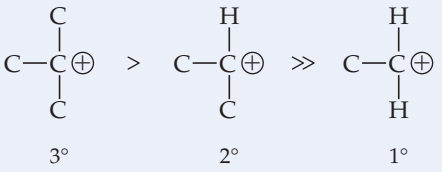
▲ **The mechanism of the addition of HBr to an alkene.** The reaction takes place in two steps and involves a carbocation intermediate. In the first step, two electrons move from the C═C double bond to form a C—H bond. In the second step, Br^- uses two electrons to form a bond to the positively charged carbon.

To begin, recognize that almost all organic reactions can be visualized as occurring between an electron-rich species and an electron-poor species. In the first step, the electron-rich alkene reacts with H^+ from the acid HBr. The carbon–carbon double bond partially breaks, and two electrons move from the double bond to form a new single bond (indicated by the curved red arrow in the figure). The remaining double-bond carbon, having had electrons that were being shared removed from it, now has only six electrons in its outer shell and bears a positive charge. Carbons that possess a positive charge, or *carbocations,* are highly reactive. As soon as this carbocation is formed, it immediately reacts with Br^- to form a neutral product.

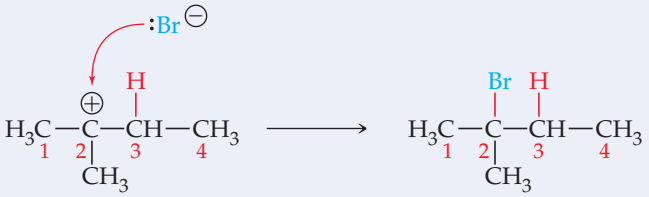
For ethene both carbons have identical substitution. What about the case where the double bond is unsymmetrically substituted, say, with 2-methylbut-2-ene? Here, we perform the same analysis as the one we did for ethene.

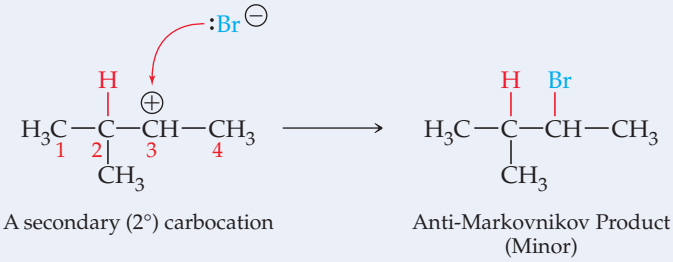


The double bond, being electron rich, attacks the electron-poor H^+ and in doing so, causes a carbocation to form; however, here we have two possibilities. If the H^+ attaches to C2, the carbocation will form on C3 (Path 1); if the H^+ attaches to C3, the carbocation will form on C2 (Path 2). Since this is an equilibrium process (the H^+ can just as easily be removed to regenerate the alkene) we should see both, but is one favored over the other? The answer to that can be arrived at by examining the two carbocations. Carbocations are electron-deficient species, so anything that can help stabilize one over another will cause a preference for that species to be seen. Carbons are known to donate electron density through the single bond; therefore, the more carbons attached to a carbocation, the less electron poor it is the more stable it will be, making it more favorable. The more favorable the carbocation, the more product will arise from it. Studies have shown that tertiary (3°) carbocations are more stable than secondary (2°) carbocations, which are much more stable than primary (1°) carbocations (which are almost never formed).



Thus, when the bromide reacts, two possible products are formed, with the major product arising from the more stable carbocation.





You should notice that the major product is that predicted by Markovnikov's rule. This now shows you the scientific basis for his observations: The major product arises because the intermediate it is derived from is more stable than any other intermediate (here, the 3° carbocation). This concept of the stability of intermediates lies at the very core of organic chemistry and is so powerful that it allows chemists to successfully predict the outcomes of diverse organic reactions.

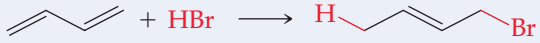
A description of the individual steps by which old bonds are broken and new bonds are formed in a reaction is called a **reaction mechanism.** Mechanisms allow chemists to classify thousands of seemingly unrelated organic reactions into only a few categories and help us to understand what is occurring during a reaction. Their study is essential to our ever-expanding ability to understand biochemistry and the physiological effects of drugs.

Reaction mechanism A description of the individual steps by which old bonds are broken and new bonds are formed in a reaction.

MR Problem 13.1 Remembering Markovnikov's rule, draw the structure of the carbocation formed during the reaction of 2-methylpropene with HCl.

MR Problem 13.2 Refer to Problem 13.62: Assuming that Markovnikov's rule is followed, predict which of the two structures you drew is formed, and draw the carbocation involved as an intermediate.

MR Problem 13.3 Consider the molecule buta-1,3-diene (shown next). When this is reacted with HBr at 25 °C, the major product obtained is 1-bromobut-2-ene. Given that the first step is the formation of a carbocation and assuming that Markovnikov's rule is initially followed, propose an explanation for the formation of the product seen. (Hint: Think about resonance.)



Worked Example 13.8 Reaction of Alkenes: Hydration

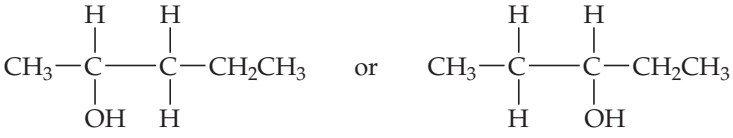
What products do you expect from the following hydration reaction?

$$CH_3CH{=}CHCH_2CH_3 + H_2O \xrightarrow{H_2SO_4} ?$$

ANALYSIS Water is added to the double bond, with an H atom added to one carbon and an —OH group added to the other carbon of the double bond.

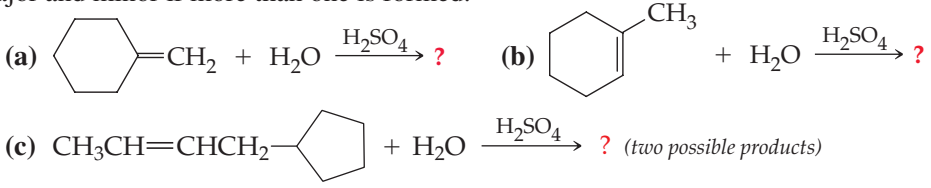
SOLUTION

Because this is *not* an unsymmetrically substituted alkene, we can add the —OH group to either carbon:



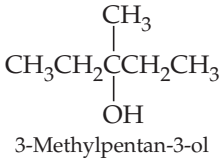
PROBLEM 13.15

What products do you expect from the following hydration reactions? Label them as major and minor if more than one is formed.



PROBLEM 13.16

Draw the structures of the two different alkenes from which 3-methylpentan-3-ol, shown in the margin, can be made. Draw them in both condensed and line format.



3-Methylpentan-3-ol

13.7 Alkene Polymers

Learning Objective:

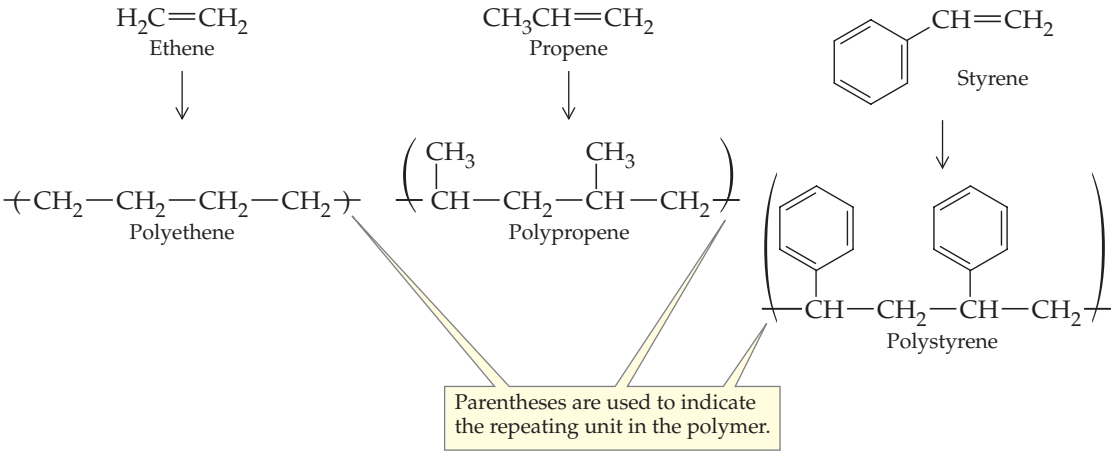
- Predict what polymer forms given an alkene monomer.

Polymer A large molecule formed by the repetitive bonding together of many smaller molecules (or monomers).

Monomer A small molecule that is used to prepare a polymer.

A **polymer** is a large molecule formed by the repetitive bonding together of many smaller molecules called **monomers.** As we will see in later chapters, biological polymers such as cellulose, starch, proteins, and DNA occur throughout nature. Although the basic idea is the same, synthetic polymers are much simpler than biopolymers because the starting monomer units are usually small, simple organic molecules.

Many simple alkenes undergo *polymerization* reactions when treated with the proper catalyst. Ethene yields polyethene upon polymerization, propene yields polypropene, and styrene yields polystyrene. The polymer product might have anywhere from a few hundred to a few thousand monomer units incorporated into a long, repeating chain.

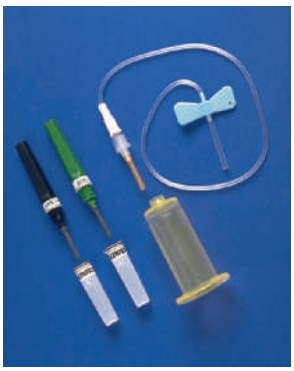


The fundamental reaction in the polymerization of an alkene monomer resembles the addition reactions of a carbon–carbon double bond described in the preceding sections. One of the most common methods used to make polymers involves the use of radicals (see Section 12.8). The reaction begins by addition of a species called an *initiator* to an alkene; this results in the breaking of one of the bonds making up the double bond. A reactive intermediate that contains an unpaired electron (known as a *radical*) is formed in this step, and it is this reactive intermediate that adds to a second alkene molecule. This produces another reactive intermediate, which adds to a third alkene molecule, and so on. Because the result is continuous addition of one monomer after another to the end of the growing polymer chain, polymers formed in this way are *chain-growth polymers.* The basic repeating unit is enclosed in parentheses, and the subscript *n* indicates how many repeating units are in the polymer.

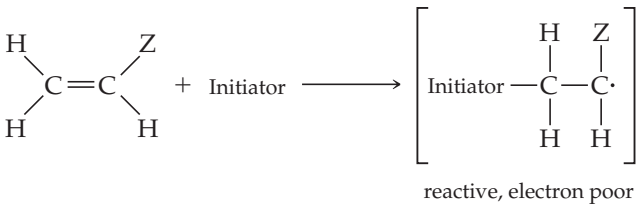
Variations in the substituent group Z attached to the double bond impart different properties to the product, as illustrated by the alkene polymers listed in Table 13.1. Polymer rigidity is controlled by addition of a small amount of a cross-linking agent, typically 1–2% of a dialkene (an alkene containing two double bonds), whose role is to covalently link two chains of monomer units together.

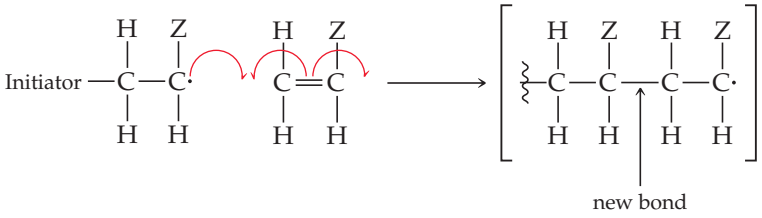
The properties of a polymer depend not only on the monomer but also on the average size of the huge molecules in a particular sample and on how extensively they cross-link and branch. The long molecules in straight-chain polyethene pack closely together, giving a rigid material called *high-density polyethene,* which is mainly used in bottles for products such as milk and motor oil. When polyethene molecules contain many branches (due to the Z groups present), they cannot pack together as tightly and instead form a flexible material called *low-density polyethene,* which is used mainly in packaging materials.

The use of polymers has changed the nature of activities ranging from plumbing and clothing to items such as skis and snowboards. In the health-care fields, the use of inexpensive, disposable equipment is now common.



▲ These disposable polypropene medical supplies are used once and then discarded.





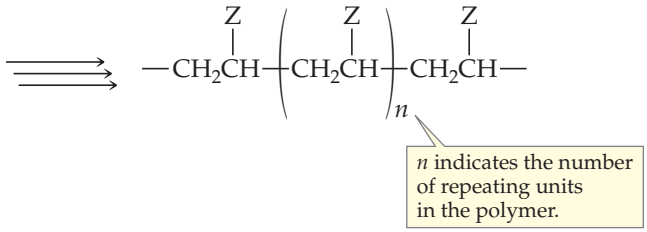
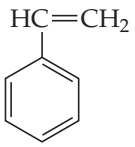


Table 13.1 Some Alkene Polymers and Their Uses

Monomer Name	Monomer Structure	Polymer Name	Uses
Ethene	$H_2C{=}CH_2$	Polyethene	Packaging, bottles
Propene	$H_2C{=}CH{-}CH_3$	Polypropene	Bottles, rope, pails, medical tubing
Vinyl chloride	$H_2C{=}CH{-}Cl$	Poly(vinyl chloride)	Insulation, plastic pipe
Styrene	$H_2C{=}CH{-}C_6H_5$	Polystyrene	Foams, molded plastics
Styrene and 1,3-butadiene	$H_2C{=}CH{-}C_6H_5$ and $H_2C{=}CHCH{=}CH_2$	Styrene-butadiene rubber (SBR)	Synthetic rubber for tires
Acrylonitrile	$H_2C{=}CH{-}C{\equiv}N$	Orlon, Acrilan	Fibers, outdoor carpeting
Methyl methacrylate	$H_2C{=}C(CH_3)COCH_3$	Plexiglas, Lucite	Windows, contact lenses, fiber optics
Tetrafluoroethylene	$F_2C{=}CF_2$	Teflon	Nonstick coatings, bearings, replacement heart valves and blood vessels

Worked Example 13.9 Reactions of Alkenes: Polymerization

Write the structure of a segment of polystyrene, used in foams and molded plastics. The monomer is



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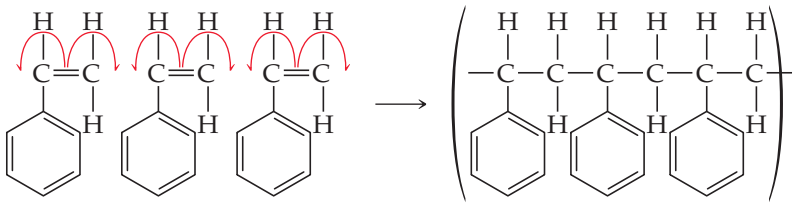
ANALYSIS The polymerization reaction resembles the addition of two monomer units to either end of the double bond.

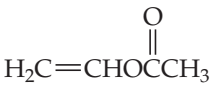
SOLUTION

Draw three molecules of styrene with the double bonds aligned next to each other; then add the monomer units together with single bonds, eliminating the double bonds in the process.



PROBLEM 13.17

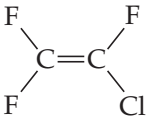
The structure of vinyl acetate is shown below (the partial structure $H_2C{=}CH{-}$ is known as a *vinyl group*). When polymerized it produces poly(vinyl acetate), a polymer used for the springy soles in running shoes. Draw the structure of the polymer obtained if three vinyl acetate units underwent polymerization.

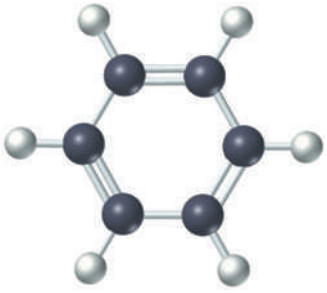


Vinyl acetate

PROBLEM 13.18

Polychlorotrifluoroethylene (PCTFE (Kel-F)) is a polymer that has the lowest water vapor transmission rate of any plastic, making it an excellent moisture barrier. It can also be used for injection molding of plastic items, while polytetrafluoroethylene (PTFE (Teflon)) cannot. Given the monomer shown below, draw a representative structure for PCTFE.





Aromatic The class of compounds containing benzene-like rings.

13.8 Aromatic Compounds and the Structure of Benzene

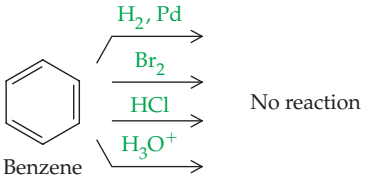
Learning Objectives:

- Identify the structures of aromatic compounds.
- Explain the importance and function of resonance in aromatic compounds.

Chemists initially used the word *aromatic* to describe fragrant substances from fruits, trees, and other natural sources, but they soon realized, however, that many of the substances grouped as aromatic behave differently from most other organic compounds. Today, chemists use the term **aromatic** to refer to the class of compounds that contain benzene-like rings.

Benzene, the simplest aromatic compound, is a flat, symmetrical molecule with the molecular formula C_6H_6. It is often represented as cyclohexatriene, a 6-membered carbon ring with three double bonds. Though useful, the problem with this representation is that it gives the wrong impression about benzene's chemical reactivity and bonding. Because benzene appears to have three double bonds, you might expect it to react with H_2, Br_2, HCl, and H_2O to give the same kinds of addition products that alkenes do. But this expectation would be wrong. Benzene and other aromatic compounds are

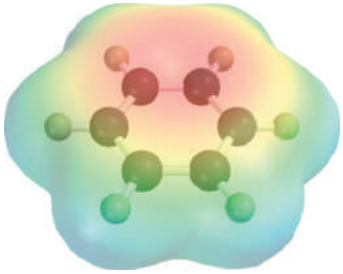
much less reactive than alkenes and do not undergo the usual addition reactions seen in alkenes.



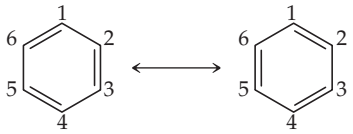
Benzene's relative lack of chemical reactivity is a consequence of its structure. If you were to draw a six-membered ring with alternating single and double bonds, where would you place the double bonds? There are two equivalent possibilities (Figure 13.2b), neither of which is fully correct by itself. Experimental evidence shows that all six carbon–carbon bonds in benzene are identical, so a picture with three double bonds and three single bonds cannot be correct.

The properties of benzene are best explained by assuming that its true structure is an *average* of the two equivalent conventional Lewis structures. Rather than being held between specific pairs of atoms, the double-bond electrons are instead free to move over the entire ring. Each carbon–carbon bond is thus intermediate between a single bond and a double bond. This is known as **resonance,** where the true structure of a molecule is an average among two or more possible conventional structures, and a special double-headed arrow ($\longleftrightarrow$) is used to show the resonance relationship. Resonance allows the electrons in the double bonds to be *delocalized* over the entire molecule, thus lowering the reactivity of the double bonds. It is important to note that *no atoms move between resonance structures, only pairs of electrons* (in this case, double bonds).

Because the real structure of benzene is intermediate between the two forms shown in Figure 13.2b, it is difficult to represent benzene with the standard conventions using lines for covalent bonds. Thus, we sometimes represent the double bonds as a circle inside the six-membered ring, as shown in Figure 13.2c. It is more common, though, to draw the ring with three double bonds, with the understanding that it is an aromatic ring with equivalent bonding all around. We use this convention in this book.

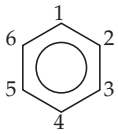


(a)



Two equivalent structures, which differ in the position of their double-bond electrons. Neither structure is correct by itself.

(b)



(c)

▲ **Figure 13.2**
Some representations of benzene.
(a) An electrostatic potential map shows the equivalency of the carbon–carbon bonds. Benzene is usually represented by the two equivalent structures in (b) or by the single structure in (c).

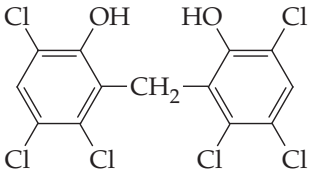
Simple aromatic hydrocarbons like benzene are nonpolar, insoluble in water, volatile, and flammable. Unlike alkanes and alkenes, however, several aromatic hydrocarbons have biological effects. Benzene itself has been implicated as a cause of leukemia, and the dimethyl-substituted benzenes are central nervous system depressants.

Everything we have said about the structure and stability of the benzene ring also applies to the ring when it has substituents, such as in the germicidal agent hexachlorophene and the flavoring ingredient vanillin.

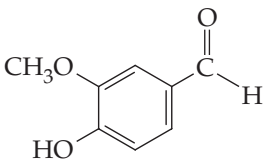
The benzene ring is also present in many biomolecules (including plant dyes and pigments, see the Chemistry in Action on p. 448) and retains its characteristic properties in these compounds as well. In addition, aromaticity is not limited to rings that

▲ Benzaldehyde, an aromatic compound, gives cherries their odor.

Resonance The phenomenon where the true structure of a molecule is an average among two or more conventional Lewis structures that differ only in the placement of double bonds.

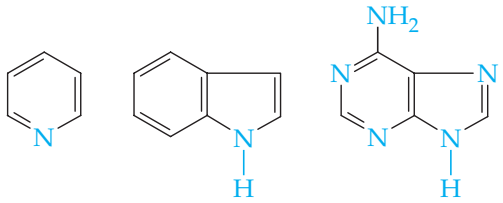


Hexachlorophene
(a germicide)



Vanillin
(vanilla flavoring)

contain only carbon. For example, many compounds classified as aromatics have one or more nitrogen atoms in the ring. Pyridine, indole, and adenine are three examples:



Pyridine Indole Adenine

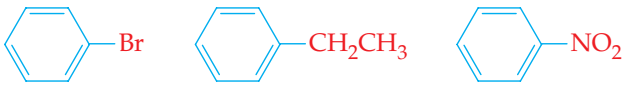
These and all other compounds that contain a substituted benzene ring, or a similarly stable six-membered ring in which double-bond electrons are equally shared around the ring, are classified as aromatic compounds. While the rules regarding exactly what makes a molecule aromatic are not as simple as we discuss here, for the purposes of this text, we say that a 6-membered ring with alternating single and double bonds will be aromatic.

13.9 Naming Aromatic Compounds

Learning Objective:

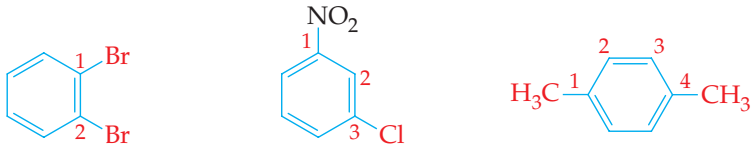
- Name simple monosubstituted or disubstituted aromatic compounds.

Substituted benzenes are named using *-benzene* as the parent. Thus, C_6H_5Br is bromobenzene, $C_6H_5CH_2CH_3$ is ethylbenzene, and so on. No number is needed for monosubstituted benzenes because all the ring positions are identical.



Bromobenzene Ethylbenzene Nitrobenzene

When a benzene has more than one substituent present, the positions of those substituents are indicated by numbers, just as in naming cycloalkanes. Disubstituted benzenes (and only disubstituted benzenes) are unique in that the relational descriptors *o- (ortho), m- (meta),* and *p- (para)* may be used in place of 1,2-, 1,3-, and 1,4-, respectively. The terms *ortho-, meta-,* or *para-* (or their single-letter equivalents) are then used as prefixes.



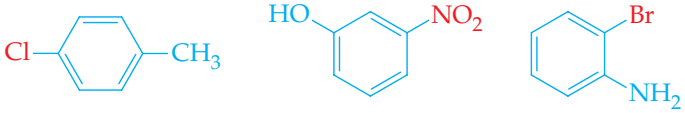
1,2-Dibromobenzene
ortho-Dibromobenzene
o-Dibromobenzene

3-Chloronitrobenzene
meta-Chloronitrobenzene
m-Chloronitrobenzene

1,4-Dimethylbenzene
para-Dimethylbenzene
p-Dimethylbenzene

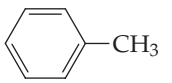
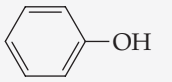
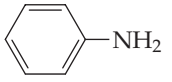
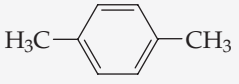
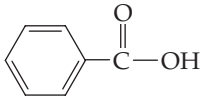
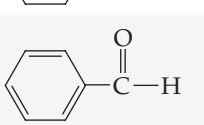
While any one of these three nomenclature schemes are acceptable, we will almost exclusively use *o-*, *m-*, and *p-* in naming these disubstituted compounds.

Many substituted aromatic compounds have common names in addition to their systematic names. For example, methylbenzene is familiarly known as *toluene,* hydroxybenzene as *phenol,* aminobenzene as *aniline,* and so on, as shown in Table 13.2. Frequently, these common names are also used together with *o- (ortho), m- (meta),* or *p- (para)* prefixes. For example,



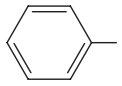
p-Chlorotoluene *m*-Nitrophenol *o*-Bromoaniline

Table 13.2 Common Names of Some Aromatic Compounds

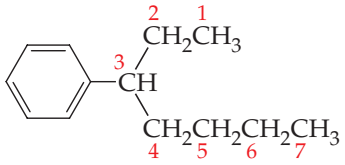
Structure	Name
	Toluene
	Phenol
	Aniline
	*para*-Xylene (*p*-Xylene)
	Benzoic acid
	Benzaldehyde

Occasionally, the benzene ring itself may be considered a substituent group attached to another parent compound. When this happens, the name **phenyl** (pronounced *fen*-nil and commonly abbreviated Ph—) is used for the C_6H_5— unit.

Phenyl The C_6H_5— group.



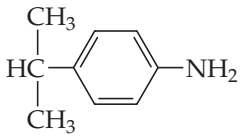
A phenyl group
C_6H_5—



3-Phenylheptane

Worked Example 13.10 Naming Organic Compounds: Aromatic Compounds

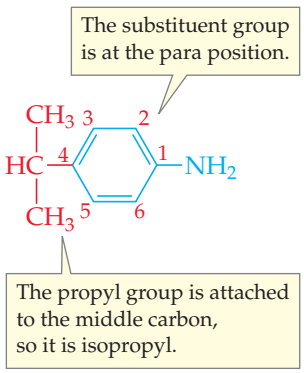
Name the following aromatic compound:



ANALYSIS First, identify the parent organic compound, then identify the location of substituent groups on the benzene ring either by number or by *ortho (o-), meta (m-),* or *para (p-).*

SOLUTION

The parent compound is a benzene ring with an amine group (*aminobenzene,* which is commonly known as *aniline*). The substituent group is attached at the C4, or para, position relative to the amino group. The propyl group is attached to the benzene ring by the middle carbon, so it is *isopropyl.*



Name: *para*-isopropylaniline, or 4-isopropylaminobenzene

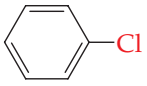
Worked Example 13.11 Molecular Structures: Aromatic Compounds

Draw the structure of *m*-chloroethylbenzene.

ANALYSIS *m*-Chloroethylbenzene has a benzene ring with two substituents, chloro and ethyl, in a meta relationship (i.e., on C1 and C3).

SOLUTION

Since all carbons in the benzene ring are equivalent, draw a benzene ring and attach one of the substituents—for example, chloro—to any position.



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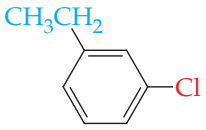
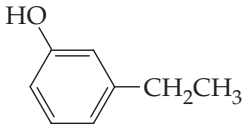
Now go to a meta position two carbons away from the chloro-substituted carbon, and attach the second (ethyl) substituent.

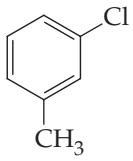


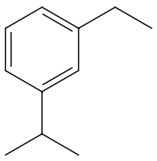
m-Chloroethylbenzene

PROBLEM 13.19

What are the IUPAC names for the following compounds?

(a) 

(b) 

(c) 

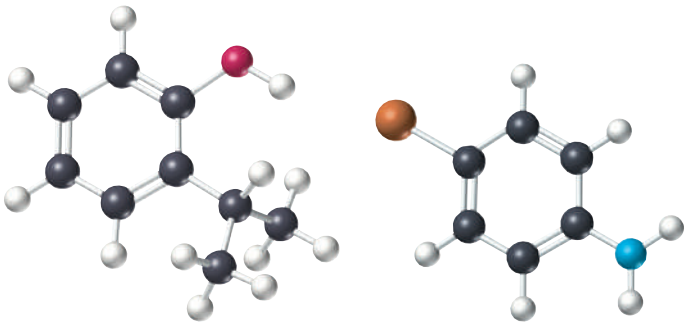
PROBLEM 13.20

Draw structures corresponding to the following names (refer to Table 13.2 if necessary):

(a) *m*-Chloronitrobenzene
(b) *o*-Nitrotoluene
(c) *p*-Methylaniline
(d) *p*-Nitrophenol

KEY CONCEPT PROBLEM 13.21

Name the following compounds (red = O, blue = N, brown = Br):



(a) **(b)**

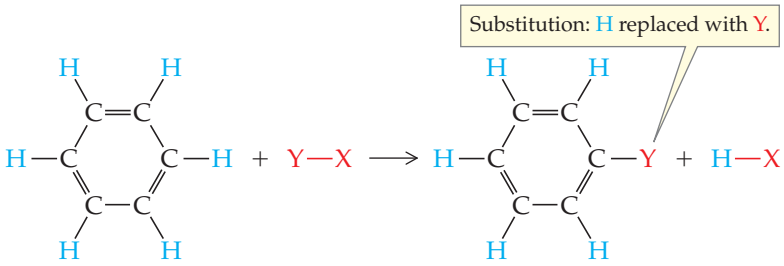
13.10 Reactions of Aromatic Compounds

Learning Objective:

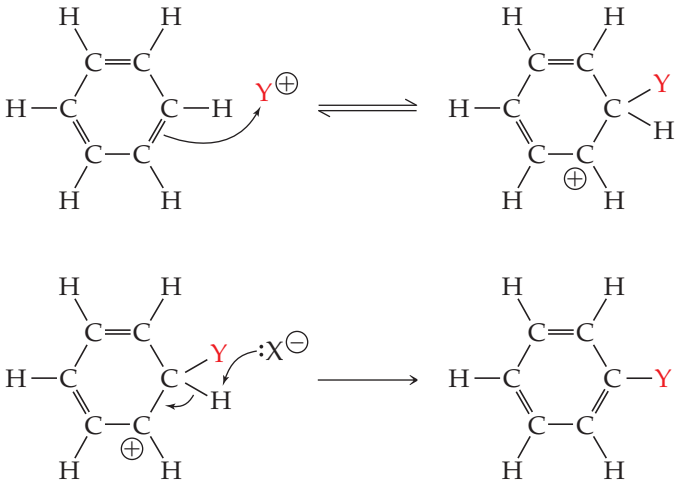
- Predict the products obtained when aromatic compounds react with concentrated HNO_3, Cl_2, Br_2, or concentrated H_2SO_4.

Unlike alkenes, which undergo addition reactions, aromatic compounds usually undergo a special type of substitution reaction known as an *electrophilic aromatic substitution* (EAS) reaction. That is, a group Y substitutes for one hydrogen atom on the

aromatic ring without changing the ring itself. It does not matter which of the six ring hydrogens in benzene is replaced because all six are equivalent.

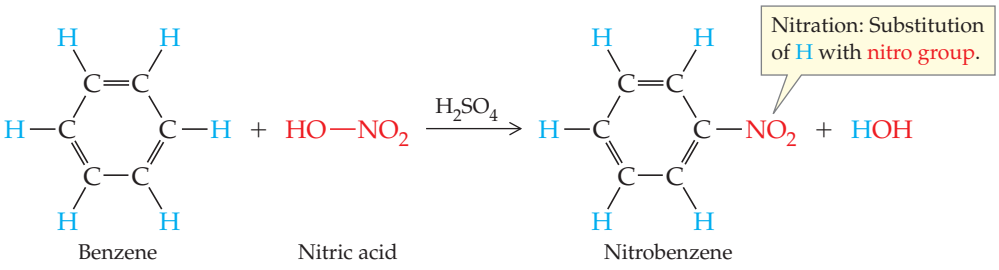


The mechanism responsible for this type of reaction is similar to that seen for alkenes, with the key difference being regeneration of the extremely stable aromatic ring.



Nitration is the substitution of a *nitro group* ($-NO_2$) for one of the ring hydrogens. The reaction occurs when benzene reacts with nitric acid in the presence of sulfuric acid as catalyst.

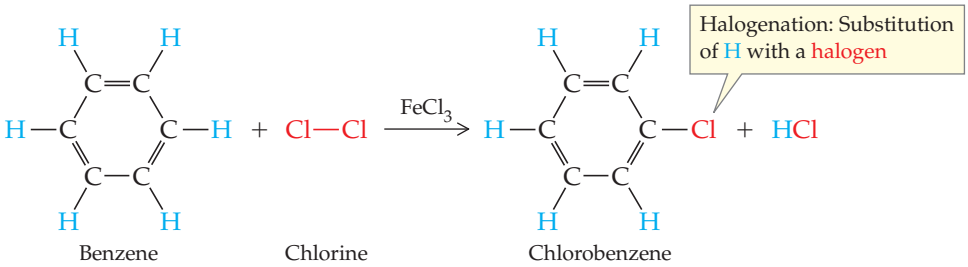
Nitration The substitution of a nitro group ($-NO_2$) for a hydrogen on an aromatic ring.



Nitration of aromatic rings is a key step in the synthesis both of explosives like TNT (trinitrotoluene) and of many important pharmaceutical agents, since the $-NO_2$ group can be readily converted to an $-NH_2$. Nitrobenzene itself is the industrial starting material for the preparation of aniline, which is used to make many of the brightly colored dyes in clothing.

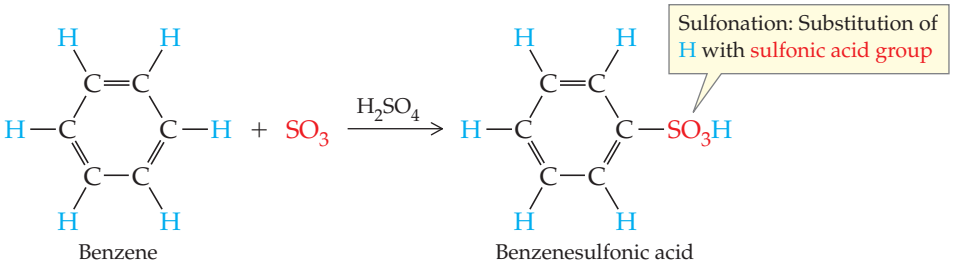
Halogenation (aromatic) The substitution of a halogen group (—X) for a hydrogen on an aromatic ring.

Halogenation (aromatic) is the substitution of a halogen atom, usually bromine or chlorine, for one of the ring hydrogens. The reaction occurs when benzene reacts with Br_2 or Cl_2 in the presence of $FeBr_3$ or $FeCl_3$ as catalyst.



Sulfonation The substitution of a sulfonic acid group (—SO_3H) for a hydrogen on an aromatic ring.

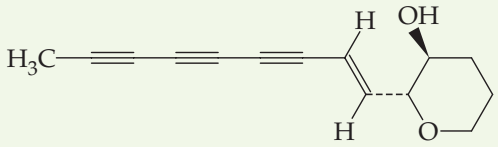
Sulfonation is the substitution of a sulfonic acid group (—SO_3H) for one of the ring hydrogens. The reaction occurs when benzene reacts with concentrated sulfuric acid and SO_3.



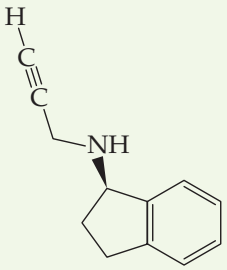
CHEMISTRY IN ACTION

Enediyne Antibiotics: A Newly Emerging Class of Antitumor Agents

While we discuss alkynes only briefly in this chapter and this text as a whole, it is not because alkynes are not important in organic chemistry. Alkynes are not usually found in nature; however, when they are isolated from natural sources, such as plants and bacteria, they have unexpected physiological properties, including toxicity. For example, ichthyothereol, a trialkyne, isolated from the leaves of a small herb found in the Amazon and Central America, inhibits energy production in mitochondria, and while being toxic to fish, mice, and dogs, has no effect on humans. This has caused chemists to investigate what might happen if the alkyne function were introduced into other biologically active molecules, which has led to the discovery of pharmaceuticals such as Rasagiline, a monoamine oxidase inhibitor effective in treating Parkinson's disease. This compound, due to its neuroprotective nature, is also offering a novel approach to Alzheimer's drug therapy. Rasagiline seems to enhance memory and learning, while also improving mood, motivation, and age-related memory decline and provides a great lead for the discovery of new medicines to treat this debilitating disease. Due to successes such as Rasagiline, chemists and biochemists have intensified the hunt for naturally occurring alkynes. This expanding pursuit for new alkyne-containing natural products has led to the discovery of a very unlikely class of antitumor antibiotics known as the enediynes, which we first learned about at the beginning of the chapter. Initially discovered in a fermentation broth derived from the bacteria *Micromonospora,* they represent a new chemical structure class for antibiotics.



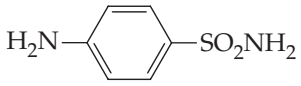
Ichthyotherol



Rasagiline

The enediyne family of compounds represents the most potent antitumor agents known. The toxic nature of these compounds arises from their ability to cause scission of DNA strands in their target. The enediyne antibiotics fall into three basic families: the calicheamicins, the dynemicins (shown next), and the most complex of the group, the chromoproteins. All members have three distinct regions within them: (1) an anthraquinone-like portion; (2) a chemical "warhead" comprised of two triple

Aromatic-ring sulfonation is a key step in the synthesis of such compounds as the sulfa-drug family of antibiotics:



Sulfanilamide—a sulfa antibiotic

PROBLEM 13.22

What products will be formed when toluene is reacted with the reagents shown here?

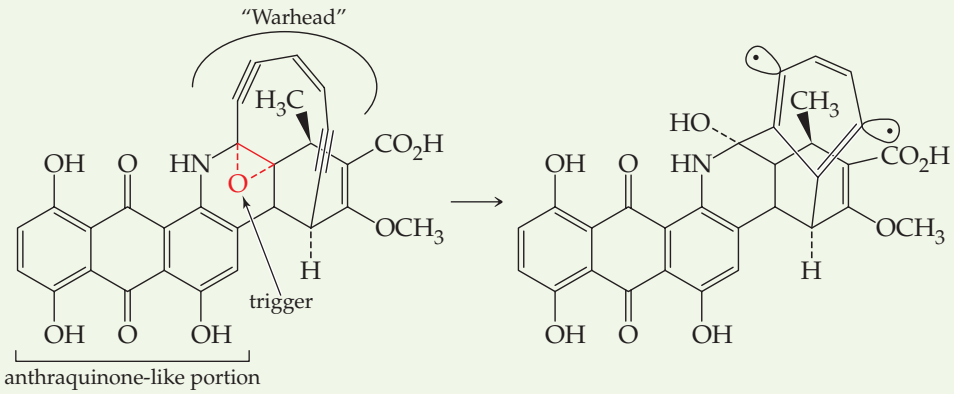
(a) Br_2 and $FeBr_3$

(b) HNO_3 and H_2SO_4 catalyst

(c) SO_3 in H_2SO_4

PROBLEM 13.23

Reaction of Br_2 and $FeBr_3$ with phenol can lead to *three* possible substitution products. Show the structure of each and name them.



Dynemicin A

bonds, conjugated through a double bond, within a 9–10-membered ring; and (3) a "trigger." In Dynemicin A (shown above), that trigger is the three-membered epoxide ring (highlighted in red). The anthraquinone portion intercalates into the major groove of DNA; the trigger is then activated by some nucleophilic species (such as an oxygen, nitrogen, or sulfur atom) that attacks and then opens the epoxide ring. Once opened, the warhead undergoes a rearrangement reaction, producing an extremely reactive diradical aromatic species, which then induces the breakage of the DNA strands.

All of the enediynes are very toxic, as are all antitumor agents. One way to utilize them in the war on cancer would be to attach them to an antibody specifically prepared to target the tumor cells the doctor wishes to destroy. This method, known as "immunotargeting," would allow the preparation of a "magic bullet," which would attack only the tumor cells and nothing else. One of the reasons that the enediyne antibiotics are so attractive is that they have activity against drug-resistant tumors. Many cancer cells have natural resistance to a number of the drugs usually used to treat them or will develop resistance over the course of a treatment. This, coupled with a lack of selectivity to antitumor agents (antitumor drugs affect all cells, not just cancer) is one of the major causes of the ineffectiveness of anticancer therapies. Compounds such as Dynemicin A and others discovered through studies of the enediynes could represent a new weapon in our assault on an old and deadly foe: cancer.

The meaning of the wedged and dashed bonds will be clarified in Section 14.10 when we discuss stereochemistry.

CIA Problem 13.4 What beneficial properties of Rasagiline make it useful for the treatment of Alzheimer's disease?

CIA Problem 13.5 Why would attaching an enediyne-containing molecule to an antibody be an attractive way to treat cancer cells?

CIA Problem 13.6 What are the major causes of the ineffectiveness of anticancer therapies?

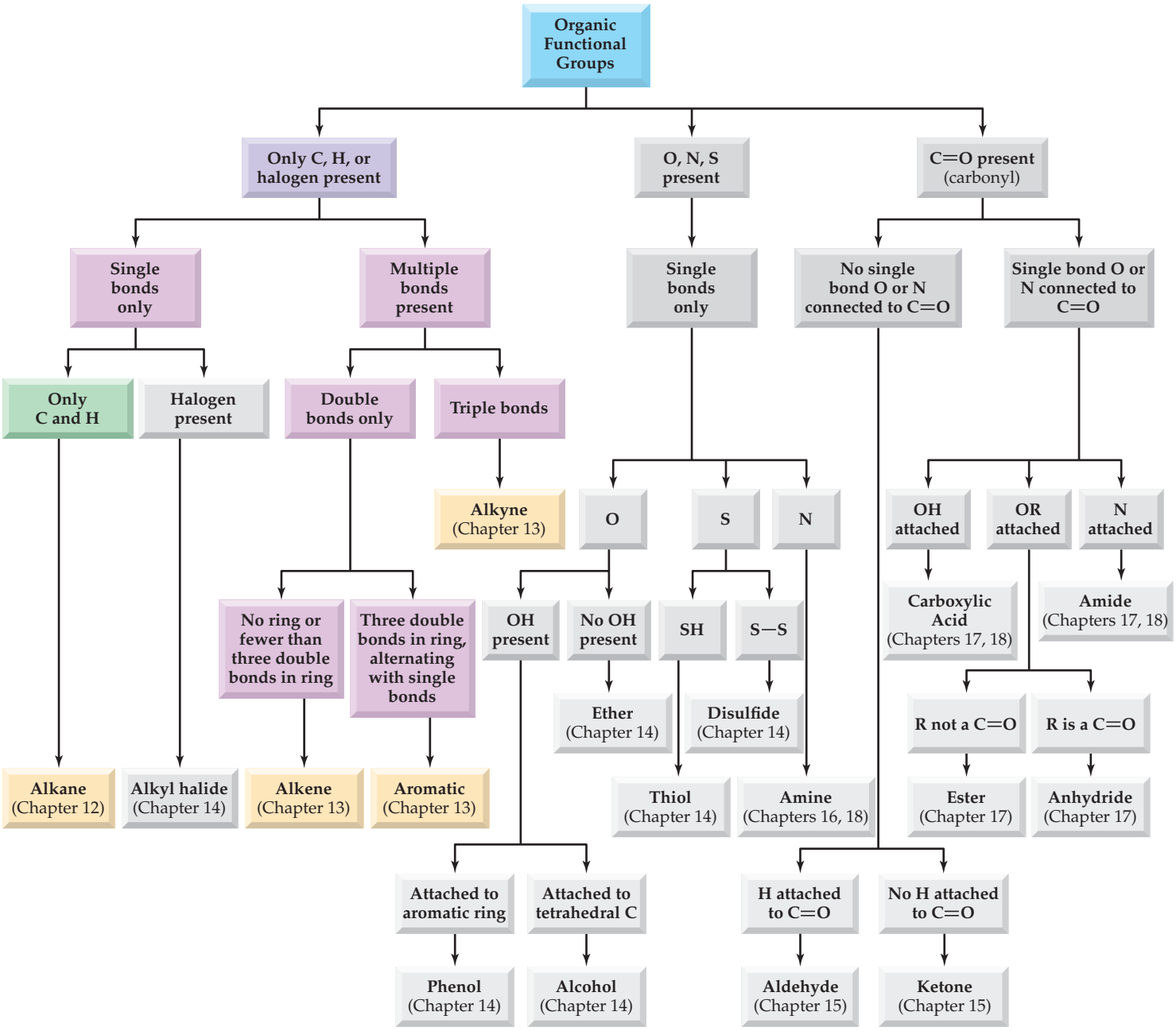
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Identify the functional groups present in alkenes and alkynes.** *Alkenes* are hydrocarbons that contain a carbon–carbon double bond, and *alkynes* are hydrocarbons that contain a carbon–carbon triple bond *(see Problems 27, 29–31, 34, 35, and 43).*
- **Differentiate between saturated and unsaturated molecules.** A *saturated* molecule is one that contains only tetravalent carbon atoms and no double or triple bonds. Compounds are said to be *unsaturated* because they have fewer hydrogens than corresponding alkanes. The term is usually used to indicate the presence of double or triple bonds *(see Problems 30 and 31).*
- **Name a simple alkene or alkyne given its condensed or line structure.** Alkenes and alkynes are named in a manner almost identical to that used for naming alkanes (Section 12.6), except now the functional group takes priority in numbering the carbon chain. Alkenes are named using the family ending *-ene;* alkynes use the family ending *-yne (see Problems 34–37).*
- **Draw the condensed or line structure of an alkene or alkyne given its name.** Organic compounds can be represented by *structural formulas* in which all atoms and bonds are shown, by *condensed structures* in which not all bonds are drawn, or by *line structures* in which the carbon skeleton is represented by lines and the locations of C and H atoms are understood *(see Problems 38, 39, 48, 61, and 70).*
- **Identify cis–trans isomers of alkenes.** Alkenes can be thought of as having sides and ends. Cis–trans isomers are seen in substituted alkenes as a consequence of the lack of rotation around carbon–carbon double bonds. In the cis isomer, the two substituents are on the same side of the double bond; in the trans isomer, they are on opposite sides of the double bond *(see Problems 44–51, 71, 81, 82, and 84).*
- **Identify the physical properties of alkenes and alkynes.** Alkenes and alkynes are generally nonpolar, insoluble in water (hydrophobic), and unreactive. They possess low melting and/or boiling points due to their weak intermolecular forces. Alkenes are generally nontoxic and therefore have limited physiological effects *(see Problems 72 and 73).*
- **Identify the different types of organic reactions.** Addition reactions occur when two reactants add together to form a single product with no atoms left over. Elimination reactions occur when a single reactant breaks into two products, forming an alkene or an alkyne in the process. Substitution reactions occur when two reactants exchange atoms or groups to give two new products. Rearrangement reactions occur when a single reactant undergoes a reorganization of bonds and atoms to yield a single isomeric product *(see Problems 52–57).*
- **Predict the addition products obtained when alkenes react with H_2, Cl_2, HCl, or H_2O.** Alkenes and alkynes undergo addition reactions to their multiple bonds. Addition of hydrogen to an alkene *(hydrogenation)* yields an alkane product, addition of Cl_2 or Br_2 *(halogenation)* yields a 1,2-dihaloalkane product, addition of HBr and HCl *(hydrohalogenation)* yields an alkyl halide product, and addition of water *(hydration)* yields an alcohol product *(see Problems 58–62 and 76–80).*
- **Identify "symmetrically substituted" and "unsymmetrically substituted" alkenes.** Alkenes can be classified as symmetrically substituted if each carbon of the double bond has the same number of hydrogens directly attached to each carbon and unsymmetrically substituted if the carbons do not *(see Problems 46–48, 50, 70, and 71).*
- **Utilize Markovnikov's rule when addition reactions to unsymmetrically substituted alkenes occur.** Markovnikov's rule predicts that in the addition of HX or H_2O to a double bond, the H becomes attached to the carbon with more hydrogens and the X or OH becomes attached to the carbon with fewer Hs *(see Problems 58 and 60).*
- **Predict what polymer forms given an alkene monomer.** Many simple alkenes undergo *polymerization,* a reaction that resembles addition to a carbon–carbon double bond, as described in the preceding sections. An *initiator* adds to an alkene to form a radical; this results in the breaking of one of the bonds making up the double bond. This reactive intermediate adds to a second alkene molecule to produce another reactive intermediate, which adds to a third alkene molecule, and so on. The resulting polymer is the result of the continuous addition of one monomer after another to the end of the growing polymer chain *(see Problems 63, 64, and 83).*
- **Identify the structures of aromatic compounds.** *Aromatic compounds* contain six-membered, benzene-like rings and are usually written with three double bonds. In fact, however, there is equal bonding between neighboring carbon atoms in benzene rings because the double-bond electrons are symmetrically spread around the entire ring *(see Problems 31–33, 37, and 39).*
- **Explain the importance and function of resonance in aromatic compounds.** Aromatic compounds exhibit resonance: Lewis structures that are interconvertable by only the movement of pairs of electrons; no atoms can move. Resonance allows for the delocalization of electrons by spreading electron density over the entire molecule. Because of this, delocalized electrons are less reactive than those found in a normal alkene or alkyne *(see Problems 29 and 31).*
- **Name simple monosubstituted or disubstituted aromatic compounds.** Disubstituted benzenes have the suffix *-benzene* as the parent name, and positions of the substituents are indicated with the prefixes *ortho-* (1,2 substitution), *meta-* (1,3 substitution), or *para-* (1,4 substitution) *(see Problems 26, 33, 37, 39, and 69).*
- **Predict the products obtained when aromatic compounds react with concentrated HNO_3, Cl_2, Br_2, or concentrated H_2SO_4.** Aromatic compounds are unusually stable but can be made to undergo substitution reactions, in which one of the ring hydrogens is replaced by another group ($C_6H_6 \rightarrow C_6H_5Y$). Among these substitutions are *nitration* (substitution of $-NO_2$ for $-H$), *halogenation* (substitution of $-Br$ or $-Cl$ for $-H$), and *sulfonation* (substitution of $-SO_3H$ for $-H$) *(see Problems 42 and 65–68).*

KEY WORDS

Addition reaction, *p. 445*
Alkene, *p. 437*
Alkyne, *p. 437*
Aromatic, *p. 460*
Cis–trans isomer, *p. 442*
Cycloalkene, *p. 437*
Elimination reaction, *p. 446*
Halogenation (alkene), *p. 451*
Halogenation (aromatic), *p. 466*
Hydration, *p. 455*
Hydrogenation, *p. 450*
Hydrohalogenation, *p. 452*
Markovnikov's rule, *p. 452*
Monomer, *p. 458*
Nitration, *p. 465*
Phenyl, *p. 463*
Polymer, *p. 458*
Reaction mechanism, *p. 457*
Rearrangement reaction, *p. 447*
Resonance, *p. 461*
Saturated, *p. 437*
Substitution reaction, *p. 446*
Sulfonation, *p. 466*
Unsaturated, *p. 437*

CONCEPT MAP: ORGANIC CHEMISTRY FAMILIES



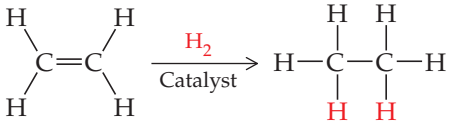
▲ **Figure 13.3** **Functional Group Concept Map.** This is the same concept map we saw at the end of Chapter 12, except the functional groups discussed in this chapter, alkenes, alkynes, and aromatic compounds, have now been colorized.

SUMMARY OF REACTIONS

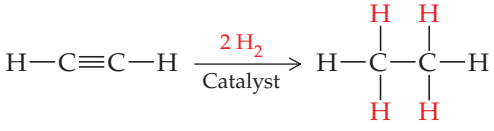
1. Reactions of alkenes and alkynes (Section 13.6):

(a) Addition of H_2 to yield an alkane (hydrogenation):

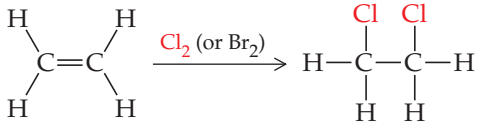
An alkene:



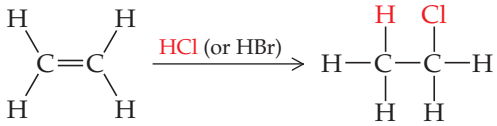
An alkyne:



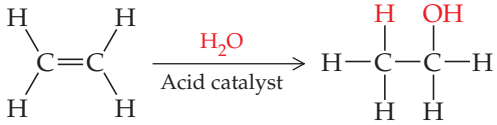
(b) Addition of Cl_2 or Br_2 to yield a dihalide (halogenation):



(c) Addition of HCl or HBr to yield an alkyl halide (hydrohalogenation):

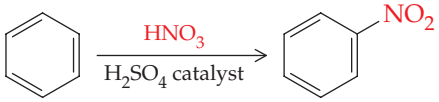


(d) Addition of H_2O to yield an alcohol (hydration):

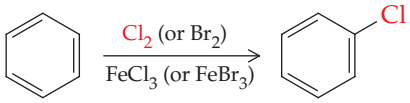


2. Reactions of aromatic compounds (Section 13.10):

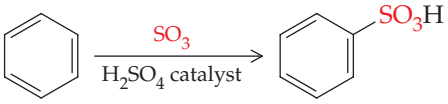
(a) Substitution of an $—NO_2$ group to yield a nitrobenzene (nitration):



(b) Substitution of a Cl or Br atom to yield a halobenzene (halogenation):

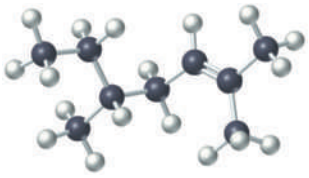


(c) Substitution of an $—SO_3H$ group to yield a benzenesulfonic acid (sulfonation):

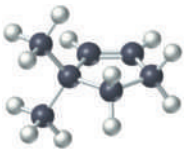


UNDERSTANDING KEY CONCEPTS

13.24 Name the following alkenes, and predict the products of their reaction with (1) HBr, (2) H_2O, and (3) an acid catalyst.

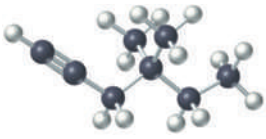


(a)

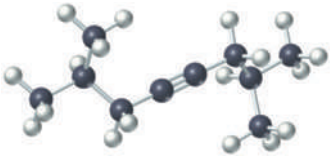


(b)

13.25 Name the following alkynes:

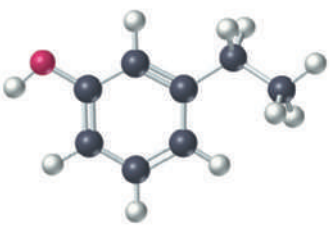


(a)

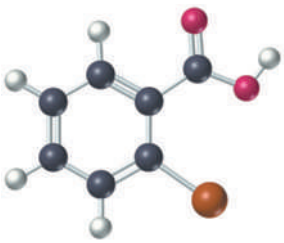


(b)

13.26 Give IUPAC names for the following substances (red = O, brown = Br):

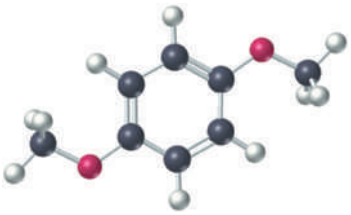


(a)

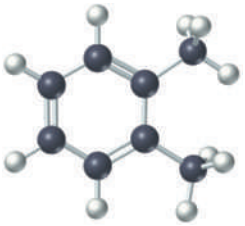


(b)

13.27 Draw the product from reaction of the following substances with (1) Br_2 and $FeBr_3$ and (2) SO_3 and H_2SO_4 catalyst (red = O):



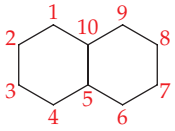
(a)



(b)

13.28 Alkynes undergo hydrogenation to give alkanes, just as alkenes do. Draw and name the products that would result from hydrogenation of the alkynes shown in Problem 13.25.

13.29 We saw in Section 13.8 that benzene can be represented by either of two resonance forms, which differ in the positions of the double bonds in the aromatic ring. Naphthalene, a polycyclic aromatic compound, can be represented by *three* forms with different double-bond positions. Draw all three structures, showing the double bonds in each (the following numbered skeletal structure of naphthalene shows only the connections among atoms).



ADDITIONAL PROBLEMS

NAMING ALKENES, ALKYNES, AND AROMATIC COMPOUNDS (SECTIONS 13.1, 13.2, 13.9)

13.30 **(a)** What do the terms saturated and unsaturated mean?
(b) Draw an example of a saturated four carbon compound and an unsaturated four carbon compound.

13.31 **(a)** What does the term "aromatic" refer to when discussing organic molecules?
(b) What is resonance and why is it important in aromatic compounds?

13.32 What family-name endings are used for alkenes, alkynes, and substituted benzenes?

13.33 What prefixes are used in naming the following?

(a) A 1,3-disubstituted benzene

(b) A 1,4-disubstituted benzene

13.34 Write structural formulas for compounds that meet the following descriptions:

(a) A 6-carbon alkene whose longest chain is 4 carbons in length (three possibilities)

(b) An alkyne with 5 carbons total (three possibilities)

(c) A monosubstituted benzene with a total of 8 carbons (one possibility)

(d) A disubstituted benzene with a total of 8 carbons (three possibilities)

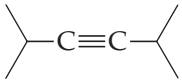
13.35 Write structural formulas for compounds that meet the following descriptions:

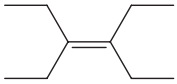
(a) An alkene, C_6H_{12}, that cannot have cis–trans isomers and whose longest chain is 5 carbons long

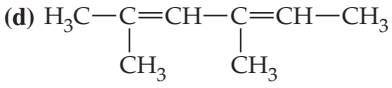
(b) An alkene with a chemical formula of $C_{10}H_{12}$ that has cis–trans isomers and contains a benzene ring.

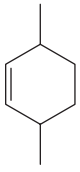
13.36 What are the IUPAC names of the following compounds?

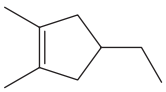
(a) $CH_3CH{=}CHCH_2CH$

(b) 

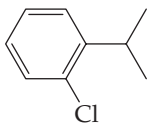
(c) 

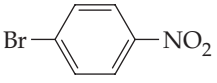
(d) 

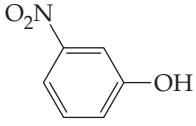
(e) 

(f) 

13.37 Give IUPAC names for the following aromatic compounds:

(a) 

(b) 

(c) 

13.38 Draw structures corresponding to the following IUPAC names:

(a) *trans*-Pent-2-ene

(b) *trans*-3,4-Dimethylhex-3-ene

(c) 2-Methylbuta-1,3-diene

(d) *trans*-Hept-3-ene

(e) *p*-Nitrotoluene

(f) *o*-Chlorophenol

(g) 1,2-Dimethylcyclobutene

(h) 3,3-Diethyl-6-methylnon-4-ene

13.39 Draw structures corresponding to the following names:

(a) Aniline

(b) Phenol

(c) *o*-Xylene

(d) 2,4,6-Trinitrobenzene

(e) *p*-Chlorobenzoic acid

(f) *m*-Nitroaniline

(g) *o*-Chlorobenzaldehyde

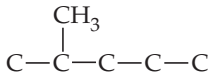
(h) Anisole (methoxybenzene)

13.40 Seven alkynes have the formula C_6H_{10}. Draw them, using line structures.

13.41 Draw and name all phenols with the formula C_7H_8O.

13.42 When ethylbenzene is reacted with nitric acid, three possible benzenes containing both a nitro group and an ethyl group are obtained. Draw and name them.

13.43 There are four different pentenes having the following general structure:



The four differ only in the placement of the double bond. Draw and name all four. Ignore cis–trans isomers.

ALKENE CIS–TRANS ISOMERS (SECTION 13.3)

13.44 What requirement(s) must be met for an alkene to show cis–trans isomerism?

13.45 Why do alkynes not show cis–trans isomerism?

13.46 Draw line structures for the following alkenes. Which can exist as cis–trans isomers? For those that can, draw both isomers.

(a) 2-Methyloct-2-ene **(b)** Hept-3-ene

(c) 3,4-Dimethylhex-3-ene

13.47 Which compound(s) in Problem 13.43 can exist as cis–trans isomers? Label each as being either a symmetrically or unsymmetrically substituted alkene.

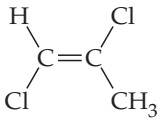
13.48 Draw structures of the following compounds:

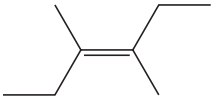
(a) *cis*-Hept-3-ene

(b) *cis*-4-Methylpent-2-ene

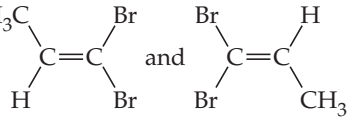
(c) *trans*-2,5-Dimethylhex-3-ene

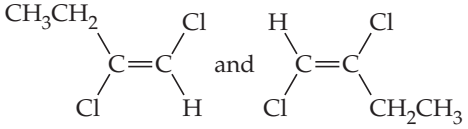
13.49 Each of the following has a cis or trans isomeric form. Draw it.

(a) 

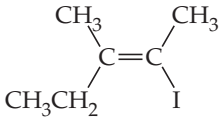
(b) 

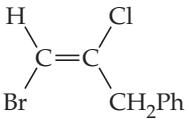
13.50 Which of the following pairs are isomers, and which are identical?

(a) 

(b) 

13.51 Draw the other cis–trans isomer for the following molecules:

(a) 

(b) 

KINDS OF REACTIONS (SECTION 13.5)

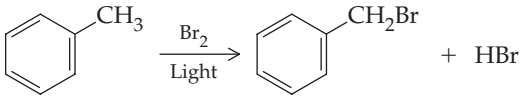
13.52 What is the difference between a substitution reaction and an addition reaction?

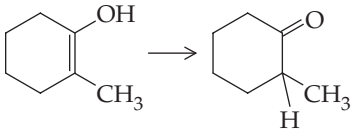
13.53 Give an example of an addition reaction.

13.54 If 2-methylpent-2-ene were converted into hex-1-ene, what kind of reaction would that be?

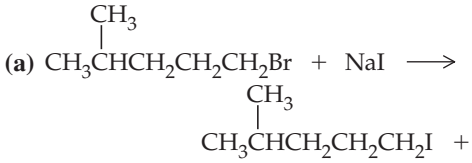
13.55 If bromocyclohexane were converted into cyclohexene, what kind of reaction would that be?

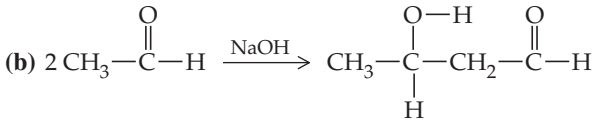
13.56 Identify the type of reaction for the following:

(a) 

(b) 

13.57 Identify the type of reaction for the following:

(a) 

(b) 

REACTIONS OF ALKENES AND ALKYNES (SECTIONS 13.6–13.7)

13.58 Write equations for the reaction of pent-2-ene with the following:

(a) H_2 and Pd catalyst

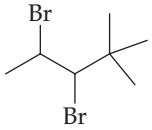
(b) Br_2

(c) HCl

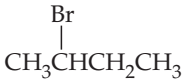
(d) H_2O and H_2SO_4 catalyst

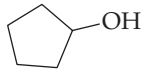
13.59 Write equations for the reaction of 1-methylcyclohexene with the reagents shown in Problem 13.58.

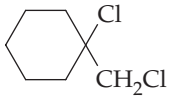
13.60 What alkene could you use to make the following products? Draw the structure of the alkene, and tell what other reagent is also required for the reaction to occur.

(a) 

(b) $CH_3CH_2CH_3$

(c) 

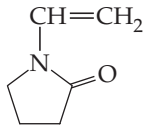
(d) 

(e) 

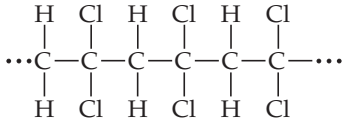
13.61 2,2,3,3-Tetrabromopentane can be prepared by an addition reaction of excess Br_2 with an alkyne. Draw the structure of the alkyne and name it.

13.62 4-Methylpent-1-yne reacts with HBr in a 1:1 molar ratio to yield two different addition products, both being bromopentenes and having the chemical formula C_5H_9Br. Draw the structures of two possible products.

13.63 Polyvinylpyrrolidone (PVP) is often used in hair sprays to hold hair in place. Draw a few units of the PVP polymer. The vinylpyrrolidone monomer unit has the following structure:



13.64 Saran, used as a plastic wrap for foods, is a polymer with the following structure. What is the monomer unit of Saran?



REACTIONS OF AROMATIC COMPOUNDS (SECTION 13.10)

13.65 For each of the following reagents, decide whether chlorobenzene will react with it or not, and, if it does, draw and name the products expected from the reaction.

(a) Br_2 and $FeBr_3$

(b) HBr

(c) HNO_3 and H_2SO_4 catalyst

13.66 Write equations for the reaction of *p*-dichlorobenzene with the following:

(a) Br_2 and $FeBr_3$

(b) HNO_3 and H_2SO_4 catalyst

(c) H_2SO_4 and SO_3

(d) Cl_2 and $FeCl_3$

13.67 Aromatic compounds do not normally react with hydrogen in the presence of a palladium catalyst but will if very high pressures (200 atm) and high temperatures are used. Under these conditions, toluene adds three molecules of H_2 to give an alkane addition product. What is a likely structure for the product?

13.68 The explosive trinitrotoluene (TNT) is made by carrying out three successive nitration reactions on toluene. If these nitrations only occur in the ortho and para positions relative to the methyl group, what is the structure of TNT?

CONCEPTUAL PROBLEMS

13.69 Salicylic acid (*o*-hydroxybenzoic acid) is used as starting material to prepare aspirin. Draw the structure of salicylic acid.

13.70 The following names are incorrect by IUPAC rules. Draw the structures represented by the following names, and write their correct names. Label each as being symmetrically or unsymmetrically substituted.

(a) 2-Methyl-4-hexene

(b) 1,3-Dimethyl-1-hexyne

(c) 2-Isopropyl-1-propene

(d) 1,4,6-Trinitrobenzene

(e) 1,2-Dimethyl-3-cyclohexene

(f) 3-Methyl-2,4-pentadiene

13.71 Which of the compounds in Problem 13.70 are capable of cis–trans isomerism? Draw each isomer.

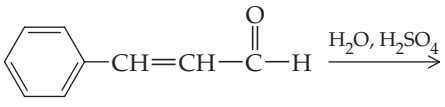
13.72 Assume that you have two unlabeled bottles, one with cyclohexane and one with cyclohexene. How could you tell them apart by carrying out chemical reactions?

13.73 Assume you have two unlabeled bottles, one with cyclohexene and one with benzene. How could you tell them apart by carrying out chemical reactions?

13.74 The compound *p*-dichlorobenzene has been used as an insecticide. Draw its structure.

13.75 Menthene, a compound found in mint plants, has the formula $C_{10}H_{18}$ and the IUPAC name 1-isopropyl-4-methylcyclohexene. What is the structure of menthene?

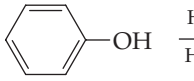
13.76 Cinnamaldehyde, the pleasant-smelling substance found in cinnamon oil, has the following structure:



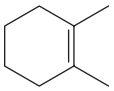
What products would you expect to obtain from reaction of cinnamaldehyde with water and sulfuric acid catalyst?

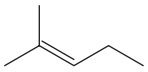
13.77 Predict the products of the following reactions:

(a) $CH_3CH_2CH{=}CHCHCH_3$ (CH_3 on the CHCH$_3$ carbon), H_2, Pd → ?

(b)  (HNO_3, H_2SO_4 → ?)

(3 possible disubstituted products)

(c)  (H_2O, H_2SO_4 → ?)

(d)  (H_2O, H_2SO_4 → ?)

(e) $CH_3C{\equiv}CCH_2CH_3$ (H_2, Pd → ?)

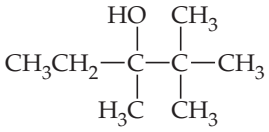
13.78 Two products are possible when pent-2-ene is treated with HBr. Write the structures of the possible products, and explain why they are made in about equal amounts.

13.79 Ocimene, a compound isolated from the herb basil, has three double bonds and the IUPAC name 3,7-dimethylocta-1,3,6-triene.

(a) Draw its structure.

(b) Draw the structure of the compound formed if enough HBr is added to react with all the double bonds in ocimene.

13.80 Describe how you could prepare the following compound from an alkene. Draw the formula of the alkene, name it, and list the inorganic reactants or catalysts needed for the conversion.



13.81 Which of the following compounds are capable of cis–trans isomerism?

(a) $CH_3CHCH{=}CHCH_3$ (CH_3 on the CHCH$_3$ carbon)

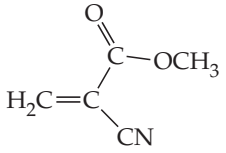
(b) $CH_3CH_2CHCH_3$ (CH=CH$_2$ on the CHCH$_3$ carbon)

(c) $CH_3CH{=}CHCHCH_2CH_3$ (Cl on the CHCH$_2$CH$_3$ carbon)

GROUP PROBLEMS

13.82 Why do you suppose small-ring cycloalkenes like cyclohexene do not exist as cis–trans isomers, whereas large ring cycloalkenes like cyclodecene *do* show isomerism?

13.83 "Superglue" is an alkene polymer made from the monomer unit.



Draw a representative segment of the structure of superglue.

13.84 Draw all possible C_5H_{10} alkene isomers having a longest chain of four carbons and a methyl group. (Hint: Adapt the method described in Worked Example 12.12 to arrive at your answers.)

14

Some Compounds with Oxygen, Sulfur, or a Halogen

CONTENTS

CONCEPTS TO REVIEW

A. Polar Covalent Bonds (Section 4.9)

B. Oxidation and Reduction (Section 5.5)

C. Hydrogen Bonds (Section 8.2)

D. Acid Dissociation Constants (Sections 10.6 and 10.7)

E. Functional Groups (Section 12.2)

F. Naming Alkanes (Section 12.6)

G. Types of Organic Reactions (Section 13.5)

▲ As a mother cuddles her newborn, it is unthinkable that she could harm her child, yet drinking during pregnancy can do just that.

Ethanol, the substance found in liquor, beer, and other alcoholic beverages, is often the first thing that people think of when the term "alcohol" is mentioned. Ethanol is also used as an antiseptic, a solvent, and as a fuel. While images of parties and celebrations come to mind, ethanol can be widely abused and severely toxic if consumed in excess. Ethanol consumption can have especially dire consequences on the most fragile of all life, a human fetus. Fetal alcohol syndrome (FAS) is one of the

leading causes of preventable birth defects in the United States. In fact, in 2015, the Centers for Disease Control and Prevention (CDC) stated that no amount of alcohol is safe to consume at any time during pregnancy. Drinking during pregnancy can lead to a number of neurological problems in newborns, as you will learn in the Chemistry in Action "Fetal Alcohol Syndrome: Ethanol as a Toxin" at the end of this chapter.

But do not let the dangers of ethanol consumption fool you; *alcohols* are arguably the most important functional group family in organic chemistry and are present in a large number of organic compounds of biological importance. Alcohols are versatile in organic synthesis; they can be used as a starting material to prepare almost any other functional group family, such as the alkyl halides, ketones, aldehydes, and carboxylic acids. In this chapter, we will concentrate on the functional groups, like alcohols, that contain single bonds to the electronegative atoms oxygen, sulfur, and the halogens.

14.1 Alcohols, Phenols, and Ethers

Learning Objectives:

- Describe the structural differences between alcohols, phenols, and ethers.
- Explain why alcohols have higher boiling points than compounds of similar molecular mass.

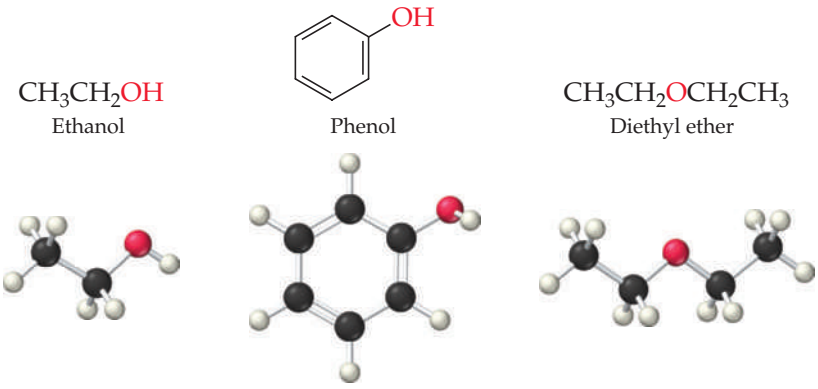
CONCEPTS TO REVIEW Recall from Table 12.3 that **R** is used to symbolize an organic substituent; it is the **R**est of the molecule.

An **alcohol** is a compound that has an —OH group (a *hydroxyl group*) bonded to a tetrahedral, carbon atom; a **phenol** has an —OH group bonded directly to an aromatic, benzene-like ring; and an **ether** has two carbon groups (whether alkyl, aromatic or a combination of both) bonded to the same oxygen atom.

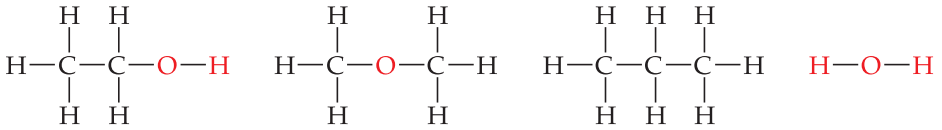
Alcohol A compound that has an —OH group bonded to a saturated, carbon atom, R—OH.

Phenol A compound that has an —OH group bonded directly to an aromatic, benzene-like ring, Ar—OH.

Ether A compound that has an oxygen atom bonded to two organic groups, R—O—R.



Compounds in all three families can be thought of as organic relatives of water in which one or both of the H_2O hydrogens have been replaced by an organic substituent. The structural similarity between alcohols and water also leads to similarities in many of their physical properties. For example, compare the boiling points of ethanol, dimethyl ether, propane, and water.

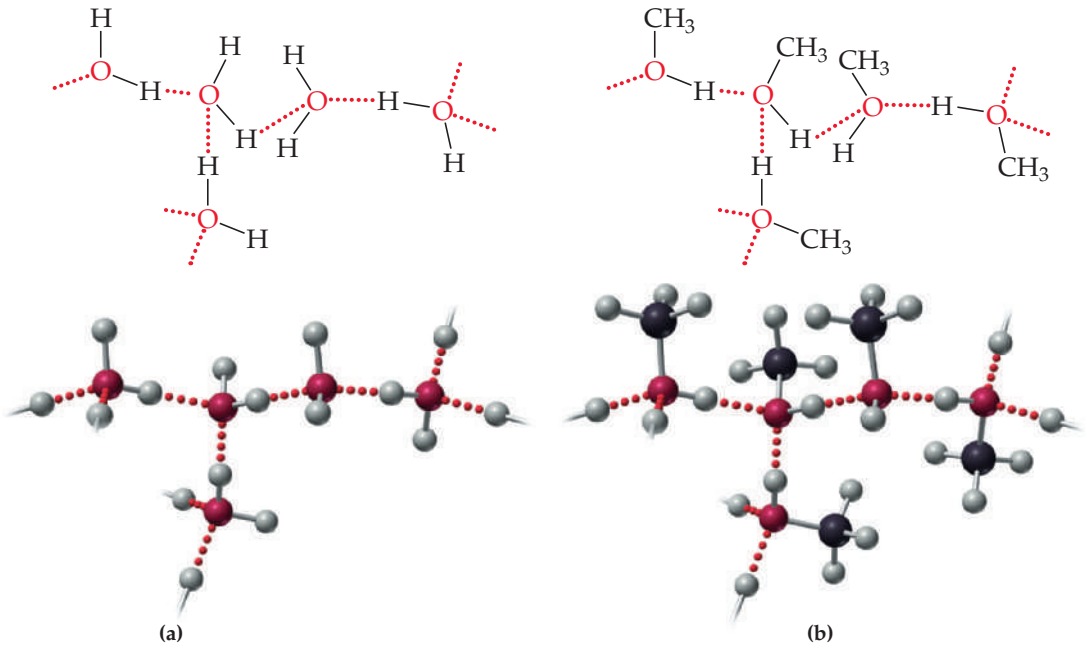


Ethanol, dimethyl ether, and propane have similar molecular masses, yet ethanol boils more than 100 °C (373 K) higher than the other two. In fact, the boiling point of ethanol is close to that of water. Why should this be?

The high boiling point of water is due to hydrogen bonding—the attraction between a lone pair of electrons on the electronegative oxygen in one molecule and the positively polarized —OH hydrogen on another molecule. This attraction holds molecules

Review the effect of hydrogen bonding on boiling point in Section 8.2.

together and prevents their easy escape into the vapor phase. In a similar manner, hydrogen bonds form between alcohol (or phenol) molecules (Figure 14.1). Alkanes and ethers do not have hydroxyl groups, however, and cannot form hydrogen bonds. As a result, they have lower boiling points. Ethers, with the exception of their polarity, resemble alkanes in many of their chemical and physical properties.

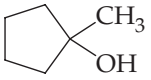


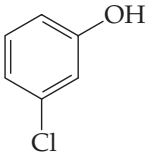
▶ Figure 14.1
The formation of hydrogen bonds in water (a) and in alcohols (b).
Because of the hydrogen bonds (shown in red), the easy escape of molecules into the vapor phase is prevented, resulting in high boiling points.

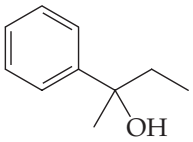
PROBLEM 14.1

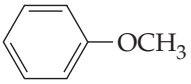
Identify each of the following compounds as an alcohol, a phenol, or an ether:

(a) $CH_3CH_2CHCH_3$ (OH)

(b) 

(c) 

(d) 

(e) 

(f) $(CH_3)_2CH—O—CH_2CH_3$

PROBLEM 14.2

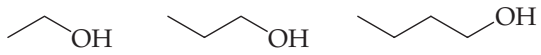
Ethers have some slight solubility in water. Explain this using the concept of hydrogen bonding.

14.2 Naming Alcohols

Learning Objectives:

- Write systematic names for simple alcohols.
- Draw the structure of an alcohol given its name, in both condensed and line structure format.
- Classify an alcohol as primary, secondary, or tertiary.
- Define and identify a glycol.

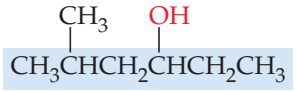
Common names of many alcohols containing one hydroxyl (—OH) group identify the alkyl group and then add the word *alcohol*. Thus, the two-carbon alcohol is ethyl alcohol, the three-carbon alcohol is propyl alcohol, and so on:



Ethyl alcohol Propyl alcohol Butyl alcohol

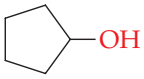
The International Union of Pure and Applied Chemistry (IUPAC) system names alcohols in a similar manner to that used for alkanes (Section 12.6) but uses index number of the hydroxyl (—OH) group and the *-ol* ending for the parent compound.

STEP 1: Name the parent compound. Find the longest chain that has the hydroxyl substituent attached, and name the chain by replacing the *-e* ending of the corresponding alkane with *-ol:*



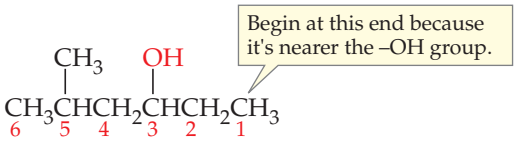
Name as a *hexanol*—a six-carbon chain containing a hydroxyl group.

If the compound is a cyclic alcohol, add the *-ol* ending to the name of the parent cycloalkane. For example,

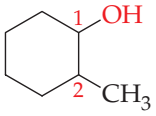


Cyclopentanol

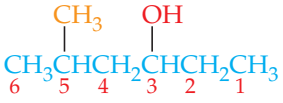
STEP 2: Number the carbon atoms in the main chain. The carbon bearing the —OH must be assigned the lowest index number possible when numbering the chain. Begin at the end nearer the hydroxyl group, ignoring the location of other substituents for now:



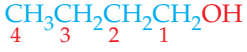
In a cyclic alcohol, begin with the carbon that bears the —OH group and proceed in a direction that gives the other substituents the lowest possible numbers:



STEP 3: Write the name, placing the number that locates the hydroxyl group immediately before the "ol" ending of the alcohol name. Number all other substituents according to their positions, and list them alphabetically. Note that in a cyclic alcohol, it is not necessary to use the number 1 to specify the location of the —OH group:

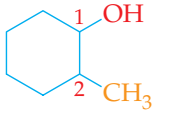


5-Methylhexan-3-ol



Butan-1-ol

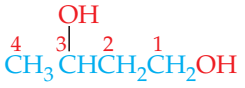
4-Chloro-6-methylheptan-2-ol



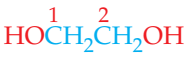
2-Methylcyclohexanol

Diols and Glycols

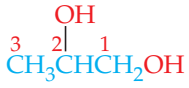
Dialcohols, or *diols,* are compounds that contain two hydroxy groups in the same molecule. The IUPAC names these alcohols by attaching the ending *diol* to the alkane name. The names will contain two numbers indicating the carbons bonded to the two different —OH groups, with the numbering starting at the end closest to one of the —OH groups:



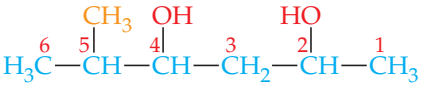
Butane-1,3-diol



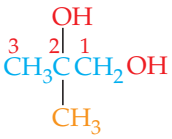
Ethane-1,2-diol
(Ethylene glycol)



Propane-1,2-diol
(Propylene glycol)



5-Methylhexane-2,4-diol
(*not 2-Methyl-3,5-hexanediol*)



2-Methylpropane-1,2-diol
(Isobutylene glycol)

Vicinal Referring to groups on adjacent carbons.

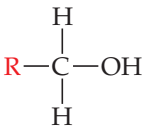
Glycol A dialcohol, or diol, having the two —OH groups on adjacent carbons.

When the two —OH groups are on adjacent carbons (commonly called **vicinal** diols), diols are often referred to by the common name **glycols.** Strictly speaking, any diol having the —OH groups on adjacent carbons can be called a glycol, but the term "glycol" is preferably reserved for two compounds, ethylene glycol and propylene glycol. Ethylene glycol is the simplest glycol. Propylene glycol is often used as a solvent for medicines that need to be inhaled or rubbed onto the skin, and, as noted in the previous section, it is also used as a replacement for ethylene glycol in antifreeze. Since glycols are commonly prepared from alkenes, the usual convention for naming simple glycols is to use the name of the alkene from which the diol is made, with the name "glycol" added.

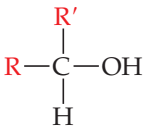
Classification of Alcohols

Alcohols are classified as primary, secondary, or tertiary according to the number of carbon substituents bonded to the hydroxyl-bearing carbon. This classification is useful, as many of the reactions of alcohols are a function of their substitution. Alcohols with one substituent are said to be *primary* (1°), those with two substituents are *secondary* (2°), and those with three substituents are *tertiary* (3°). The substituent groups need not be the same, so we will use the representations R, R′ (read it *R prime*), and R″ (read *R double prime*) to indicate different substituent groups.

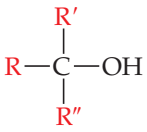
This same classification is used to describe the carbons in alkanes; see Section 12.6.



A primary alcohol
(one R group on
OH-bearing carbon)



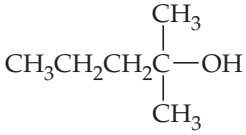
A secondary alcohol
(two R groups on
OH-bearing carbon)



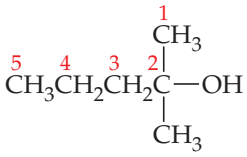
A tertiary alcohol
(three R groups on
OH-bearing carbon)

Worked Example 14.1 Naming Organic Compounds: Alcohols

Give the systematic name of the following alcohol, and classify it as primary, secondary, or tertiary:



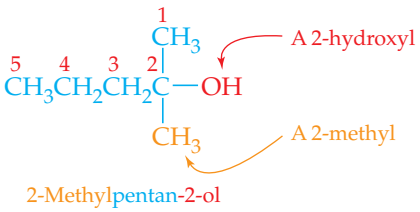
ANALYSIS First, identify the longest carbon chain, and number the carbon atoms beginning at the end nearer the —OH group. The longest chain attached to the —OH has five carbon atoms:



Name as a pentanol.

Next, identify and number the hydroxyl group and the substituents. Finally, write the name of the compound.

SOLUTION



Since the —OH group is bonded to a carbon atom that has three alkyl substituents, this is a tertiary alcohol.

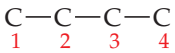
Worked Example 14.2 Drawing Organic Compounds: Alcohols

Draw the structures of (a) 2,3-dimethylbutan-2-ol and (b) 3-ethylcyclopentanol. Classify each as primary, secondary, or tertiary.

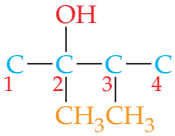
ANALYSIS For both, begin by determining the longest carbon chain; number the carbon atoms and put groups on appropriate atoms. If no index number is given for the —OH group, it is assumed to be on the first carbon.

SOLUTION

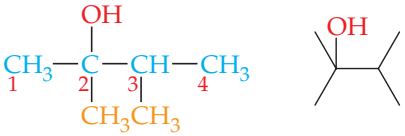
(a) This alcohol is a butanol, so it has a longest chain of four carbons:



Since it is a butan-2-ol, the —OH group is bonded to carbon 2; the methyl groups are bonded to carbons 2 and 3:



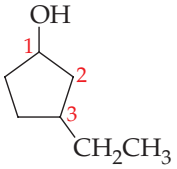
Filling out the remaining Hs gives us the following (in both condensed and line structure formats):



2,3-dimethylbutan-2-ol

Since the —OH group is bonded to a carbon atom that has three other carbons bonded to it, this is a tertiary alcohol.

(b) The name tells us that the —OH group is bonded to a cyclopentane ring; since no position number is given, the —OH group is on carbon 1. Putting in the ethyl group on carbon 3 gives us the following:



Since the —OH group is bonded to a carbon atom that has two other carbons bonded to it, this is a secondary alcohol.

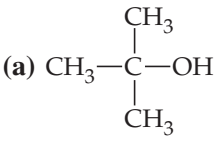
PROBLEM 14.3

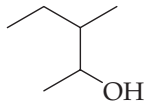
Draw structures corresponding to the following names:

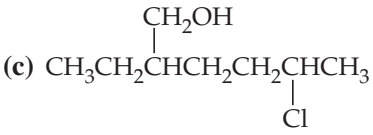
(a) 3-Methylhexan-1-ol
(b) 1-Methyl-3-propylcyclopentanol
(c) 2,2-Dimethylhexan-3-ol
(d) Heptan-3-ol
(e) 2,3-Diethylcyclohexanol

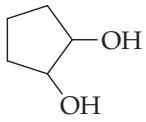
PROBLEM 14.4

Give systematic names for the following compounds:

(a) 

(b) 

(c) 

(d) 

PROBLEM 14.5

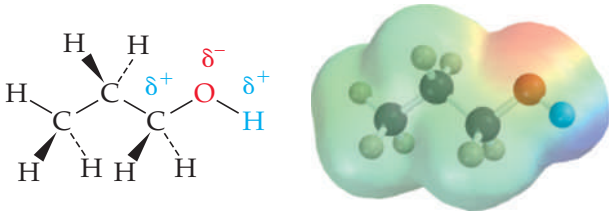
Identify each alcohol in Problems 14.3 and 14.4 as primary, secondary, or tertiary.

14.3 Properties of Alcohols

Learning Objectives:

- Describe the properties of alcohols.
- Describe hydrophobic and hydrophilic alcohols.

Alcohols are much more polar than hydrocarbons because of the electronegative oxygen atom that withdraws electrons from the neighboring atoms. As a result, both its polarity and ability to hydrogen bond have a strong influence on alcohol properties.

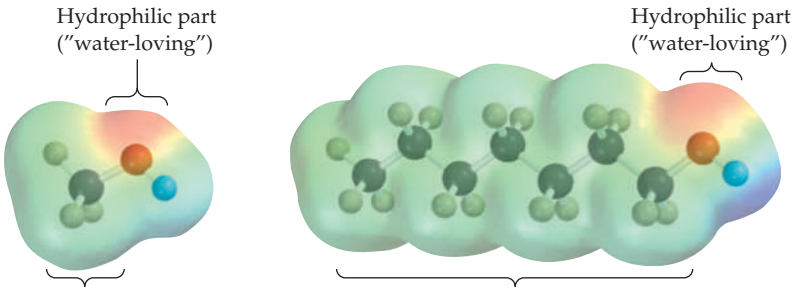


1-Propanol

Straight-chain alcohols with up to 12 carbon atoms are liquids, and each boils at a considerably higher temperature than the related alkane. Alcohols containing one to three carbons, such as methanol, ethanol, and propanol, resemble water in their solubility behavior. Methanol and ethanol are miscible with water, with which they can form hydrogen bonds, and these two alcohols can dissolve small amounts of many ionic compounds. Both are also miscible with many organic solvents because of the presence of the carbon group.

From a water solubility standpoint, all alcohols can be thought of as having two distinct parts: a "water-loving," or *hydrophilic,* part (the —OH) and a "water-fearing," or *hydrophobic,* part (the hydrocarbon chain attached to the alcohol carbon). The larger the hydrocarbon part is, such as in heptan-1-ol, the more alkane-like the alcohols are and the less water-soluble they become. Heptan-1-ol is nearly insoluble in water and cannot dissolve ionic compounds but does dissolve alkanes. In order for water and another liquid to be miscible, water molecules must be able to entirely surround a mole-

cule of the other liquid; the larger the hydrophobic (or alkane-like) portion of an alcohol molecule is, the harder this is to accomplish.



Methanol has a small hydrophobic part ("water-fearing") and is therefore water-like.

Heptan-1-ol has a large hydrophobic part ("water-fearing") and is therefore alkane-like.

$CH_3—OH$ $CH_3CH_2CH_2CH_2CH_2CH_2CH_2—OH$

Alcohols with two or more —OH groups (diols or triols) can form more than one hydrogen bond. Therefore, they are higher boiling and more water-soluble than similar alcohols with only one —OH group. Compare butan-1-ol and butane-1,4-diol, for example:

$CH_3CH_2CH_2CH_2OH$ (Butan-1-ol): bp 117 °C (390 K), water solubility of 7 g/100 mL.

$HOCH_2CH_2CH_2CH_2OH$ (Butane-1,4-diol): Added –OH raises bp to 230 °C (503 K) and gives miscibility with water

A general rule of thumb for solubility of uncharged organic molecules containing oxygens is the following: organic molecules having a carbon to oxygen ratio of 1:1 to 3:1 are soluble in water (such as methanol, ethanol, and propanol), while those having ratios of 5:1 and greater are insoluble (molecules with a 4:1 ratio have slight solubility).

Many alcohols have common uses, both commercially and medically. Table 14.1 lists six of them, along with their properties and uses.

LOOKING AHEAD In Chapters 17, 18, and 23, we will revisit this concept of hydrophilic and hydrophobic when we discuss carboxylic acids, proteins, and lipids, respectively.

PROBLEM 14.6

Rank the following according to boiling point, highest to lowest:

(a) $CH_3CH_2CH_2OH$ **(b)** $CH_3CH_2(OH)CH_2OH$

(c) $CH_3CH_2CH_3$ **(d)** $CH_2(OH)CH(OH)CH_2OH$

PROBLEM 14.7

For each of the following molecules, (i) redraw using line structure format, (ii) identify its hydrophobic and hydrophilic parts, and (iii) predict its solubility in water.

(a) $CH_3(CH_2)_{10}CH_2OH$ **(b)** $CH_3CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_3$ **(c)** $CH_3CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_2OH$

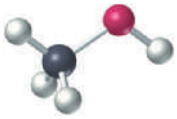
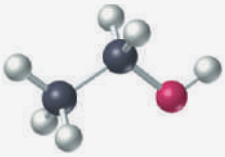
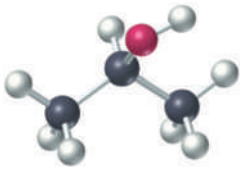
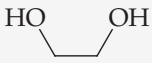
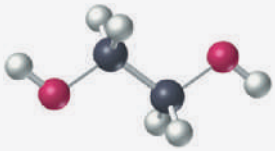
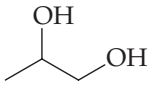
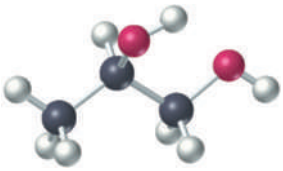
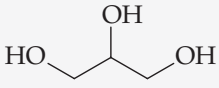
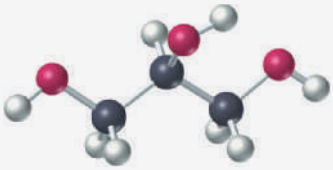
14.4 Reactions of Alcohols

Learning Objectives:

- Predict the products obtained upon dehydration of an alcohol.
- Predict the oxidation products of a primary, secondary, and tertiary alcohol.

Alcohols are one of the most important classes of organic molecules because of their versatility in the preparation of other organic molecules. We will examine two of the more important reactions of alcohols here: *dehydration* (an elimination reaction; see Section 13.5) and *oxidation*.

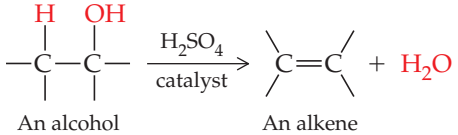
Table 14.1 Some Common Alcohols and Their Uses

Alcohol	Structure	Common Properties and Applications
Methanol (Methyl Alcohol) CH_3OH		• Commonly known as *wood alcohol* • Made by reaction of carbon monoxide with hydrogen • Used industrially as a solvent; also a starting material for preparing formaldehyde ($H_2C{=}O$) (Chapter 15) • Colorless, miscible with water • Toxic to humans when ingested or inhaled
Ethanol (Ethyl Alcohol) CH_3CH_2OH		• One of the oldest known organic chemicals • 100% ethanol is known as *absolute alcohol* • Formed by fermentation of starches or complex sugars • Alcohol present in all alcoholic beverages • A central nervous system (CNS) depressant • Toxic to a developing fetus (see the Chemistry in Action feature "Fetal Alcohol Syndrome: Ethanol as a Toxin," p. 501) • Ethanol for nonconsumption is *denatured* by addition of a toxic substance (like methanol); denatured alcohol is exempt from the tax applied to the sale of consumable alcohol • Industrially made by hydration of ethene (Chapter 13) • Gasohol (or E85) is a blend of ethanol and gasoline and is a desirable fuel as it produces fewer air pollutants
Isopropanol (Isopropyl Alcohol; Propan-2-ol) 		• Also known as *rubbing alcohol* • Used as a 70% mixture with water for rubdowns; cools the skin through evaporation and causes pores to close • Used as a solvent for medicines, as a sterilant for instruments, and as a skin cleanser before drawing blood or giving injections • Not as toxic as methanol but much more toxic than ethanol
Ethane-1,2-diol (Ethylene glycol) 		• A *diol* (meaning it has two —OH groups) • A slightly sweet, colorless liquid that is miscible with water and insoluble in nonpolar solvents • Originally used as an engine antifreeze and coolant; now is primarily used to manufacture plastic films and fibers • A CNS depressant • Lethal to humans, dogs, and cats at doses of about 1.5–3 mL/kg of body weight
Propane-1,2-diol (Propylene Glycol) 		• A diol • Essentially nontoxic; it is used to replace ethane-1,2-diol in automobile antifreezes and coolants • Used as a moisturizer, solvent, and preservative in food products • Used in various edible items such as coffee-based drinks, liquid sweeteners, ice cream, whipped dairy products, and soda. • One of the major "e-liquid" ingredients in electronic cigarettes • Used as a solvent in many pharmaceutical oral, injectable, and topical formulations
Propane-1,2,3-triol (Glycerol) 		• Also known as *glycerin* • A *triol* (three —OH groups in the molecule). • A sweet tasting, colorless liquid that is miscible with water. • Nontoxic, useful in making candy and prepared foods. • Also used in cosmetics as a moisturizer, in plastics manufacturing, in antifreeze and shock-absorber fluids. • Provides the structural backbone of animal fats and vegetable oils (Chapter 23)

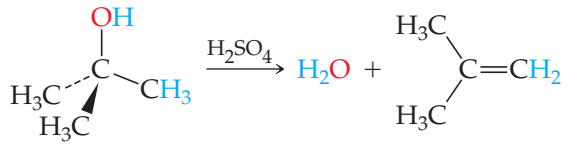
Dehydration

Dehydration The loss of water from an alcohol to yield an alkene.

Alcohols undergo loss of water **(dehydration)** upon treatment with a strong acid catalyst; the reaction is typically driven to completion by heating. The —OH group is lost from one carbon and an —H is lost from an adjacent carbon to yield an alkene product and water.

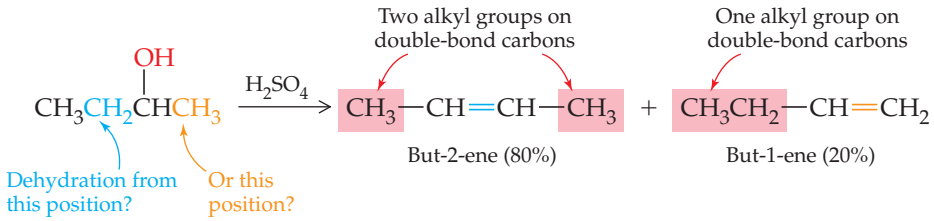


For example,



tert-Butyl alcohol 2-Methylpropene

A mixture of products forms when more than one alkene results from dehydration. A good rule of thumb is that the major product is the more substituted alkene, or the alkene that has the greater number of alkyl groups directly attached to the double-bond carbons. For example, when the dehydration of butan-2-ol is carried out in the laboratory, a mixture containing 80% but-2-ene and only 20% but-1-ene is obtained:

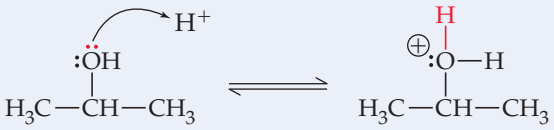


MASTERING REACTIONS

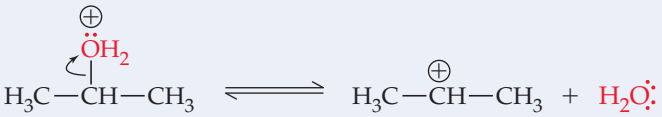
How Eliminations Occur

We have previously discussed the mechanism by which addition reactions occur (p. 456); let us now examine what is essentially the reverse of this reaction, an *elimination.* Eliminations can occur in one of two ways: as a one-step process (known as an *E2 reaction*) or as a two-step process (known as an *E1 reaction*). We will concentrate our efforts here on the latter, the E1 process.

When an alcohol is treated with a strong mineral acid (such as H_2SO_4), the first thing that happens is that the oxygen atom of the alcohol protonates in an equilibrium process:

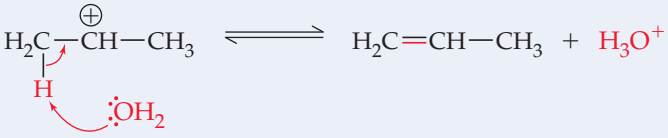


Notice that the —OH has been converted into what is essentially a water molecule. This portion can then leave, and what remains is a carbocation:



The favorability of this process is a direct function of the stability of the carbocation formed (see Mastering Reactions: How Addition Reactions Occur, p. 456). As a result, 3° alcohols will undergo this process more readily than 2° alcohols, and 1° alcohols undergo the process slowly at best.

The carbocation can then readily undergo loss of H^+ to form the alkene:



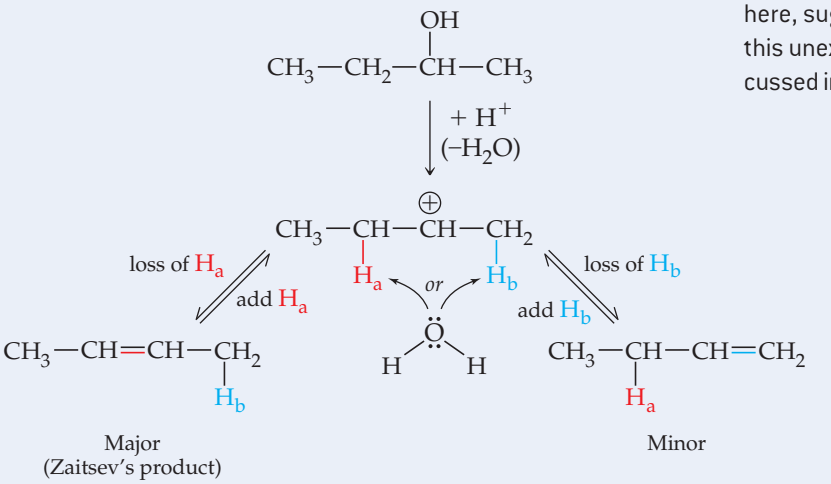
Here, water acting as a Lewis base can remove a hydrogen directly adjacent to the carbocation, forming the alkene. This sets up an equilibrium between the protonated alcohol, the carbocation, and the alkene. Recall that the reaction is typically heated; since the alkene formed has a lower boiling point than the alcohol, it simply escapes from the heated mixture, causing the reaction to proceed to the right (Le Châtelier's principle, Section 7.9).

This back and forth process may occur many times before the alkene is able to escape from the reaction, which helps to explain another observation: If it is possible to form more than one alkene isomer, the one having the more substituted double

(*continued*)

bond will be favored. This observation is known as *Zaitsev's Rule.* Consider the dehydration of butan-2-ol; after the initial formation of the carbocation, there are two possible eliminations that can then occur (discussed in the following text).

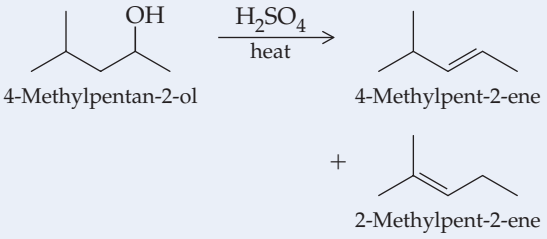
Each alkene is in equilibrium with the carbocation, but the more substituted alkene (here, but-2-ene) is thermodynamically more stable than the less substituted alkene. Once formed, it will be less likely to re-form the carbocation than the less substituted alkene will. Thus, the more substituted alkene accumulates, becoming the major product of the reaction, while the less substituted alkene is the minor product.



MR Problem 14.1 We discussed in Chapter 13 that H_2SO_4 catalyzes the addition of water to alkenes to form alcohols. In this chapter, however, we saw that H_2SO_4 is also used to dehydrate alcohols to make alkenes. Looking at the two mechanisms, explain with drawings what role sulfuric acid plays in both and why its role in both makes sense.

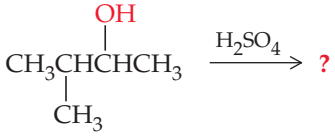
MR Problem 14.2 Provide the mechanism for the dehydration of 1-methylcyclopentanol.

MR Problem 14.3 When 4-methylpentan-2-ol is heated in H_2SO_4, two alkenes are formed in significant amounts: 4-methylpent-2-ene, the expected product and 2-methylpent-2-ene, the unexpected product. Using just the mechanism you learned here, suggest a reasonable explanation for the formation of this unexpected alkene. (Hint: Think about the equilibria discussed in this feature.)

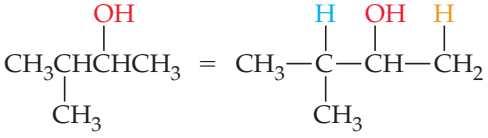


Worked Example 14.3 Organic Reactions: Dehydration

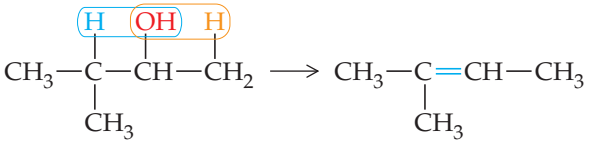
What products would you expect from the following dehydration reaction? Which product will be major and which will be minor?

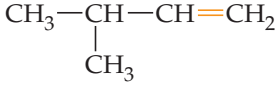


ANALYSIS Find the hydrogens on carbons next to the OH-bearing carbon, and rewrite the structure to emphasize these hydrogens:



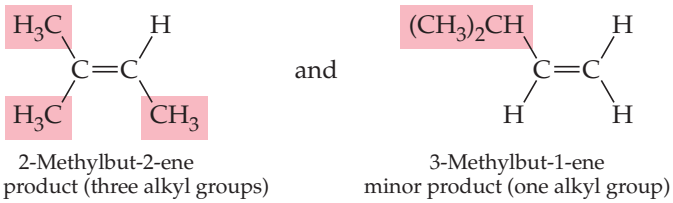
Then, remove the possible combinations of —H and —OH, drawing a double bond each —H and —OH could be removed:



and 

Finally, determine which alkene has the larger number of alkyl substituents on its double-bond carbons and is therefore the major product.

SOLUTION

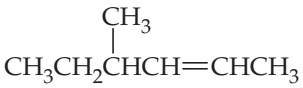


2-Methylbut-2-ene
major product (three alkyl groups)

3-Methylbut-1-ene
minor product (one alkyl group)

Worked Example 14.4 Organic Reactions: Dehydration

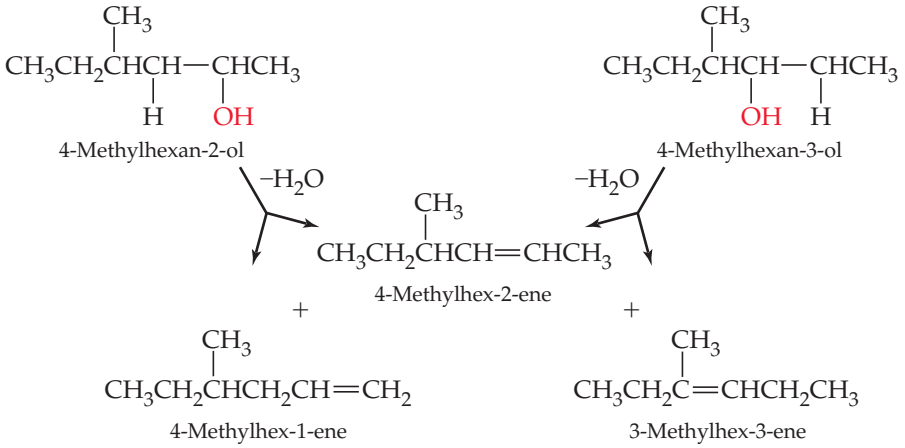
Which alcohol(s) yield 4-methylhex-2-ene on dehydration? Are there any other alkenes that arise from dehydration of these alcohols?



4-Methylhex-2-ene

ANALYSIS The double bond in the alkene is formed by removing —H and —OH from adjacent carbons of the starting alcohol. This removal occurs in two possible ways, depending on which carbon is bonded to the —OH and to the —H.

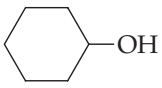
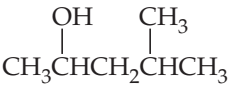
SOLUTION



Dehydration of 4-Methylhexan-2-ol yields 4-Methylhex-2-ene as the major product, along with 4-Methylhex-1-ene. Dehydration of 4-Methylhexan-3-ol also gives 4-Methylhex-2-ene but as the minor product, along with 3-Methylhex-3-ene as the major product.

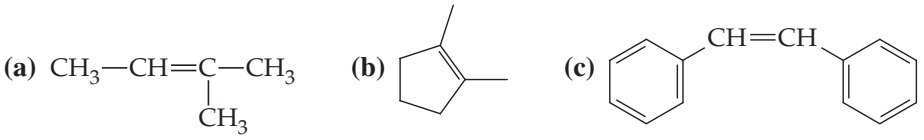
PROBLEM 14.8

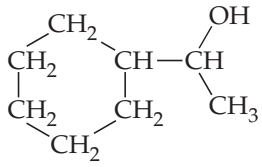
What alkenes might be formed by dehydration of the following alcohols? If more than one product is possible in a given case, indicate which is major.

(a) $CH_3CH_2CH_2OH$ **(b)**  **(c)** 

PROBLEM 14.9

What alcohols yield the following alkenes as the major product on dehydration?





KEY CONCEPT PROBLEM 14.10

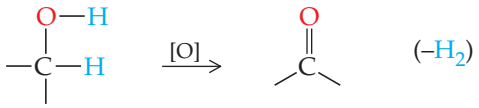
Two different alkenes will be formed by dehydration of the alcohol shown in the margin. Draw their structures using both condensed and line structure format, and label each as being either the major or minor product.

Oxidation

Primary and secondary alcohols are converted into *carbonyl*-containing compounds on treatment with an oxidizing agent. A **carbonyl group** (pronounced car-bo-*neel*) is a functional group that has a carbon atom joined to an oxygen atom by a double bond, C=O. In a laboratory, many different oxidizing agents can be used—potassium permanganate ($KMnO_4$), potassium dichromate ($K_2Cr_2O_7$), or even oxygen gas in some cases—and it often does not matter which specific reagent is chosen. Thus, we will simply use the symbol [O] to indicate a generalized oxidizing agent.

Recall that an *oxidation* is defined in inorganic chemistry as the loss of one or more electrons by an atom, and a *reduction* as the gain of one or more electrons. These terms have the same meaning in organic chemistry, but because of the size and complexity of organic compounds, a more general distinction is made when discussing organic molecules. An *organic oxidation* is one that increases the number of C—O bonds and/or decreases the number of C—H bonds. (Note that in determining whether or not an organic oxidation has taken place, a C=O is counted as *two* C—O bonds. Thus, whenever C—O in a molecule changes to a C=O bond, the number of C—O bonds has increased, and therefore an oxidation has taken place.) Conversely, an *organic reduction* is one that decreases the number of C—O bonds and/or increases the number of C—H bonds.

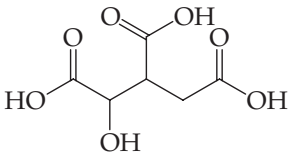
In the oxidation of an alcohol, two hydrogen atoms are removed from the alcohol and converted into water during the reaction by the oxidizing agent [O]. One hydrogen comes from the —OH group, and the other hydrogen from the carbon atom bonded to the —OH group. In the process, a new C—O bond is formed and a C—H bond is broken:



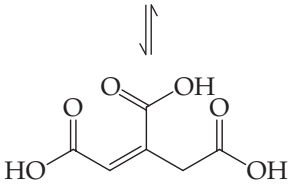
An alcohol — A carbonyl compound

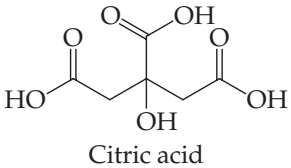
Different kinds of carbonyl-containing products are formed, depending on the structure of the starting alcohol and on the reaction conditions. Primary alcohols (RCH_2OH) are converted first into *aldehydes* (RCH=O) if carefully controlled

In Section 21.8, we will see the conversion of citric acid to isocitric acid, a key step in the citric acid cycle. This reaction, which looks simply like an —OH group moving from one carbon to the next, actually occurs via an enzyme-catalyzed dehydration reaction followed by readdition of water to the alkene formed.



Isocitric acid



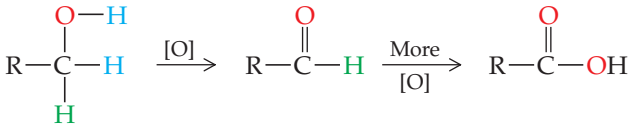


Citric acid

Carbonyl group The C=O functional group.

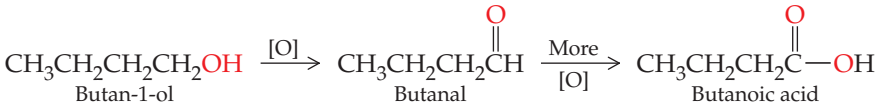
Review redox reactions in Section 5.6.

conditions are used; then, if an excess of oxidant is present, aldehydes are further converted into *carboxylic acids* (pronounced car-box-*ill*-ic) (RCO_2H):



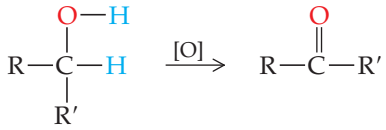
A primary alcohol — An aldehyde — A carboxylic acid

For example,



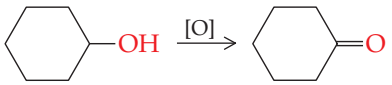
Butan-1-ol — Butanal — Butanoic acid

Secondary alcohols (R_2CHOH) are converted into *ketones* ($R_2C{=}O$) on treatment with oxidizing agents; further oxidation does not normally occur:



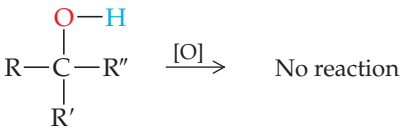
A secondary alcohol — A ketone

For example,



Cyclohexanol — Cyclohexanone

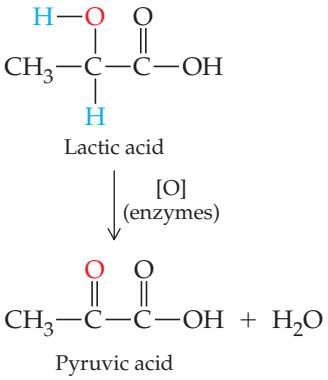
Tertiary alcohols do not normally react with oxidizing agents because they do not have a hydrogen on the carbon atom to which the —OH group is bonded:



A tertiary alcohol

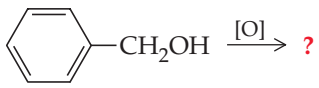
In Section 15.5, we will discuss the oxidation of aldehydes to make carboxylic acids. Carboxylic acids will be discussed in Chapter 17.

In Chapter 22, we will see that alcohol oxidations are critically important steps in many key biological processes. When lactic acid builds up in tired, overworked muscles, for example, the liver removes it by oxidizing it to pyruvic acid. Our bodies, of course, do not use $K_2Cr_2O_7$ or $KMnO_4$ for the oxidation; instead, they use specialized, highly selective enzymes to carry out this chemistry. Regardless of the details, though, the net chemical transformation is the same whether carried out in a laboratory flask or in a living cell.



Worked Example 14.5 Organic Reactions: Oxidation

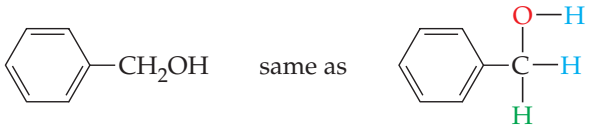
What is the product of the following oxidation reaction?



Benzyl alcohol

Recall from Table 12.2 that a commonly used abbreviation for the aromatic group is Ph. Thus benzyl alcohol could also have been written as $PhCH_2OH$.

ANALYSIS The starting material is a primary alcohol, so it will be converted first to an aldehyde and then to a carboxylic acid. To find the structures of these products, first redraw the structure of the starting alcohol to identify the hydrogen atoms on the hydroxyl-bearing carbon:

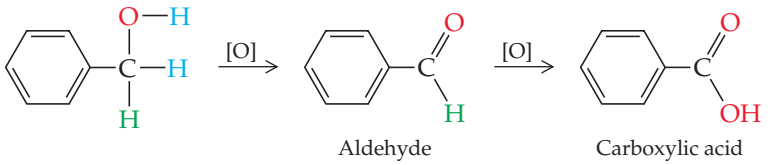


Next, remove two hydrogens, one from the —OH group and one from the hydroxyl-bearing carbon. In their place, make a C=O double bond. This is the aldehyde product that forms initially. Finally, convert the aldehyde to a carboxylic acid by replacing the hydrogen in the —CH=O group with an —OH group.

—continued on next page

—continued from previous page

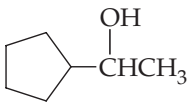
SOLUTION



Aldehyde Carboxylic acid

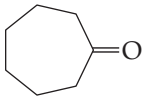
PROBLEM 14.11

What products would you expect from oxidation of the following alcohols?

(a) $CH_3CH_2CH_2OH$ **(b)** $CH_3\overset{\overset{OH}{|}}{C}HCH_2CH_2CH_3$ **(c)** 

PROBLEM 14.12

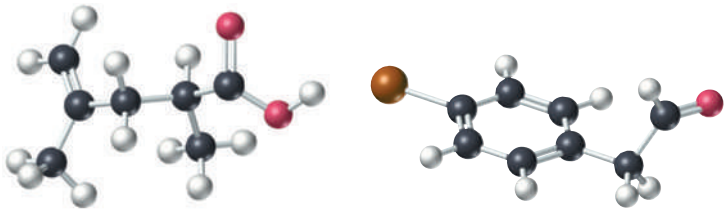
From what alcohols might the following carbonyl-containing products have been made?

(a) $CH_3\overset{\overset{O}{\|}}{C}CH_3$ **(b)** 

(c) $CH_3\overset{\overset{CH_3}{|}}{C}H\overset{\overset{O}{\|}}{C}H_2COH$

KEY CONCEPT PROBLEM 14.13

From what alcohols might the following carbonyl-containing products have been made (red = O, reddish-brown = Br)?



(a) **(b)**

14.5 Phenols

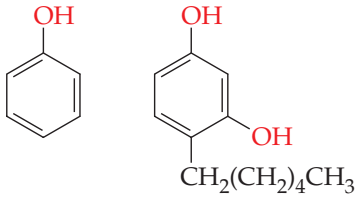
Learning Objective:

- Identify a phenol.

The word *phenol* is the name for both a specific compound (hydroxybenzene, C_6H_5OH) as well as a family of compounds. Phenol itself, formerly called carbolic acid, is a medical antiseptic that was first used by Joseph Lister in 1867. Lister showed that the occurrence of postoperative infection dramatically decreased when phenol was used to cleanse the operating room and the patient's skin. Because phenol numbs the skin, it also became popular in topical drugs for pain and itching and in treating sore throats.

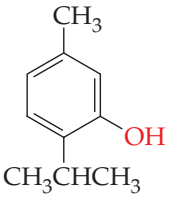
The medical use of phenol is now restricted because it can cause severe skin burns and has been found to be toxic, both by ingestion and by absorption through the skin. Only solutions containing less than 1.5% phenol or lozenges containing a maximum of 50 mg of phenol are now allowed in nonprescription drugs. Many mouthwashes and

throat lozenges contain alkyl-substituted phenols such as thymol as active ingredients for pain relief. The presence of an alkyl group lowers the absorption of the compound through skin (among other things), rendering alkyl-substituted phenols less toxic than phenol itself.



Phenol

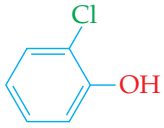
4-Hexylresorcinol
(a topical anesthetic)



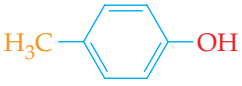
Thymol
(a topical anesthetic; occurs naturally in the herb thyme)

Some other alkyl-substituted phenols such as the cresols (methylphenols) are common as *disinfectants* in hospitals and elsewhere. In contrast to an *antiseptic*, which safely kills microorganisms on living tissue, a disinfectant should be used only on inanimate objects. The germicidal properties of phenols can be partially explained by their ability to disrupt the permeability of cell walls of microorganisms.

Phenols are usually named with the ending *-phenol* rather than *-benzene* even though the —OH group is bonded to a benzene ring. For example,



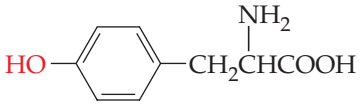
ortho-Chlorophenol
(2-Chlorophenol)



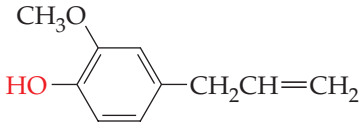
para-Methylphenol
(4-Methylphenol)

The properties of phenols, like those of alcohols, are influenced by the presence of the electronegative oxygen atom and by hydrogen bonding. Most phenols are water-soluble to some degree and have higher melting and boiling points than similarly substituted alkylbenzenes. They are generally less soluble in water than alcohols are, since the benzene ring is very hydrophobic.

Biomolecules that contain a hydroxyl-substituted benzene ring and are considered phenols include the amino acid tyrosine, as well as many other compounds.

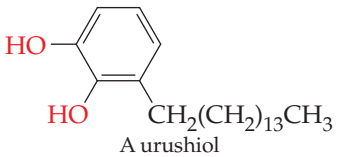


Tyrosine
(an *amino* acid)



Eugenol
(in cloves, bananas, and other fruits; used for toothache pain)

▲ Careful! The urushiol in this poison ivy plant causes severe skin rash.



A urushiol
(skin irritant in poison ivy)

PROBLEM 14.14

Draw structures for the following:

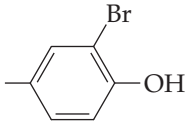
(a) 2,4-Dinitrophenol

(b) *m*-Ethylphenol

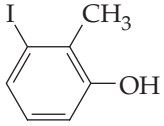
PROBLEM 14.15

Name the following compounds:

(a)



(b)



14.6 Acidity of Alcohols and Phenols

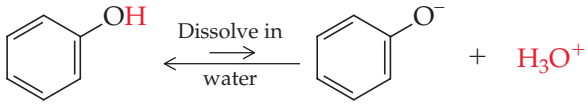
Learning Objective:

- Explain why alcohols and phenols are weak acids.

Alcohols and phenols, because of the positively polarized O—H hydrogen, dissociate slightly in aqueous solution and establish an equilibria between their neutral and anionic forms:

$$CH_3CH_2OH \underset{\text{water}}{\overset{\text{Dissolve in}}{\rightleftharpoons}} CH_3CH_2O^- + H_3O^+$$

An alcohol



A phenol

Alcohols, such as methanol and ethanol, are about as acidic as water itself (Sections 10.3 and 10.4), with K_a values near 10^{-15}. By comparison, acetic acid has a K_a of 10^{-5}. In fact, both dissociate so little in water that their aqueous solutions are neutral (pH 7). Thus, an **alkoxide ion** (RO^-), or the anion of an alcohol, is as strong a base as a hydroxide ion, OH^-. An alkoxide ion is produced by reaction of an alkali metal with an alcohol, just as a hydroxide ion is produced by reaction of an alkali metal with water. For example,

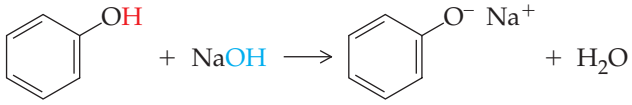
Alkoxide ion The anion resulting from the removal of the H from an alcohol, RO^-.

$$\underset{\text{Water}}{2H_2O} + 2Na \longrightarrow \underset{\text{Sodium hydroxide}}{2\,Na^+\,{}^-OH} + H_2$$

$$\underset{\text{Methanol}}{2CH_3OH} + 2Na \longrightarrow \underset{\text{Sodium methoxide}}{2\,Na^+\,{}^-OCH_3} + H_2$$

Recall from Section 10.7 what K_a refers to and what its magnitude means.

In contrast to alcohols, phenols are about 10,000 times more acidic than water. Phenol itself, for example, has $K_a = 1.0 \times 10^{-10}$. This acidic property means that phenols react with dilute aqueous sodium hydroxide to give a phenoxide ion. (Alcohols do NOT react in this way with sodium hydroxide.)



Phenol Sodium phenoxide

14.7 Ethers

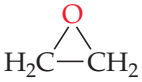
Learning Objectives:

- Identify an ether.
- Distinguish between an ether and an alcohol.

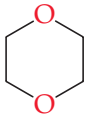
Simple ethers—compounds with two organic groups bonded to the same oxygen atom (R—O—R′)—are named by identifying the two organic groups and adding the word *ether*. (The compound frequently referred to simply as "ether" is actually diethyl ether.)

$CH_3—O—CH_3$	$CH_3—O—CH_2CH_3$	$CH_3CH_2—O—CH_2CH_3$
Dimethyl ether	Ethyl methyl ether	Diethyl ether
(bp = −24.5 °C (248.5 K))	(bp = −10.8 °C (262.2 K))	(bp = 34.5 °C (307.5 K))

Compounds that contain the oxygen atom in a ring are classified as cyclic ethers and are often referred to by their common names. You have already seen the presence of a three-membered, oxygen-containing ring (an epoxide) in the structure of the dynemicins (see the Chemistry in Action "Enediyne Antibiotics: A Newly Emerging Class of Antitumor Agents," Chapter 13, p. 466).

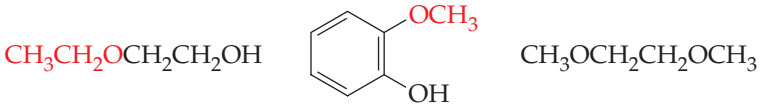

Ethylene oxide
(an epoxide)


Tetrahydrofuran
(a solvent)


1,4-Dioxane
(a solvent)

An —OR group is referred to as an **alkoxy group;** —OCH_3 is a *methoxy* group, —OCH_2CH_3 is an *ethoxy* group, and so on. These names are used when the ether functional group is present in a compound that also has other functional groups. For example,

Alkoxy group An —OR group.


2-Ethoxyethanol
(Cellusolve™)

o-Methoxyphenol

Dimethoxyethane
(glyme)

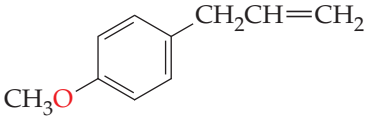
Although they contain polar C—O bonds, ethers lack the —OH group of water and alcohols, and thus do not form hydrogen bonds to one another. Simple ethers therefore boil at higher temperatures than alkanes but lower than alcohols of similar molecular mass. The oxygen atom in ethers can hydrogen bond with water, causing dimethyl ether to be water-soluble and diethyl ether to be partially miscible with water. As with alcohols, ethers with larger organic groups are often insoluble in water. Ethers make very good solvents for organic reactions where a polar solvent is needed but no —OH groups can be present.

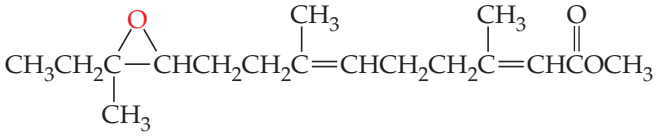
Ethers are alkane-like in many of their properties and do not react with most acids, bases, or other reagents. Ethers do, however, react readily with oxygen, and the simple ethers are highly flammable. On standing in air, many ethers form explosive *peroxides,* compounds that contain an O—O bond. Thus, ethers must be handled with care and stored in the absence of oxygen.

Diethyl ether, the best-known ether, is used primarily as a solvent but was for many years a popular anesthetic. Its value as an inhalation anesthetic was discovered in the 1840s, and it was a mainstay of the operating room until the 1940s. Although it acts quickly and is very effective, ether is far from ideal as an anesthetic because it has a long recovery time and it often induces nausea. Moreover, its effectiveness is strongly offset by its hazards. Diethyl ether is a highly volatile, flammable liquid whose vapor forms explosive mixtures with air.

Diethyl ether has been replaced by safer, less flammable anesthetics such as enflurane and isoflurane (see the Chemistry in Action "Inhaled Anesthetics" on p. 492). Both compounds were products of an intensive effort during the 1960s search for improved anesthetics, during which more than 400 halogenated ethers were synthesized.

Ethers are found throughout the plant and animal kingdoms. Some are present in plant oils and are used in perfumes; others have a variety of biological roles. Juvenile hormone, for example, is a cyclic ether that helps govern the growth of the silkworm moth. The three-membered ether ring (an *epoxide* ring) in the juvenile hormone is unusually reactive because of strained 60° bond angles.


Anethole—a flavoring agent
found in anise and fennel


Juvenile hormone—an insect hormone
found in the silkworm moth


▲ The maturation of this silkworm moth is controlled by a hormone that contains a three-membered ether ring.

CHEMISTRY IN ACTION

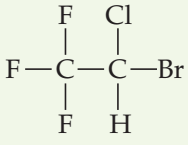
Inhaled Anesthetics

▲ William Morton performed the first public demonstration of ether as an anesthetic on October 16, 1846, at Massachusetts General Hospital.

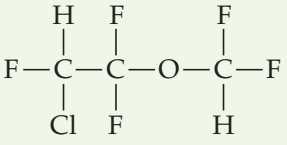
William Morton's demonstration in 1846 of ether-induced anesthesia during dental surgery represents one of the most important medical breakthroughs of all time. Before that date, all surgery had been carried out with the patient fully conscious. Use of chloroform ($CHCl_3$) as an anesthetic quickly followed Morton's work, popularized by Queen Victoria of England, who in 1853 gave birth to a child while anesthetized by chloroform.

Hundreds of substances have subsequently been shown to act as inhaled anesthetics. Halothane, enflurane, isoflurane, and methoxyflurane are at present the most commonly used agents in hospital operating rooms. All four are potent at relatively low doses, are nontoxic, and are nonflammable, an important safety feature.

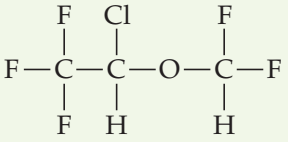
Despite their importance, surprisingly little is known about how inhaled anesthetics work in the body. Remarkably, the potency of different inhaled anesthetics correlates well with their solubility in olive oil, leading many scientists to believe that anesthetics act by dissolving in the fatty membranes surrounding nerve cells. The resultant changes in the fluidity and shape of the membranes apparently decrease the ability of sodium ions to pass into the nerve cells, thereby blocking the firing of nerve impulses.



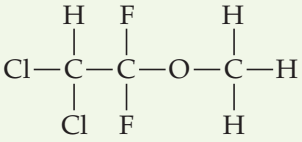
Halothane



Enflurane



Isoflurane



Methoxyflurane

Depth of anesthesia is determined by the concentration of anesthetic agent that reaches the brain. Brain concentration, in turn, depends on the solubility and transport of the anesthetic agent in the bloodstream and on its partial pressure in inhaled air. Anesthetic potency is usually expressed as a *minimum alveolar concentration* (MAC), defined as the concentration of anesthetic in inhaled air that results in anesthesia in 50% of patients. As shown in the following table, nitrous oxide, N_2O, is the least potent of the common anesthetics and methoxyflurane is the most potent; a partial pressure of only 160 Pa is sufficient to anesthetize 50% of patients.

Relative Potency of Inhaled Anesthetics

Anesthetic	MAC (%)	MAC (partial pressure, Pa)
Nitrous oxide		>101,325
Enflurane	1.7	1733
Isoflurane	1.4	1467
Halothane	0.75	760
Methoxyflurane	0.16	160

CIA Problem 14.1 What substance was used as the first general anesthetic?

CIA Problem 14.2 The solubility of inhaled anesthetics in what substance correlates to their potency?

CIA Problem 14.3 How is "minimum alveolar concentration" for an anesthetic defined?

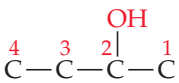
Worked Example 14.6 Molecular Structures: Drawing Ethers and Alcohols

Draw the structure for 3-methoxybutan-2-ol.

ANALYSIS First, identify the parent compound and then add numbered substituents to appropriate carbons in the parent chain.

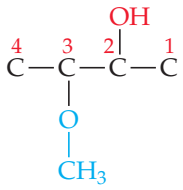
SOLUTION

The parent compound is a 4-carbon chain with the —OH attached to C2.



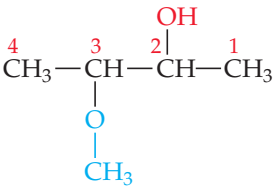
Butan-2-ol

The 3-methoxy substituent indicates that a methoxy group ($—OCH_3$) is attached to C3.



3-Methoxy

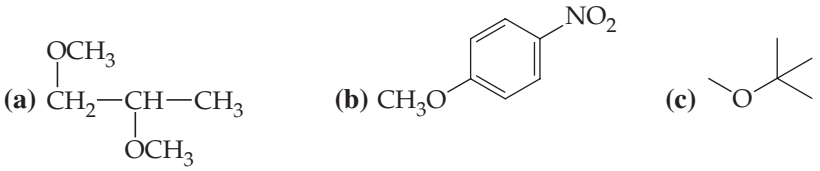
Finally, add hydrogens until each carbon atom has a total of four bonds.



3-Methoxybutan-2-ol

PROBLEM 14.16

Name the following compounds:



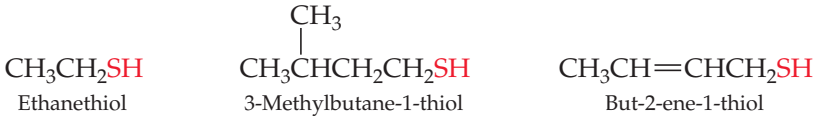
14.8 Thiols and Disulfides

Learning Objectives:

- Identify a thiol.
- Explain how a thiol is converted into a disulfide and vice versa.

Sulfur is just below oxygen in group 6A of the periodic table, and many oxygen-containing compounds have sulfur analogs. For example, **thiols** ($R—SH$), also called *thioalcohols* or *mercaptans,* are sulfur analogs of alcohols (an analog is a molecule that has a structure very similar to that of another one in all but one or two key aspects). The IUPAC name of a thiol is formed by adding *-thiol* to the parent hydrocarbon name. Otherwise, thiols are named in the same way as alcohols.

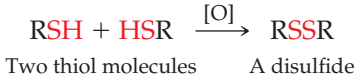
Thiol A compound that contains an —SH group, R—SH.



The most outstanding characteristic of thiols is their terrible odor. The scent of a skunk's spray is caused by two of the simple thiols shown above, 3-methylbutane-1-thiol and but-2-ene-1-thiol. Thiols are also responsible for the scent of garlic and onions, or when there is a natural gas leak. Natural gas itself is odorless, but a low concentration of methanethiol (CH_3SH) is added as a safety measure to make leak detection easy.

Thiols react with mild oxidizing agents, such as Br_2 in water or even O_2, to yield **disulfides,** RS—SR. Two thiols join together in this reaction, the hydrogen from each is lost, and a bond forms between the two sulfurs:

Disulfide A compound that contains a sulfur–sulfur bond, RS—SR.



▲ Skunks repel predators by releasing several thiols with appalling odors.

For example,

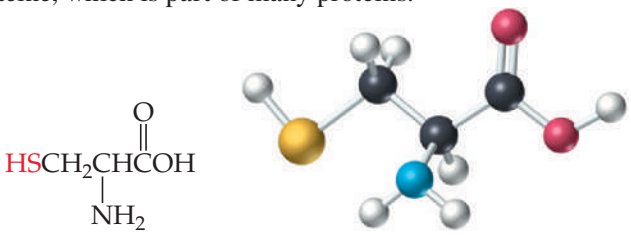
$$H_3C-S-H + H-S-CH_3 \xrightarrow{[O]} CH_3-S-S-CH_3 + H_2O$$

Methanethiol — Dimethyl disulfide

The reverse reaction occurs when a disulfide is treated with a reducing agent, represented by [H]:

$$RSSR \xrightarrow{[H]} RSH + RSH$$

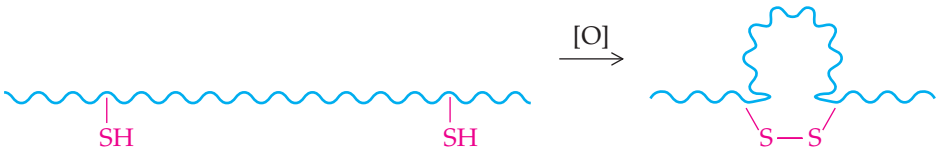
Thiols are important biologically because they occur as a functional group in the amino acid cysteine, which is part of many proteins:



Cysteine
(an amino acid)

The easy formation of S—S bonds between two cysteines helps pull large protein molecules into the shapes they need to function. The proteins in hair, for example, are unusually rich in —S—S— and —SH groups. When hair is "permed," some disulfide bonds are broken and others are then formed. As a result, the hair proteins are held in a different shape (Figure 14.2). The hair straightening procedure known as "rebonding" works in a similar way. The importance of the disulfide linkage will be discussed further in Section 18.8.

▶ **Figure 14.2**
Chemistry can curl your hair. A permanent wave results when disulfide bridges are formed between —SH groups in hair protein molecules.



PROBLEM 14.17

What disulfides would you obtain from oxidation of the following thiols?

(a) $CH_3CH_2CH_2SH$ **(b)** 3-Methylbutane-1-thiol (skunk scent)

14.9 Halogen-Containing Compounds

Learning Objective:

- Identify an alkyl or aryl halide.

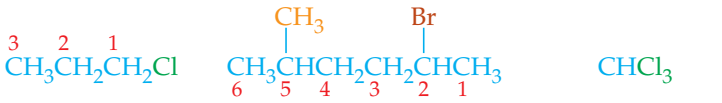
Alkyl halide A compound that has an alkyl group bonded to a halogen atom, R—X.

Aryl halide A compound that has an aromatic group bonded to a halogen atom, Ar—X.

The simplest halogen-containing compounds are the **alkyl halides,** RX, where R is an alkyl group and X is a halogen and the **aryl halides,** ArX, where Ar represents an aromatic ring. Many alkyl halides have common names that consist of the name of the alkyl group followed by the halogen name with an *-ide* ending. The compound CH_3Br, for example, is commonly called *methyl bromide*.

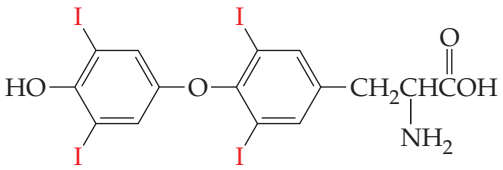
In Section 12.6, we discussed the naming of alkanes. The systematic names (IUPAC) of alkyl halides treat the halogen atom as a substituent on a parent alkane in the same way that alkyl groups are treated. The parent alkane is named in the usual way by selecting the longest continuous chain and numbering from the end nearer the first substituent, either alkyl or halogen. The *halo-* substituent name is then given as

a prefix, just as if it were an alkyl group. A few common halogenated compounds are also known by nonsystematic names, such as chloroform ($CHCl_3$). The naming of aryl halides was discussed in Section 13.9.



Halogenated organic compounds have a variety of medical and industrial uses. Chloroethane is used as a topical anesthetic because it cools the skin through rapid evaporation; halothane is an important anesthetic. Chloroform was once employed as an anesthetic and as a solvent for cough syrups and other medicines but is now considered too toxic for such uses. Bromotrifluoromethane, CF_3Br, is useful for extinguishing fires in aircraft and electronic equipment because it is nonflammable and nontoxic, and it evaporates without a trace.

Although a large number of halogen-containing organic compounds are found in nature, especially in marine organisms, few are significant in human biochemistry. One exception is thyroxine, an iodine-containing hormone secreted by the thyroid gland. A deficiency of iodine in the human diet leads to a low thyroxine level, which causes a swelling of the thyroid gland called a *goiter.* To ensure adequate iodine in the diet of people who live far from an ocean, potassium iodide is sometimes added to table salt (to create the product we know as *iodized salt*).

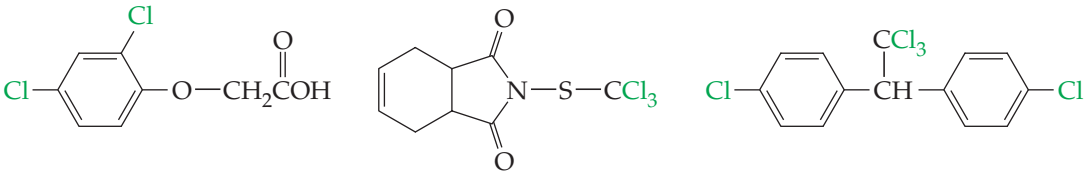


Thyroxine

Thyroid gland hormone; deficiency causes goiter

Halogenated compounds are also used widely in industry and agriculture. Dichloromethane (CH_2Cl_2, methylene chloride), trichloromethane ($CHCl_3$, chloroform), and trichloroethene ($Cl_2C{=}CHCl$) are used as solvents and degreasing agents, although their use is diminishing as less-polluting alternatives become available. Because these substances are excellent solvents for the oils in skin, continued exposure often causes dermatitis.

The use of halogenated herbicides such as 2,4-D and fungicides such as Captan has resulted in vastly increased crop yields in recent decades, and the widespread application of chlorinated insecticides such as dichlorodiphenyltrichloroethane (DDT) is largely responsible for the progress made toward worldwide control of malaria and typhus. Despite their enormous benefits, however, chlorinated pesticides present problems because they persist in the environment and are not broken down rapidly. They remain in the fatty tissues of organisms and accumulate up the food chain as larger organisms consume smaller ones. Eventually, the concentration in some animals becomes high enough to cause harm. In an effort to maintain a balance between the value of halogenated pesticides and the harm they can do, the use of many has been restricted, and others have been banned altogether.



2,4-D Captan DDT

PROBLEM 14.18

Give systematic names for the following alkyl halides:

14.10 Stereochemistry and Chirality

Learning Objective:

- Identify a chiral carbon.

In Chapters 12 and 13, you saw wedges and dashes used in drawing certain molecules, where the solid wedge indicated a bond coming out of the plane of the paper toward you and the dashed wedge indicated a bond going out of the paper away from you. This concept was first introduced in Chapter 8 when the idea of three-dimensional structure was first discussed. **Stereochemistry** is the study of molecules that have the same overall connectivity of atoms but differ in how those atoms are arranged in three-dimensional space. In Section 12.5, we discussed the concept of conformational isomers, while in Section 13.3, we learned about cis–trans isomers; in both cases the compounds differed only in how the atoms were orientated in space. Isomers that have the same formula and whose atoms have the same connections but different spatial arrangements are known as **stereoisomers.**

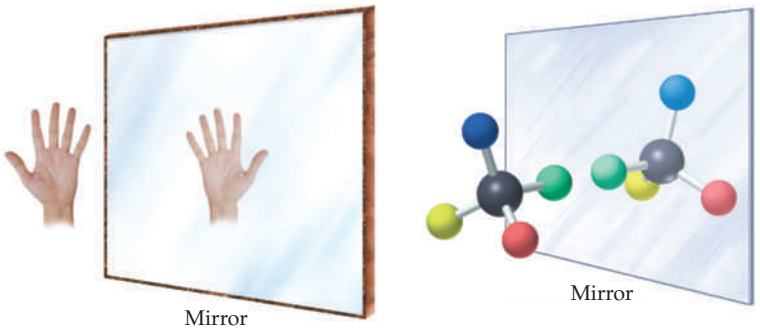
Stereochemistry The study of the relative three-dimensional spatial arrangement of the atoms in a molecule.

Stereoisomers Isomers that have the same molecular and structural formulas but different spatial arrangements of their atoms.

Configurations Stereoisomers that *cannot* be converted into one another by rotation around a single bond.

Conformational isomers of a molecule can be interconverted by simple rotations around carbon–carbon single bonds; but what if two isomers *cannot,* such as cis–trans isomers? We say that these stereoisomers have different **configurations.** Let us examine why this is important in organic and biological chemistry.

Do you write with your left or your right hand? If you are right handed, have you ever tried to write with your left hand? Your "handedness" affects almost everything you do, from writing, to hitting a golf ball, to using a fork. Just like you, molecules can also possess handedness, and it can dramatically affect their biochemical activity. To get a feel for this idea, hold your left hand up to a mirror. The image you see looks like your right hand as shown in Figure 14.3. This happens because your hands are not identical. Rather, they are mirror images.



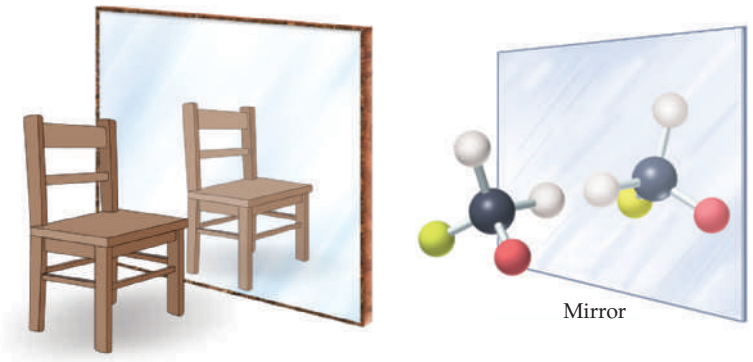
▶ **Figure 14.3**
The meaning of *mirror image*. If you hold your left hand up to a mirror, the image you see looks like your right hand. The same can be true for molecules.

Additionally, note that the mirror images of your hand cannot be superimposed on each other; one does not completely fit on top of the other. Objects that have handedness in this manner are said to be **chiral** (pronounced *ky*-ral, from the Greek *cheir,* meaning "hand").

Chiral Having right- or left-handedness with two *different* mirror-image forms.

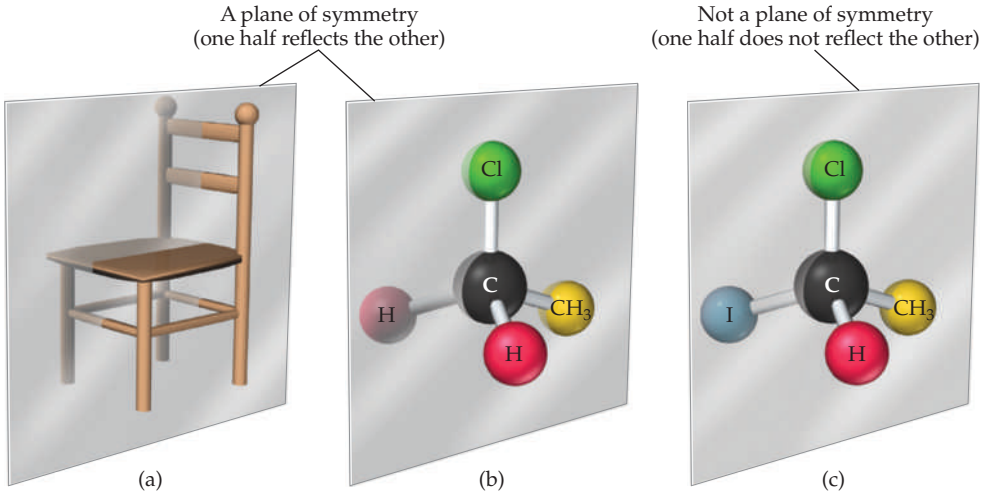
Not all objects are chiral. Consider both the chair and its mirror image as well as the molecule and its mirror image shown in Figure 14.4. When a chair is reflected in a mirror, its image is identical to chair itself. Objects that lack handedness are said to be nonchiral, or **achiral.** The molecule in this figure is also achiral. Convince yourself of this by studying the chair and the molecule in Figure 14.4. Each of these has mirror images that are superimposable because they possess a plane of symmetry. Any item that,

Achiral The opposite of chiral, having superimposable mirror images and thus no right- or left-handedness.



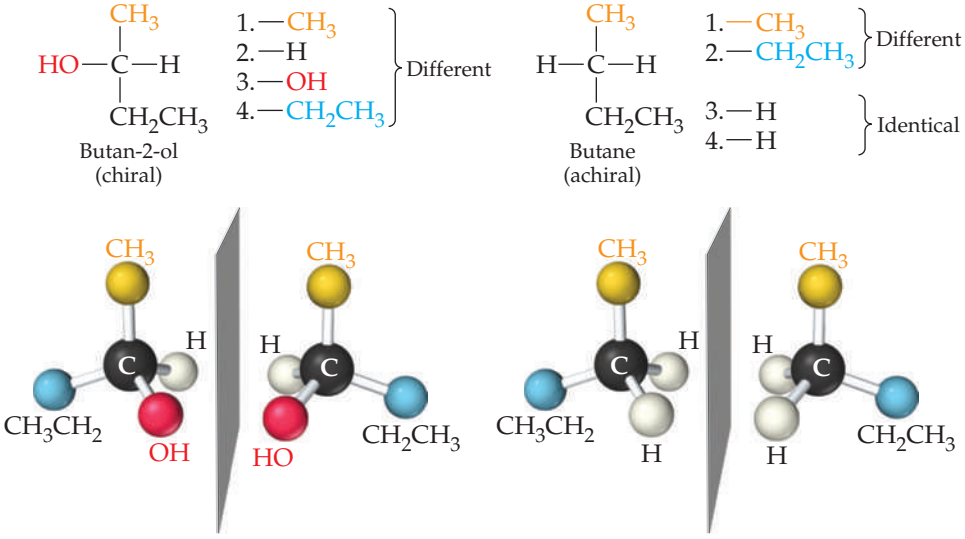
◀ **Figure 14.4**
The meaning of *superimposable.* It is easy to visualize the chair on top of its mirror image. The molecular model shown is also superimposable but not as easy to visualize.

when bisected with an imaginary mirror plane, has two halves that are mirror images of one another will be achiral. All that is required for a molecule to be achiral is one plane of symmetry. Figure 14.5 illustrates this concept.



◀ **Figure 14.5**
The meaning of *plane of symmetry.* The items from Figure 14.4 are shown here with their plane of symmetry illustrated. Note that the imaginary mirror splits both (a) the chair and (b) the molecular model into two identical pieces. Notice that the molecular model shown in (c) has no such plane of symmetry and is therefore chiral.

Can we predict whether a molecule will be chiral from structural formulas? Recall that carbon forms four bonds oriented to the four corners of an imaginary tetrahedron. The formulas for butan-2-ol and butane are shown below in a manner that emphasizes the four groups bonded to the central carbon atom. In butan-2-ol, this carbon is connected to *four different groups:* a $-CH_3$ group, an $-H$ atom, an $-OH$ group, and a $-CH_2CH_3$ group:



Don't be concerned if you struggle with the concept of chirality; you will become more comfortable with it the more you use it.

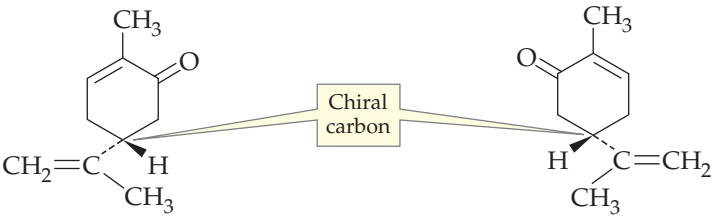
Chiral carbon atom A carbon atom bonded to four different groups. Also referred to as a chiral center or stereocenter.

A carbon atom that is BOTH tetrahedral AND has four different groups attached is referred to as a **chiral carbon atom,** or a chiral center (or stereocenter). The presence of one chiral carbon atom always produces a chiral molecule that exists in two mirror-image forms. Thus, butan-2-ol is chiral. In butane, the central carbon atom shown is bonded to two groups that are different (the $-CH_3$ and the $-CH_2CH_3$ groups) and one pair of identical groups, the two hydrogen atoms. Possessing no chiral center, butane is therefore achiral. Molecules can have more than one chiral carbon atom, but whether the molecule itself is chiral will depend on overall shape.

We will see the use rotation of polarized light to distinguish enantiomers used again in Section 20.2.

Enantiomers (optical isomers) The two mirror-image forms of a chiral molecule.

The two mirror-image forms of a chiral molecule like butan-2-ol are called either **enantiomers** (pronounced en-*an*-ti-o-mers) or **optical isomers** ("optical" because of their effect on polarized light). The chemical and physical properties of a given pair of enantiomers (such as butan-2-ol and its mirror image) are usually identical in all aspects *except* for how they are affected by polarized light. Both enantiomers of butan-2-ol, for example, have the same boiling point, the same solubility in water, the same isoelectric point, and the same density; yet when polarized light is transmitted through a solution containing one enantiomer, it rotates that light to the right (and is called the *d* or (+) enantiomer) while a solution containing the other enantiomer rotates light to the left (and is called the *l* or (−) enantiomer). Enantiomers often differ in their biological activity, odors, and tastes. For example, the very different natural flavors of spearmint and caraway seeds are attributed to these two enantiomers.

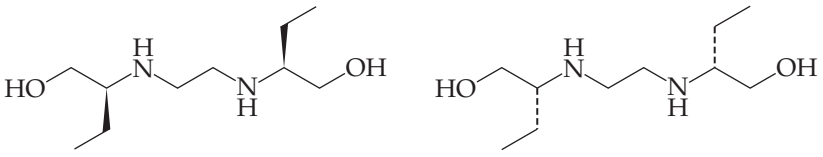


l–carvone (in spearmint)

d–carvone (in caraway)

In Chapter 18, you will be introduced to the α-amino acids, all except one of which are chiral. Chirality is also an important property of another major class of biomolecules, the carbohydrates (Chapter 20).

Most importantly, however, pairs of enantiomers often differ in their activity as drugs. For example, *l*-ethambutol is used to treat tuberculosis and is on the World Health Organization's List of Essential Medicines; however, its enantiomer, *d*-ethambutol, causes blindness:



l–Ethambutol (used to treat tuberculosis)

d–Ethambutol (causes blindness)

HANDS-ON CHEMISTRY 14.1

Being able to grasp the idea of superimposable molecules, plane of symmetry, and chirality is important when you study biochemistry, where the three-dimensional shape of the molecules is crucial to its biological activity. In this exercise, you are going to look at molecules that have zero, one, or two chiral centers and see if you can get a grasp on the concept of chirality. To accomplish all of this, you are going to use models, *but you do not need a model kit to carry out this exercise.* If you have a model kit, follow the instructions included with it to make the "building blocks" described here. If you do not have access to a model kit, follow the instructions to make "gumdrop building blocks." You will need a box of toothpicks and a bag of multicolored gumdrops (preferred), gummy bears, or mini-marshmallows; it does not matter as long as you can insert a toothpick in it and it will stay in place. Throughout this exercise, remember that (1) carbon is tetravalent (forms four bonds), (2) hydrogen and halogen (Cl, Br, and I) are monovalent (forms one bond), (3) you will want to be sure that your units have real angles and represent tetrahedrons as closely as possible, and (4) once you build a model you can rotate around single bonds but you CANNOT remove any atoms and swap them when making comparisons.

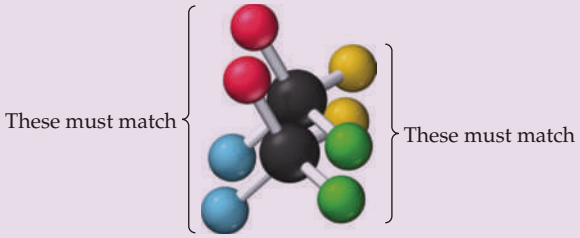
Building Blocks—for this exercise, you will need the following (use the color coding of atoms listed in Table 4.2 as your guide if possible):

Eight tetrahedral carbon units—make these by placing four toothpicks into a gumdrop in a tetrahedral array. Use gumdrops of whatever color you have assigned to being carbon (black or some other dark color). Note: There will be times you will have to remove toothpicks to make connections to other units; when you do, make the new connection in the same location as the toothpick you removed.

Six to eight "one group" unit pairs—simply stick a toothpick into a gumdrop. Make two of each color so that you have 12–16 total. The gumdrops should all be the same color.

Once you have these assembled, you can begin. Be prepared to use more toothpicks and/or gumdrops as necessary. If possible, you may want to take pictures of each model you make for review later.

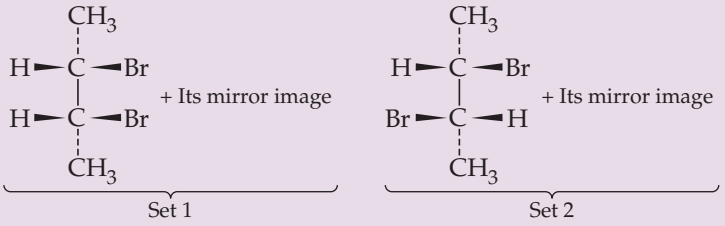
a. Start by assembling CH_2BrCl. Use different colors for each atom. Now, put your model in front of a mirror (or use a small piece of reflective material, like aluminum foil) and build the mirror image of what you just built. Can you superimpose them on top of one another? For this to be true, you must be able to do the following:



If they do superimpose, can you find a plane of symmetry in your model?

b. Repeat part a by making CHIBrCl. Can you superimpose them on top of one another? Can you find a plane of symmetry?

c. Now build the following molecules, using your tetrahedral units:

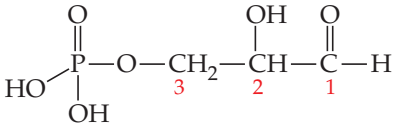


(Rather than building a CH_3, simply use a different colored ball or gumdrop to represent the entire methyl group, but use the same color for all the CH_3's in both molecules). Start by looking at Set 1. How many chiral centers does each model have? Can you superimpose one on top of the other? Try doing rotations around the C—C bond. Is there a plane of symmetry in the molecule? Repeat this for Set 2. What you should find is that the models you made for Set 1 are superimposable, whereas those for Set 2 are not.

d. (Optional) Take the first molecule of Set 1 and compare it to the first molecule of Set 2. Are they mirror images of one another? Try to superimpose these on top of one another, doing rotations around the central C—C bond if necessary. You should find that these two are neither mirror images of one another, nor are they superimposable. These are examples of *diastereomers*: Stereoisomers that have the same gross connections of atoms but differ in their spatial orientation and are NOT related to one another as mirror images. The simplest example of diastereomers is cis–trans isomers (Chapter 13). For a molecule containing only tetrahedral carbons to exist as diastereomers, it must have two or more chiral centers; this is one of the things that can happen when a molecule has more than one chiral center. You will come across this again when you study carbohydrates (Chapter 20).

Worked Example 14.7 Determining Whether a Carbon Is Chiral

(a) Glyceraldehyde-3-phosphate is a key intermediate in the metabolism of glucose (both glycolysis and gluconeogenesis). Determine which (if any) of the carbons in this molecule are chiral (The carbons have been numbered for clarity).



ANALYSIS Identify the tetrahedral carbons in the molecule; a carbon will be chiral if it is tetrahedral AND is bonded to four different groups.

SOLUTION

We can ignore C1, as it is not tetrahedral (carbons that are part of a double bond are trigonal planar). List the groups attached to each of the remaining carbon atoms.

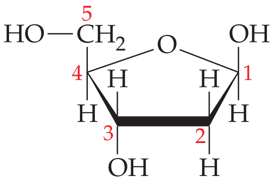
Groups on Carbon 2	Groups on Carbon 3
1. —CHO	1. —CH(OH)CHO
2. —OH	2. —H
3. —H	3. —H
4. $—CH_2OPO_3H_2$	4. $—CH_2OPO_3H_2$

—continued on next page

—*continued from previous page*

Looking at the lists we see that only carbon 2 has four different groups attached. Therefore, only C2 is chiral.

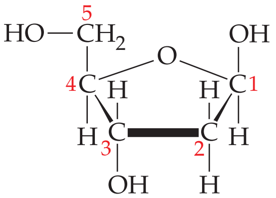
(b) 2-Deoxyribose is a carbohydrate that makes up the backbone of the biomolecule ribonucleic acid (RNA). Determine which (if any) of the carbons in this molecule are chiral (The carbons have been numbered for clarity).



ANALYSIS As in part (a), begin by identifying the tetrahedral carbons in the molecule and then list what is attached; use R, R′, and R″ to represent different carbon chains when the groups are complex and not as easy to list.

SOLUTION

When dealing with molecules in line structure format, it is sometimes easier to actually put the carbons in to avoid confusion:



All carbons in this molecule are tetrahedral. List the groups attached to each of the remaining carbon atoms; indicate *different* complex carbon chains beyond the carbon adjacent to that being examined by using R and R′. Analyze each of the carbons one at a time to determine chirality:

Groups on C1	Groups on C2	Groups on C3	Groups on C4	Groups on C5
1. —OR	1. —CH(OH)R	1. —CH_2R′	1. —CH(OH)R	1. —OH
2. —OH	2. —H	2. —OH	2. —CH_2OH	2. —H
3. —H	3. —H	3. —H	3. —H	3. —H
4. —CH_2R′	4. —CH(OH)R′	4. —CH(CH_2OH)OR	4. —OR′	4. —CH(R)(R′)

Comparing the groups on each carbon, we see that C2 and C5 are both achiral; note that both have only three different groups attached (also note that on C2 the —CH(OH)R and —CH(OH)R′ are different, noted by the use of R and R′). The other carbons have four different groups attached. Therefore, C1, C3, and C4 are chiral.

PROBLEM 14.19

2-Aminopropane is an achiral molecule, but 2-aminobutane is chiral. Explain.

PROBLEM 14.20

Which of the following molecules are chiral? (Hint: Draw each molecule and analyze it as illustrated in Worked Example 14.2.)

(a) 3-Chloropentane

(b) 2-Chloropentane

(c) $CH_3CHCH_2CHCH_2CH_3$ (with CH_3 on the second and fourth carbons)

$\quad\quad\quad | \quad\quad\quad |$

$\quad\quad CH_3 \quad\ \ CH_3$

CHEMISTRY IN ACTION

Fetal Alcohol Syndrome: Ethanol as a Toxin

As we learned in the beginning of the chapter, ethanol is classified for medical purposes as a CNS depressant. The passage of ethanol through the body begins with its absorption in the stomach and small intestine, followed by rapid distribution to all body fluids and organs. Its direct effects (being "drunk") resemble the response to anesthetics, with the amount in the bloodstream easily measurable and reported as blood alcohol concentration (BAC, expressed as a percentage of ethanol in the blood in units of grams of alcohol per deciliter of blood). At a BAC of 0.06–0.20%, motor coordination and pain perception are affected, accompanied by loss of balance, slurred speech, and amnesia; at a BAC of 0.20–0.40%, there may be nausea and loss of consciousness. At BAC levels above 0.50%, spontaneous respiration and cardiovascular regulation are affected, ultimately resulting in death. All of these effects point to alcohol as being a toxin, but one that in small enough amounts the human body can tolerate.

But what happens when the organism affected has almost no body mass nor the complete biochemistry to deal with alcohol in the blood? What happens when a fetus is exposed to alcohol? Alcohol crosses the placenta, rapidly reaching the fetus. Studies have demonstrated that BAC levels are the same in both the mother and the fetus, suggesting an unimpeded movement of alcohol across the placenta. Since the activity of alcohol dehydrogenase (ADH) in the fetal liver is less than 10% of that of an adult, a fetus depends on the mothers' liver to detoxify the alcohol. Even more chilling, amniotic fluid seems to act as a reservoir for alcohol, prolonging fetal exposure. Prenatal exposure to alcohol is associated with a wide variety of effects, the most severe of which is known as FAS. A syndrome is a specific set of medical indications and symptoms that are often linked to one another and to a specific disease. For FAS, the signs and symptoms are birth defects that result from a woman's use of alcohol during her pregnancy. Children with FAS may grow less quickly than other children, have facial abnormalities, and can have CNS problems that can include delayed development of motor skills such as rolling over, sitting up, crawling and walking, hyperactivity, attention-deficit disorder, conduct disorder, and, at the severe end of the spectrum, mental retardation.

The mechanism for the adverse effects of alcohol on virtually all organ systems of the developing fetus is unknown. Ethanol metabolism in the liver is a two-step process: oxidation of the alcohol to acetaldehyde, followed by oxidation of the aldehyde to acetic acid. These oxidations are mediated by the liver enzyme ADH. When continuously present in the bodies of chronic alcoholics, alcohol and acetaldehyde are toxic, leading to devastating physical and metabolic deterioration. Since a fetus lacks the body mass of an adult, these effects are undoubtedly magnified to perilous proportions.

▲ Danger can come in pretty packages, especially for a pregnant woman.

$$CH_3CH_2OH \xrightarrow[\text{Alcohol dehydrogenase enzyme}]{NAD^+} CH_3\overset{O}{\overset{\|}{C}}H \xrightarrow[\text{Aldehyde dehydrogenase enzyme}]{NAD^+} CH_3\overset{O}{\overset{\|}{C}}OH$$

So, is alcohol consumption safe at any level for a pregnant woman? In 2015, the CDC issued the following statement: "There is no known safe amount of alcohol use during pregnancy or while trying to get pregnant. There is also no safe time during pregnancy to drink. All types of alcohol are equally harmful, including all wines and beer. When a pregnant woman drinks alcohol, so does her baby."[1] While this overall topic generates a great deal of controversy, there is one thing to say for sure, exposure of a fetus to alcohol is not recommended. There is always the possibility that some harm to a baby might result from light or moderate drinking during pregnancy. Given this possibility, even if remote, the very safest choice for an expectant mother's fetus would be to abstain. Why take the chance?

CIA Problem 14.4 Is ethanol a stimulant or a depressant?

CIA Problem 14.5 At what BAC does speech begin to be slurred? What is the approximate lethal concentration of ethanol in the blood?

CIA Problem 14.6 What is a syndrome?

CIA Problem 14.7 What are some of the CNS disorders possible in children with FAS?

[1] *From the article "Alcohol Use in Pregnancy," Centers for Disease Control and Prevention (2014 April 17). www.cdc.gov/ncbddd/fasd/alcohol-use.html*

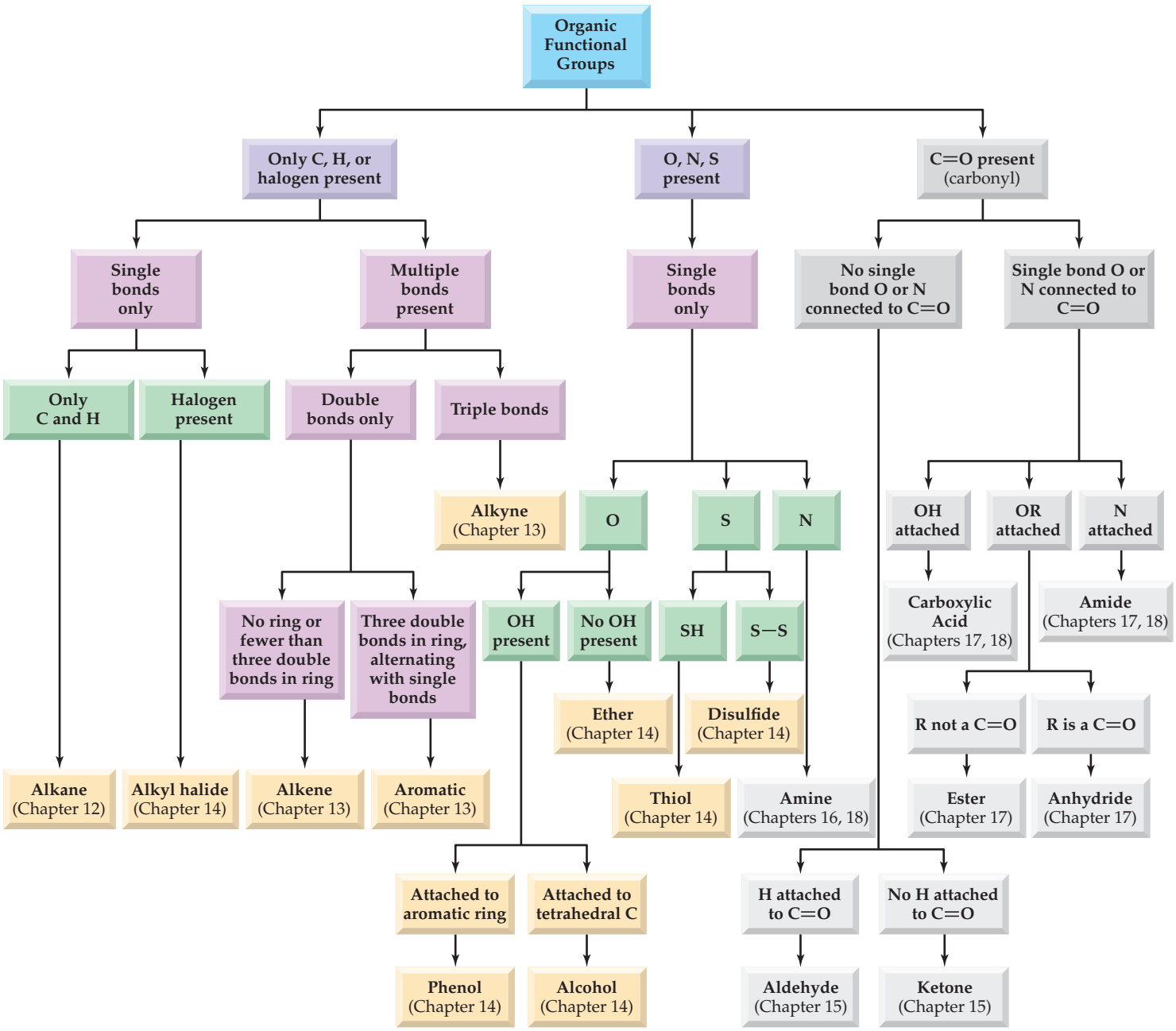
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Describe the structural differences between alcohols, phenols, and ethers.** An *alcohol* has an —OH group (a *hydroxyl* group) bonded to a saturated, carbon atom; a *phenol* has an —OH group bonded directly to an aromatic ring; and an *ether* has an oxygen atom bonded to two organic groups *(see Problems 26, 27, 30, and 31).*
- **Explain why alcohols have higher boiling points than compounds of similar molecular mass.** Alcohols, like water, can undergo hydrogen bonding. This leads to alcohols having higher boiling points than expected based on molecular mass. Alcohols with two or more —OH groups can form more than one hydrogen bond and will have even higher boiling points *(see Problems 28 and 38).*
- **Write systematic names for simple alcohols.** Alcohols are named using the *-ol* ending, and phenols are named using the *-phenol* ending *(see Problems 32, 33, 60, 68, 69, and 73).*
- **Draw the structure of an alcohol given its name, in both condensed and line structure format.** The structure of an alcohol is drawn in a similar fashion to that for an alkane; the numbering system uses index number of the hydroxyl (—OH) group as the basis for the location of all other groups in the molecule *(see Problems 34, 35, 67, and 73).*
- **Classify an alcohol as primary, secondary, or tertiary.** A primary alcohol has one carbon attached to the carbon containing the —OH group, a secondary alcohol has two carbons attached to the carbon containing the —OH group, and a tertiary alcohol has three carbons attached to the carbon containing the —OH group *(see Problems 36 and 37).*
- **Define and identify a glycol.** A diol is an alcohol containing two —OH groups. When the groups are on adjacent carbons, the diol is given the special name glycol *(see Problems 32, 34, and 39).*
- **Describe the properties of alcohols.** Alcohols are much more polar than hydrocarbons, and the presence of the —OH group provides the ability to hydrogen bond to other alcohols and to water. Due to the presence of the carbon group, alcohols are also miscible with many organic solvents *(see Problems 28, 29, 54, 55, and 62).*
- **Describe hydrophobic and hydrophilic alcohols.** Alcohols R—OH have both a hydrophilic (—OH) and hydrophobic (R—) part. *Hydrophilic* means "water-loving," and *hydrophobic* means "water-fearing." The larger the hydrophobic organic part is, the more alkane-like and less water-like alcohols become *(see Problems 36, 39, and 62).*
- **Predict the products obtained upon dehydration of an alcohol.** Alcohols undergo loss of water *(dehydration)* to yield alkenes when treated with a strong acid. When mixtures of alkenes are possible, the major product expected is the one with the most carbons directly attached to the carbon–carbon double bond *(see Problems 46, 47, 69, 74, and 75).*
- **Predict the oxidation products of a primary, secondary, and tertiary alcohol.** Alcohols undergo *oxidation* to yield compounds that contain a *carbonyl group* (C=O). Primary alcohols (RCH_2OH) are oxidized to yield either aldehydes (RCHO) or carboxylic acids (RCO_2H), secondary alcohols (R_2CHOH) are oxidized to yield ketones ($R_2C{=}O$), and tertiary alcohols are not oxidized *(see Problems 48, 49, 69, 70, and 72).*
- **Identify a phenol.** A *phenol* has an —OH group bonded directly to an aromatic ring. Phenols are notable for their use as disinfectants and antiseptics *(see Problems 33, 35, 44, and 64).*
- **Explain why alcohols and phenols are weak acids.** Like water, alcohols and phenols are weak acids that can donate H^+ from their —OH group to a strong base. Alcohols are similar to water in acidity; phenols are more acidic than water and will react with aqueous NaOH *(see Problems 29 and 64).*
- **Identify an ether.** An *ether* has an oxygen atom bonded to two organic groups. The groups can be alkyl, aromatic, or a mixture of both. Simple ethers are named by identifying the two organic groups attached to oxygen, followed by the word *ether.* Ethers are used primarily as solvents *(see Problems 30, 33, and 35).*
- **Distinguish between an ether and an alcohol.** Both alcohols and phenols are like water in their ability to form hydrogen bonds. As the size of the carbon part of the molecule increases, alcohols become less soluble in water. Ethers do not hydrogen bond and are more alkane-like in their properties *(see Problems 32–35).*
- **Identify a thiol.** *Thiols* are sulfur analogs of alcohols, containing an —SH in place of an —OH. Thiols use the name ending *-thiol (see Problems 50 and 51).*
- **Explain how a thiol is converted into a disulfide and vice versa.** Thiols react with mild oxidizing agents to yield *disulfides* (RSSR), a reaction of importance in protein chemistry. Reducing agents will convert disulfides back to thiols *(see Problems 52 and 53).*
- **Identify an alkyl or aryl halide.** *Alkyl halides* contain a halogen atom bonded to an alkyl group, R—X, while *aryl halides* have a halogen attached to an aromatic ring, Ar—X. Halogenated compounds are rare in human biochemistry but are widely used in industry as solvents and in agriculture as herbicides, fungicides, and insecticides *(see Problems 68 and 69).*
- **Identify a chiral carbon.** A chiral carbon is a carbon atom that is bonded to four different groups. Also referred to as a chiral center or stereocenter. The presence of a chiral carbon atom can lead to stereoisomers: Isomers that have the same bonded connections of atoms but differ in how those atoms are oriented in space *(see Problems 56–59, 65, and 67).*

KEY WORDS

Achiral, *p. 496*
Alcohol, *p. 475*
Alkoxide ion, *p. 490*
Alkoxy group, *p. 491*
Alkyl halide, *p. 494*
Aryl halide, *p. 494*
Carbonyl group, *p. 486*
Chiral carbon atom, *p. 498*
Chiral, *p. 496*
Configurations, *p. 496*
Dehydration, *p. 482*
Disulfide, *p. 493*
Enantiomers (optical isomers), *p. 498*
Ether, *p. 475*
Glycol, *p. 478*
Phenol, *p. 475*
Stereochemistry, *p. 496*
Stereoisomers, *p. 496*
Thiol, *p. 493*
Vicinal, *p. 478*

CONCEPT MAP: ORGANIC CHEMISTRY FAMILIES

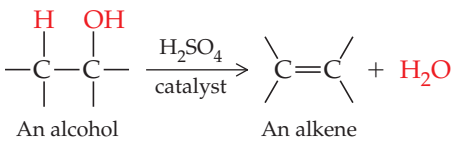


▲ **Figure 14.6** **Concept Map.** This is the same concept map we saw at the end of Chapters 12 and 13, except the functional groups discussed in this chapter, alcohols, ethers, thiols, and disulfides have now been colored.

SUMMARY OF REACTIONS

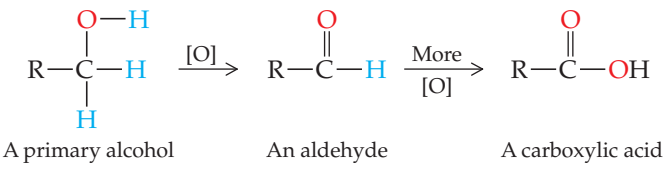
1. Reactions of alcohols (Section 14.6)

(a) Loss of H_2O to yield an alkene (dehydration):

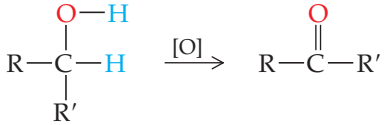


An alcohol — An alkene

(b) Oxidation to yield a carbonyl compound:



A primary alcohol — An aldehyde — A carboxylic acid



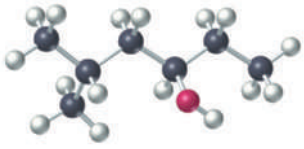
A secondary alcohol — A ketone

2. Reactions of thiols (Section 14.10); oxidation to yield a disulfide:

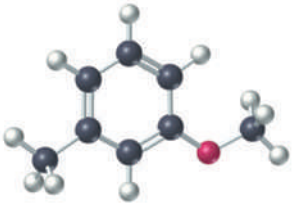
$$\underset{\text{Two thiol molecules}}{RSH + HSR} \xrightarrow{[O]} \underset{\text{A disulfide}}{RSSR}$$

UNDERSTANDING KEY CONCEPTS

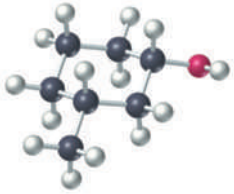
14.21 Give IUPAC names for the following compounds (black = C, red = O, white = H).



(a)

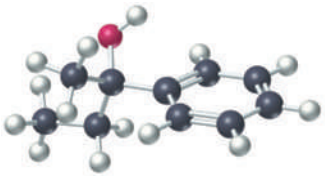


(b)

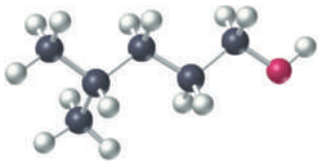


(c)

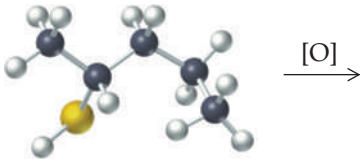
14.22 Predict the product of the following reaction:



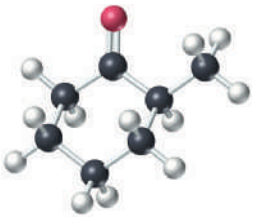
14.23 Predict the products of the following reaction:



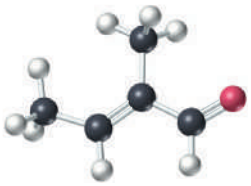
14.24 The compound pictured here is a thiol. (a) Draw its line structure, and (b) draw the structure of the disulfide formed when it is treated with an oxidizing agent (yellow = S).



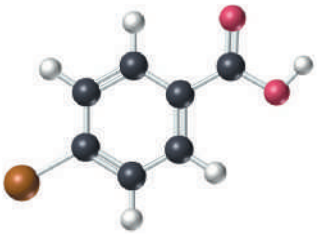
14.25 From what alcohols might the following carbonyl compounds have been made (reddish-browm = Br)?



(a)



(b)



(c)

ADDITIONAL PROBLEMS

ALCOHOLS, ETHERS, AND PHENOLS (SECTIONS 14.1–14.2 AND 14.5–14.7)

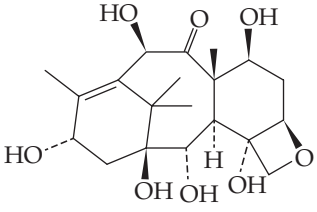
14.26 How do alcohols, ethers, and phenols differ structurally?

14.27 What is the structural difference between primary, secondary, and tertiary alcohols?

14.28 Why do alcohols have higher boiling points than ethers of the same molecular mass?

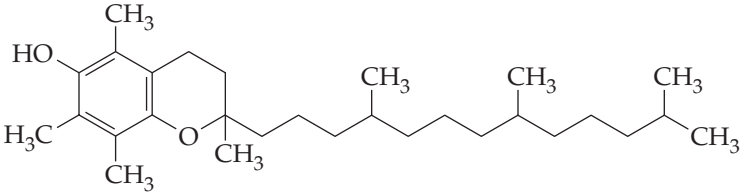
14.29 Which is the stronger acid, ethanol or phenol?

14.30 The Taxane nucleus is shown here; it is the basis of a number of new drugs used to treat cancers. Identify the functional groups present in this molecule.



Taxane nucleus

14.31 Vitamin E has the structure shown. Identify the functional group to which each oxygen belongs.



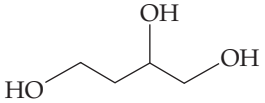
Vitamin E (a naturally occurring antioxidant)

14.32 Give systematic names for the following alcohols:

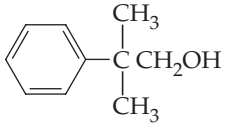
(a) $H_3C-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-OH$

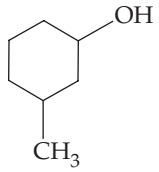
(b) $(CH_3)_2CHCH_2OH$

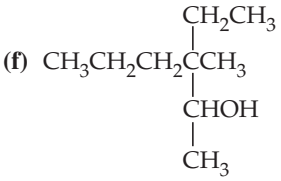
(c)



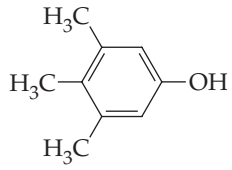
(d)

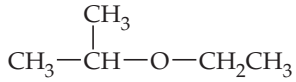


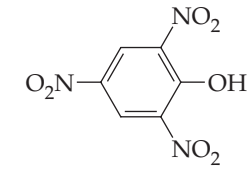
(e) 

(f) 

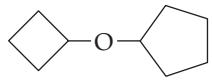
14.33 Give systematic names for the following compounds:

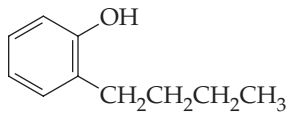
(a) 

(b) 

(c) 

(Also known as picric acid)

(d) 

(e) 

(f) $CH_3CH_2CH_2OCH_2CH_2CH_3$

14.34 Draw structures corresponding to the following names:

(a) 2,4-Dimethylheptan-2-ol

(b) 2,2-Diethylcyclohexanol

(c) 5-Ethyl-5-methylheptan-1-ol

(d) 4-Ethylhexan-2-ol

(e) 3-Methoxycyclooctanol

(f) 3,3-Dimethylheptane-1,6-diol

14.35 Draw structures corresponding to the following names:

(a) Isopropyl methyl ether

(b) *o*-Dihydroxybenzene (catechol)

(c) Phenyl *tert*-butyl ether

(d) *m*-Iodophenol

(e) 2,4-Dimethoxy-3-methylpentane

(f) 3-Methoxy-4-methylpent-1-ene

14.36 **(a)** Identify each alcohol named in Problem 14.32 as primary, secondary, or tertiary.

(b) Classify each alcohol in Problem 14.32 as water-soluble or water insoluble. Identify the hydrophobic and hydrophilic areas of each alcohol.

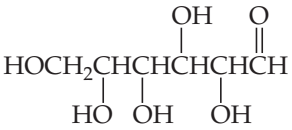
14.37 Locate the alcohol functional groups in the taxane nucleus (Problem 14.30), and identify each as primary, secondary, or tertiary.

14.38 Arrange the following 6-carbon compounds in order of their expected boiling points, and explain your ranking:

(a) Hexane **(b)** Hexan-1-ol

(c) Dipropyl ether $(CH_3CH_2CH_2—O—CH_2CH_2CH_3)$

14.39 Glucose is much more soluble in water than hexan-1-ol, even though both contain 6 carbons. Explain.



Glucose

REACTIONS OF ALCOHOLS (SECTION 14.4)

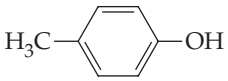
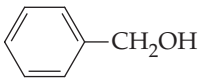
14.40 What functional group is formed on oxidation of a secondary alcohol? Demonstrate your answer using isopropanol.

14.41 What structural feature is necessary for an alcohol to undergo oxidation reactions?

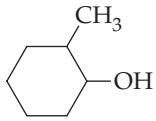
14.42 What product can form on oxidation of a primary alcohol with an excess of oxidizing agent?

14.43 What type of product is formed on reaction of an alcohol with Na metal?

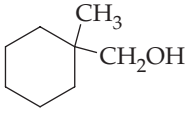
14.44 Assume that you have samples of the following two compounds, both with formula C_7H_8O. Both compounds dissolve in ether, but only one of the two dissolves in aqueous NaOH. How could you use this information to distinguish between them?

 and 

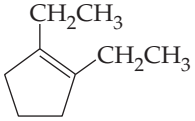
14.45 Which of the following alcohols can undergo oxidation? Draw the line structure of the product expected for those that can. Assume an excess of oxidizing agent is present.

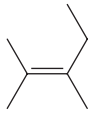
(a) 

(b) 

(c) 

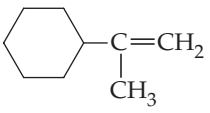
14.46 The following alkenes can be prepared by dehydration of an appropriate alcohol. Show the structure of the alcohol in each case that would provide the alkene shown as the major product.

(a) 

(b) 

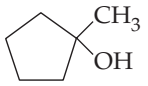
Two possible alcohols

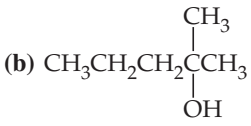
(c) 2-Phenylhex-2-ene

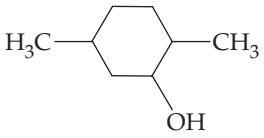
(d) 

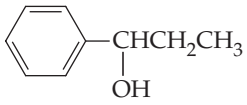
(e) Penta-1,4-diene

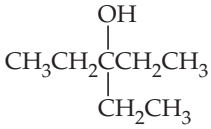
14.47 What alkenes might be formed by dehydration of the following alcohols? If more than one product is possible, indicate which you expect to be major.

(a) 

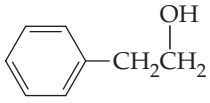
(b) 

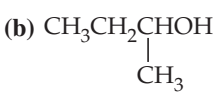
(c) 

(d) 

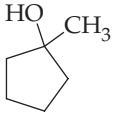
(e) 

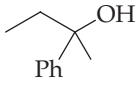
14.48 What carbonyl-containing products would you obtain from the oxidation of the following alcohols? If no reaction occurs, write "NR."

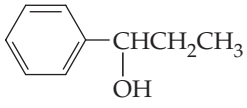
(a) 

(b) 

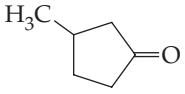
(c) Pentane-2,3-diol

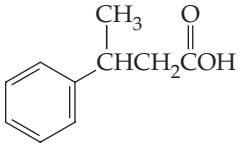
(d) 

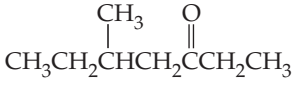
(e) 

(f) 

14.49 What alcohols would you oxidize to obtain the following carbonyl compounds?

(a) 

(b) 

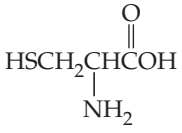
(c) 

THIOLS AND DISULFIDES (SECTION 14.8)

14.50 What is the most noticeable characteristic of thiols?

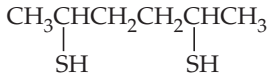
14.51 What is the structural relationship between a thiol and an alcohol?

14.52 The amino acid cysteine forms a disulfide when oxidized. What is the structure of the disulfide?



Cysteine

14.53 Oxidation of a dithiol such as hexane-2,5-dithiol forms a six-membered ring containing a disulfide group as part of the ring. Draw the structure of this cyclic disulfide (Hint: Draw the starting compound in line structure format first).



Hexane-2,5-dithiol

14.54 The boiling point of propanol is 97 °C (370 K), much higher than that of either ethanethiol (37 °C/310 K) or chloroethane (13 °C/286 K), even though all three compounds have similar molecular masses. Explain.

14.55 Propanol is very soluble in water, but ethanethiol and chloroethane are only slightly soluble. Explain.

STEREOCHEMISTRY AND CHIRALITY (SECTION 14.10)

14.56 Define the following terms:

(a) Chiral **(b)** Achiral

(c) Chiral carbon **(d)** Enantiomer

14.57 Are the following items chiral or achiral? Give a justification for your answers.

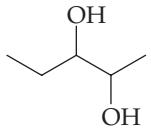
(a) A fork **(b)** This textbook

(c) Your right hand

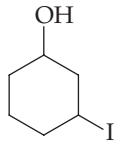
(d) A blank 3 × 5 index card

14.58 Identify the chiral center(s) in each of the following molecules:

(a) 2-Methylpentan-3-ol **(b)** 3-Chlorobutan-1-ol

(c) 

two chiral centers

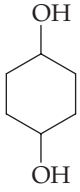
(d) 

two chiral centers

14.59 Are the following molecules chiral or achiral? If they are chiral, identify the chiral carbon atom(s).

(a) Pentan-3-ol **(b)** 2-Bromobutane

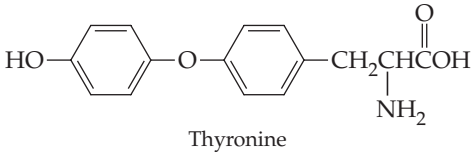
(c) 2-Methylcyclohexanol

(d) 

CONCEPTUAL PROBLEMS

14.60 Name all unbranched ether and alcohol isomers with formula $C_5H_{12}O$, and write their structural formulas.

14.61 Thyroxine (Section 14.9) is synthesized in the body by reaction of thyronine with iodine. Write the reaction, and tell what kind of process is occurring (Hint: See Section 13.5).



Thyronine

14.62 Propan-1-ol is freely soluble in water, butan-1-ol is marginally soluble, and hexan-1-ol is essentially insoluble. Explain.

14.63 Phenols undergo the same kind of substitution reactions that other aromatic compounds do (Section 13.11). Formulate the reaction of *p*-methylphenol with Br_2 to give a mixture of two substitution products.

14.64 What is the difference between an antiseptic and a disinfectant?

14.65 Which of the alcohols pictured in Problem 14.47 are achiral?

14.66 Which of the alcohols pictured in Problem 14.48 are chiral? Indicate the chiral carbons for those that are chiral.

14.67 Write the formulas and IUPAC names for the following common alcohols (Hint: See Table 14.1).

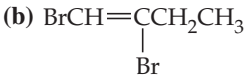
(a) Rubbing alcohol **(b)** Wood alcohol

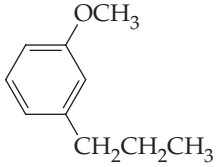
(c) Grain alcohol

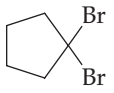
(d) Diol used as antifreeze (two answers)

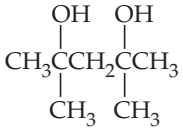
14.68 Name the following compounds:

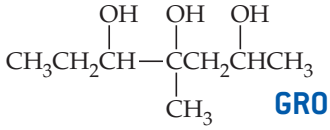
(a) 

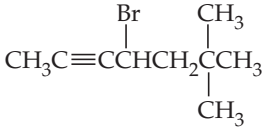
(b) 

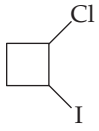
(c) 

(d) 

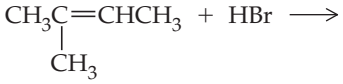
(e) 

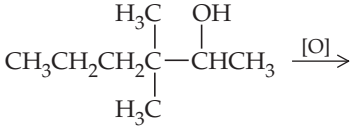
(f) 

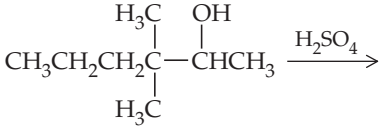
(g) 

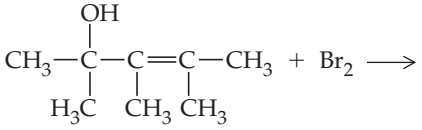
(h) 

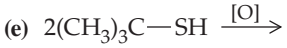
14.69 Complete the following reactions:

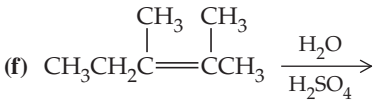
(a) 

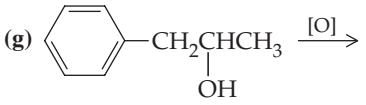
(b) 

(c) 

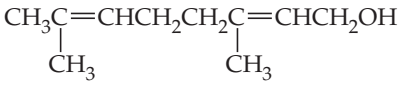
(d) 

(e) 

(f) 

(g) 

14.70 The aroma of roses is due to geraniol.



Geraniol

(a) What is the systematic name of geraniol?

(b) When geraniol is oxidized, the aldehyde citral, one of the compounds responsible for lemon scent, is formed. Write the structure of citral.

14.71 "Designer vinegars" have become very popular over the past decade. Vinegars made from champagne, merlot, and other wines are but a few of these. All wines contain ethanol, and these vinegars are simply wines containing microorganisms that have caused oxidation of the ethanol present. If vinegar is simply ethanol that has been oxidized, what is the structure of the acid formed?

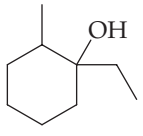
14.72 "Flaming" desserts, such as cherries jubilee, use the ethanol in brandy or other distilled spirits as the flame carrier. Write the equation for the combustion of ethanol.

GROUP PROBLEMS

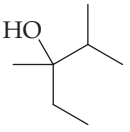
14.73 **(a)** Draw all possible cyclic $C_7H_{14}O$ alcohol isomers having a cyclohexane ring and a methyl group. (Hint: Adapt the method described in Worked Example 12.12 to arrive at your answers.)

(b) Identify all chiral centers in the isomers that you drew for part (a).

14.74 Using the alcohol shown, draw all the possible alkenes that might be formed on its dehydration. Which do you think will be the major product(s)? Which do you think will be the minor product(s)? It is alright to have more than one major and minor product.



14.75 Using the alcohol shown, draw all the possible alkenes that might be formed on its dehydration. Which alkenes can exist as cis–trans isomers? Draw them, in both condensed and line structure, and identify each as cis or trans. Explain your choices.



15

Aldehydes and Ketones

CONTENTS

CONCEPTS TO REVIEW

A. Electronegativity and Molecular Polarity (Sections 4.9 and 4.10)
B. Oxidation and Reduction (Section 5.6)
C. Hydrogen Bonds (Section 8.2)
D. Functional Groups (Section 12.2)
E. Naming Alkanes (Section 12.6)
F. Types of Organic Reactions (Section 13.5)

▲ Isolated from the bark of the Pacific Yew is the carbonyl-containing compound paclitaxel, which may lead to new medicines in cancer chemotherapy.

Many intricate biological processes, such as the reproduction of a cell, are regulated by increasingly complex molecules that contain many different functional groups, ketones and aldehydes included. As an outcome of this, the medicines needed to treat diseases have become more and more complicated. Nowhere is this more evident than in the drugs needed to treat cancer. A well-known adage in medicine is "the dose makes the poison," and these drugs embody this better than any others. Chemotherapy relies on

the use of molecules that are not only complicated but toxic as well, blurring the line between a drug and a toxin. While there are five general categories of chemotherapeutic agents, the newest of these, the mitotic inhibitors, seem to be among the most promising as they primarily affect rapidly dividing cells. These compounds prevent mitosis, the part of the cell cycle during which chromosomes are duplicated and separated into two identical sets of chromosomes, each in its own nucleus. Two members of this class of compounds contain the ketone functional group. One of these, paclitaxel, was originally isolated from the bark of the Pacific Yew tree and has shown much promise in the treatment of a number of solid tumor cancers. We will discuss the difference between a drug and a toxin, as well as chemotherapy, in the Chemistry in Action "When Is Toxicity Beneficial?" found at the end of this chapter.

Paclitaxel contains the carbonyl group (C═O); this functional group is found in many important and biologically significant molecules, including the carbohydrates (Chapter 20). In this chapter and Chapter 17, we will study the families of compounds that contain this functional group, beginning with the two simplest families of carbonyl compounds, the *aldehydes* and *ketones.*

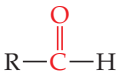
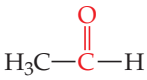
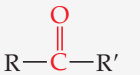
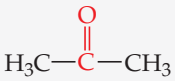
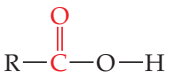
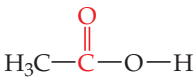
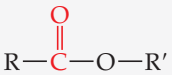
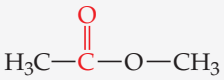
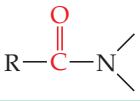
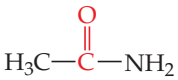
15.1 The Carbonyl Group

Learning Objective:

- Identify a carbonyl group and describe its polarity and shape.

The presence of a **carbonyl group** (C═O) distinguishes **carbonyl compounds** from other organic compounds; carbonyl compounds are then classified according to what is bonded to the carbonyl carbon, as illustrated in Table 15.1.

Table 15.1 General Classes of Carbonyl Compounds

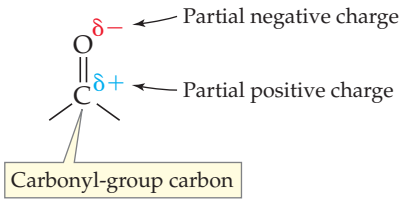
Family Name	Structure	Example	
Aldehyde			Acetaldehyde
Ketone			Acetone
Carboxylic acid			Acetic acid
Ester			Methyl acetate
Amide			Acetamide

Since oxygen is more electronegative than carbon, carbonyl groups are strongly polarized, with a partial positive charge on the carbon atom and a partial negative charge on the oxygen atom. The polarity of the carbonyl group contributes to its reactivity.

Chemists find it useful to divide carbonyl compounds into two major groups based on their chemical properties. In one group are the **aldehydes** and **ketones,** which have similar properties because their carbonyl groups are bonded to atoms that do not attract electrons strongly—carbon and hydrogen. In the second group are *carboxylic acids, esters,* and *amides* (the *carboxyl* family). The carbonyl-group carbon in these compounds is bonded to an atom (other than carbon or hydrogen) that *does* attract electrons strongly, typically an oxygen or nitrogen atom. This second group of carbonyl-containing compounds is discussed in Chapter 17.

Carbonyl group A functional group that has a carbon atom joined to an oxygen atom by a double bond.

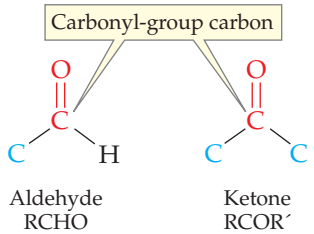
Carbonyl compound Any compound that contains a carbonyl group (C═O).



CONCEPTS TO REVIEW Remember that electronegativity is the ability of an atom to attract electrons to itself (see Figure 4.6).

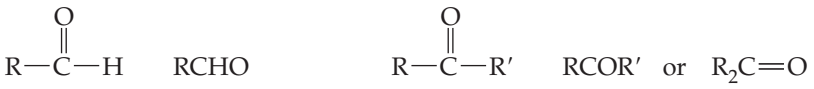
Aldehyde A compound that has a carbonyl group bonded to at least one hydrogen, RCHO.

Ketone A compound that has a carbonyl group bonded to two carbons in organic groups that can be the same or different, $R_2C{=}O$, RCOR′.



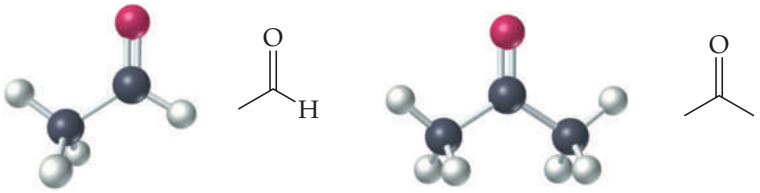
There are various ways of representing carbonyl compound structures on paper. All carbonyl groups are planar (or flat). The bond angles between the three substituents on the carbonyl carbon atom are 120° or close to it. Because of this trigonal planar arrangement of atoms around the carbonyl group, the bonds of the carbonyl carbon are often drawn at 120° angles to remind us that such angles are present in the molecules. Structures like those in Table 15.1, on the other hand, which emphasize the location of the double bond, do not fit well on a single line of type, so the simplified formulas shown next are often used for aldehydes and ketones.

Aldehydes *Ketones*



For example,

120° angles, in a trigonal planar



CH_3CHO
Acetaldehyde
(Ethanal)

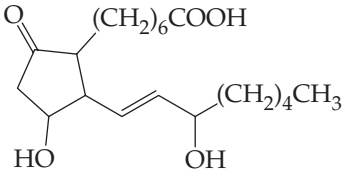
CH_3COCH_3
Acetone
(Propan-2-one)

The aldehyde group, you will notice, can only be connected to one carbon atom and therefore is always at the end of a carbon chain (—CHO is the common abbreviation for the aldehyde functional group; be careful not to confuse it with an alcohol, which you may see written as —COH). In line structure format, the aldehyde H must be explicitly shown. The ketone group, by contrast, must be connected to two carbon groups, and thus always occurs within a carbon chain.

PROBLEM 15.1

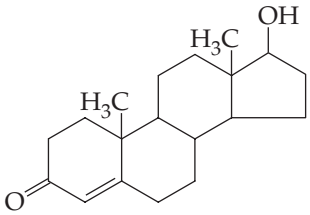
Which of the following molecules contain aldehyde or ketone functional groups? You may want to refer to Table 15.1, Table 12.1, and Figure 15.3 to help in your identification. Copy the formulas and circle these functional groups.

(a)



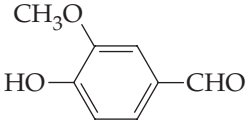
Prostaglandin E_1

(b)



Testosterone
(a male hormone)

(c)



Vanillin
(a flavoring agent)

(d) $C_4H_9COCH_3$

(e) C_4H_9CHO

LOOKING AHEAD Aldehyde or ketone groups are present in biomolecules with a wide range of functions, from the steroid hormones that regulate sexual function (Section 28.5), to the carbohydrate backbones that are essential to nucleic acids and the genetic code (Section 26.2). Most distinctively, the structure and reactions of aldehydes and ketones are fundamental to the chemistry of carbohydrates, those in our diet and those that provide energy and structure to our bodies (Chapters 20, 21, and 22).

PROBLEM 15.2

Draw the structures of compounds (d) and (e) in Problem 15.1 to show all individual atoms and all covalent bonds. Assume that all carbons are connected in a continuous chain. Redraw each in line structure format.

15.2 Naming Simple Aldehydes and Ketones

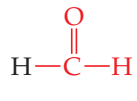
Learning Objective:

- Name and draw simple aldehydes and ketones given a structure or a name.

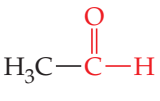
The aldehyde and ketone functional groups are typically found in molecules that contain more than one functional group. As a result, we will limit our discussion of nomenclature to only the simplest of aldehydes and ketones, focusing on the common names wherever possible.

The simplest aldehydes have common names, which end in *aldehyde;* for example, formaldehyde, acetaldehyde, and benzaldehyde. To name aldehydes systematically in the International Union of Pure and Applied Chemistry (IUPAC) system, the final *-e* of the name of the parent alkane is replaced by *-al.* The three-carbon aldehyde derived from propane is named systematically as propanal, the four-carbon aldehyde as butanal, and so on. When substituents are present, the chain is numbered beginning with 1 for the carbonyl carbon, as illustrated next for 3-methylbutanal.

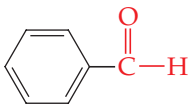
Aldehydes



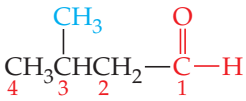
Formaldehyde



Acetaldehyde



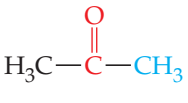
Benzaldehyde



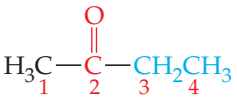
3-Methylbutanal

Most simple ketones are best known by common names that use the names of the two alkyl groups bonded to the carbonyl carbon followed by the word *ketone*—for example, methyl ethyl ketone, shown next. An exception to this common-name scheme is seen for the simplest ketone, acetone. Ketones are named systematically by adding *-one* (pronounced own) to the alkane name. The numbering of the alkane chain begins at the end nearest the carbonyl group. As shown here for butan-2-one and pentan-2-one, the location of the carbonyl group is indicated by placing the number of the carbonyl carbon in front of the *-one* suffix. Using this nomenclature scheme, acetone would be named propan-2-one.

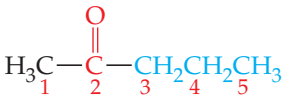
Ketones



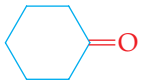
Acetone
(Propan-2-one)



Methyl ethyl ketone
(Butan-2-one)



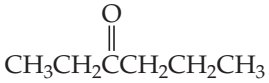
Methyl propyl ketone
(Pentan-2-one)



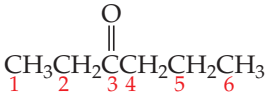
Cyclohexanone

Worked Example 15.1 Naming a Ketone Given Its Structure

Give both the systematic (IUPAC) name and the common name for the following compound:



ANALYSIS The compound is a ketone, as shown by the single carbonyl group bonded to two alkyl groups: an ethyl group on the left (CH_3CH_2-) and a propyl group on the right ($-CH_2CH_2CH_3$). The IUPAC system identifies and numbers carbon chains to indicate where the carbonyl group is located, counting in the direction that gives the carbonyl carbon the lowest number possible.



The common name uses the names of the two alkyl groups.

SOLUTION

The IUPAC name is hexan-3-one. The common name is ethyl propyl ketone.

PROBLEM 15.3

Draw structures corresponding to the following names:

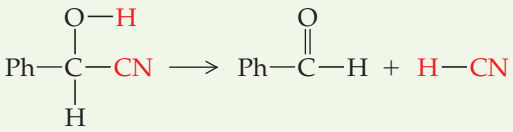
(a) Octanal
(b) Methyl phenyl ketone
(c) 4-Methylhexanal
(d) Methyl *tert*-butyl ketone

CHEMISTRY IN ACTION

Chemical Warfare among the Insects

Life in the insect world is a jungle. Predators abound, just waiting to make a meal of any insect that happens along. To survive, insects have evolved extraordinarily effective means of chemical protection. Take the humble millipede *Apheloria corrugata*, for example. When attacked by ants, the millipede protects itself by discharging benzaldehyde cyanohydrin.

In the laboratory, cyanohydrins [RCH(OH)C≡N] are formed by addition of the toxic gas HCN (hydrogen cyanide) to ketones or aldehydes, not unlike the addition of HCl or H_2O to alkenes (Section 13.6 and Mastering Reactions: Carbonyl Additions on p. 527). The reaction with HCN to yield a cyanohydrin is reversible, just like the reaction of a ketone or aldehyde with an alcohol to yield a hemiacetal, as we'll see in Section 15.7. Thus, the benzaldehyde cyanohydrin secreted by the millipede decomposes to yield benzaldehyde and HCN. This action protects the millipede because while the cyanohydrin itself is safe, the decomposition reaction releases deadly hydrogen cyanide gas, a remarkably clever and very effective kind of chemical warfare.



▲ The beautifully colored millipede *Apheloria corrugata* can produce as much as 0.6 mg of HCN to defend itself against attacks.

CIA Problem 15.1 Draw the structures of the cyanohydrins expected to be formed when HCN is added to compounds (a) and (b) in Problem 15.4.

CIA Problem 15.2 HCN is quite toxic. How do you suppose the millipede uses this weapon without killing itself?

PROBLEM 15.4

Give systematic, IUPAC names for the following compounds. Redraw each in line structure format.

(a) $CH_3CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}H$
(b) $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_3$
(c) $CH_3CH_2\overset{\overset{CH_3}{|}}{C}HCH_2CH_2\overset{\overset{O}{\|}}{C}H$
(d) Dipropyl ketone

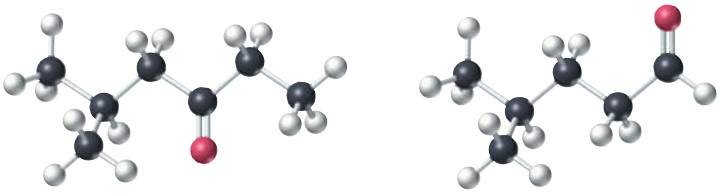
PROBLEM 15.5

Draw the line structures and provide common names for the following ketones:

(a) 1-Phenylpropanone
(b) 2-Methylpentan-3-one
(c) 1-Cyclohexyl-3,3-dimethylbutan-2-one

KEY CONCEPT PROBLEM 15.6

Which of these two molecules is a ketone and which is an aldehyde? Write the condensed and line structure formulas for both of them.



15.3 Properties of Aldehydes and Ketones

Learning Objective:

- Describe the polarity, hydrogen bonding, and water solubility of aldehydes and ketones.

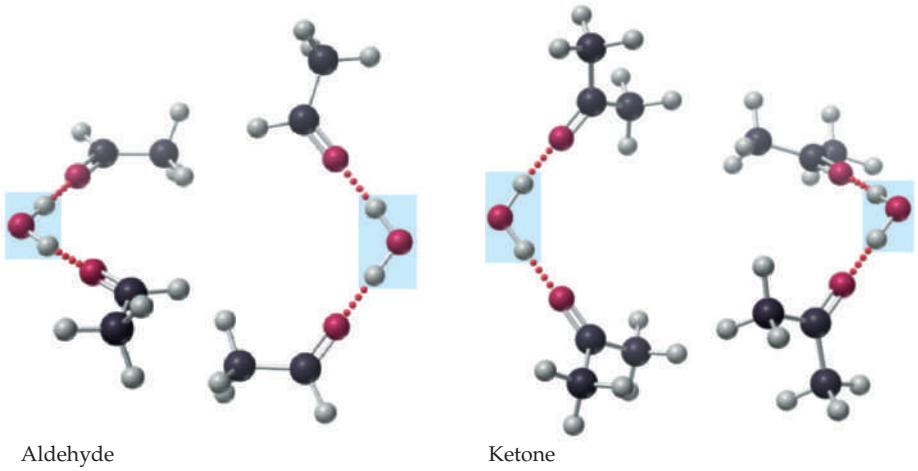
The polarity of the carbonyl group makes aldehydes and ketones moderately polar compounds (Section 15.1). As a result, they boil at a higher temperature than alkanes with similar molecular masses. Since they have no hydrogen atoms bonded to oxygen or nitrogen, individual molecules do not hydrogen bond with each other, which makes aldehydes and ketones lower boiling than alcohols. In a series of compounds with similar molecular masses, the alkane is lowest boiling, the alcohol is highest boiling, and the aldehyde and ketone fall in between.

$CH_3CH_2CH_2CH_3$	$CH_3CH_2C(=O)H$	$CH_3C(=O)CH_3$	$CH_3CH_2CH_2OH$
Butane	Propanal	Acetone	Propanol
(bp 0 °C (273 K))	(bp 50 °C (323 K))	(bp 56 °C (329 K))	(bp 97 °C (370 K))

Formaldehyde (HCHO), the simplest aldehyde, is a gas; acetaldehyde (CH_3CHO) boils close to room temperature. The other simple aldehydes and ketones are liquids and those with more than 12 carbon atoms are solids. The lower-boiling aldehydes and ketones are flammable and can form explosive mixtures with air.

Aldehydes and ketones are soluble in common organic solvents, and those with fewer than four carbon atoms show significant solubility in water because they are able to accept hydrogen bonds from water molecules (Figure 15.1). Once again, as in the case of alcohols, as the number of carbons compared to oxygens increases, the solubility decreases (Section 14.3). This is even more dramatic with ketones and aldehydes; while alcohols have the ability to both accept and donate hydrogen bonds with water, ketones and aldehydes can only accept them.

◀◀ Since solubility in a solvent requires the molecule to be completely surrounded by that solvent, as the hydrophobic portion of the molecule becomes larger, the ability of water to solvate it decreases (Section 14.3).



Aldehyde Ketone

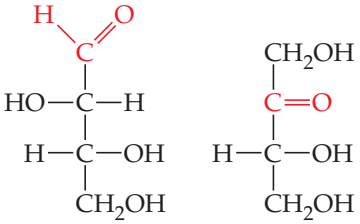
◀ Figure 15.1
Hydrogen bonding with water (highlighted in blue) of an aldehyde (CH_3CHO) and a ketone (CH_3COCH_3). The dotted red lines indicate the hydrogen bond formed between the carbonyl group oxygen and the hydrogen of water.

Simple ketones are excellent solvents because they dissolve both polar and nonpolar compounds. With increasing numbers of carbon atoms, aldehydes and ketones become more alkane-like and less water-soluble.

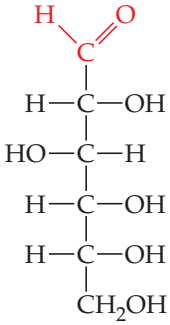
Properties of Aldehydes and Ketones

- Aldehyde and ketone molecules are polar due to the presence of the carbonyl group.
- Since aldehydes and ketones cannot hydrogen bond with one another, they have lower boiling points than alcohols but higher boiling points than alkanes because of dipole–dipole interactions (Section 8.2).
- Common aldehydes and ketones are typically liquids.
- Simple aldehydes and ketones are water-soluble due to hydrogen bonding with water molecules, and ketones are good solvents for many polar and nonpolar solutes.
- Many aldehydes and ketones have distinctive odors.
- Simple ketones are less toxic than simple aldehydes.

In the biochemistry chapters that lie ahead, you will find that all of the simplest sugars—the monosaccharides (Section 20.4)—contain either an aldehyde group or a ketone group. Glucose, the 6-carbon sugar shown below, plays a major role in metabolism as the primary fuel molecule for energy generation (Section 22.2).



Aldehyde and ketone 4-carbon sugars



Glucose

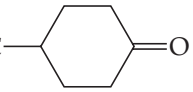
KEY CONCEPT PROBLEM 15.7

For each compound shown next (a–d), indicate whether the compound is polar or nonpolar, and whether it is soluble or insoluble in water.

(a) $CH_3CCH_2CH_3$ (O)

(b) CH_3CH_2CH (O)

(c) $CH_3CH_2CH_2CH_2CH_3$

(d) 

KEY CONCEPT PROBLEM 15.8

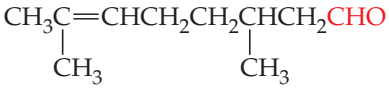
Why do aldehydes and ketones have lower boiling points than alcohols with similar molecular masses? Why are their boiling points higher than those of alkanes with similar molecular masses?

15.4 Some Common Aldehydes and Ketones

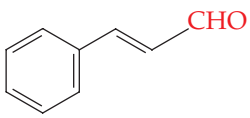
Learning Objective:

- Identify common aldehydes and ketones and their uses.

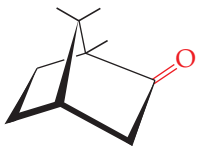
Many aromas and flavors derive largely from naturally occurring aldehydes and ketones. Some examples are carvenone (dill oil), fenchone (fennel oil), junionone (juniper berry oil), piperitone (eucalyptus oil), citronellal (lemon oil), vanillin (vanilla), and cinnamaldehyde (cinnamon). The structures of a few naturally occurring aldehydes and ketones with distinctive odors are shown next; all are used in soaps, cosmetics, and perfumes.



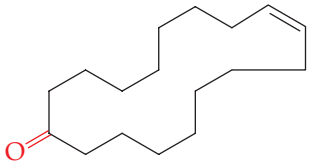
Citronellal (insect repellant, also used in perfumes; from citronella and lemon grass oils)



Cinnamaldehyde (cinnamon flavor in foods, drugs; from cinnamon bark)



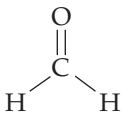
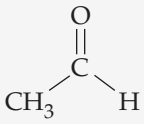
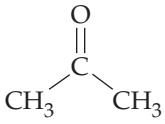
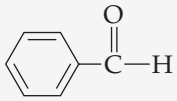
Camphor (moth repellant from camphor tree)



Civetone (musky odor in perfumes; from the scent gland of the civet cat)

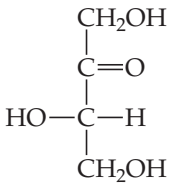
Chemically, the aldehyde and ketone functional groups are used as starting points for the synthesis of many complex organic molecules and pharmaceuticals, such as the anticancer drugs discussed in the Chemistry in Action "When Is Toxicity Beneficial?" at the end of the chapter. Four of the most common aldehydes and ketones used industrially are formaldehyde, acetaldehyde, acetone, and benzaldehyde; Table 15.2 shows their properties and uses.

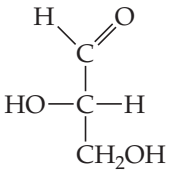
Table 15.2 Common Aldehydes and Ketones and Their Uses.

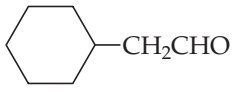
Common Name	Structure	Properties and Uses
Formaldehyde (Methanal, HCHO)		• Colorless gas with a pungent, suffocating odor; commonly sold as an aqueous solution under the name *formalin.* • Low concentrations in the air can cause eye, throat, and bronchial irritation, and higher concentrations can trigger asthma attacks. Skin contact can produce dermatitis. • Formed during incomplete combustion of hydrocarbon fuels; partly responsible for the irritation caused by smog. • Formaldehyde is very toxic by ingestion; can cause kidney damage and death. • Formed when methanol is broken biochemically; one reason methanol is so toxic. • Once commonly used as a preservative for biological specimens. • Major industrial use of formaldehyde is in the production of polymers used as adhesives for binding plywood, foam insulation for buildings, textile finishes, and hard and durable manufactured objects. • Because of concern over the toxicity and possible carcinogenicity of formaldehyde from polymeric materials, their use in most household applications is limited.
Acetaldehyde (Ethanal, CH_3CHO)		• Sweet-smelling, flammable liquid. • Present in ripe apples and other fruits; formed by the oxidation of ethanol. • Less toxic than formaldehyde; large doses can cause respiratory failure. • Chronic exposure produces symptoms like those of alcoholism. • Small amounts are produced in the normal breakdown of carbohydrates (Chapter 20). • Used historically in the production of acetic acid and acetic anhydride (Chapter 17). • Used industrially for the preparation of polymeric resins and as a reagent used in the silvering of mirrors.
Acetone (CH_3COCH_3)		• Highly volatile liquid; a serious fire and explosion hazard when allowed to evaporate in closed spaces. • One of the most widely used of all organic solvents. • Dissolves most organic compounds and is miscible with water. • No chronic health risk associated with casual acetone exposure. • Sold for general-purpose cleanup work in home improvement stores. • Used as a solvent in many varnishes, lacquers, and nail polish removers. Produced in the liver when the biochemical breakdown of fats and carbohydrates is out of balance (ketosis; Section 24.7).
Benzaldehyde (PhCHO)		• Simplest aromatic aldehyde. • Colorless liquid; pleasant almond or cherry-like odor; first extracted from bitter almonds. • Used as a flavoring and fragrance in food, cosmetics, pharmaceuticals, and soap and is "generally regarded as safe" by the Food and Drug Administration (FDA). • Used industrially as a forerunner to other organic compounds, ranging from pharmaceuticals to plastic additives.

KEY CONCEPT PROBLEM 15.9

Identify the functional groups in the following compounds:

(a) 

(b) 

(c) 

(d) $H_2NCH_2CH_2COCH_3$

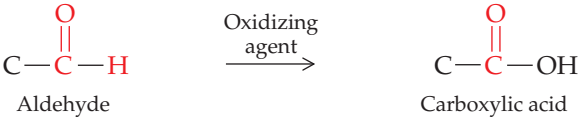
15.5 Oxidation of Aldehydes

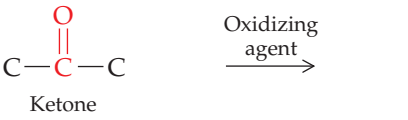
Learning Objective:

- Identify the products formed from the oxidation of aldehydes (and see that ketones do not oxidize in the same way).

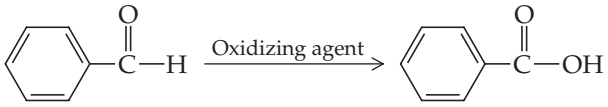
Alcohols can be oxidized to aldehydes or ketones (Section 14.6), and aldehydes can be further oxidized to carboxylic acids. In aldehyde oxidation, the hydrogen bonded to the carbonyl carbon (shown in gold) is replaced by an —OH group. Ketones, because they do not have this hydrogen, do not react cleanly with oxidizing agents (except with those strong enough to destroy the molecule).

Oxidation of aldehydes and ketones





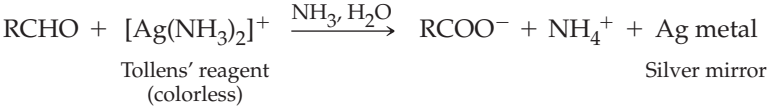
For example,



Of the mild oxidizing agents that convert aldehydes to carboxylic acids, oxygen in the air is the simplest. Aldehydes typically have a musty odor due to their partial oxidation to carboxylic acids, which generally have a strong, unpleasant odor. To prevent air oxidation, aldehydes are often stored under a layer of nitrogen gas, limiting contact with oxygen in the air.

Because ketones cannot be oxidized, treatment with a mild oxidizing agent is used as a test to distinguish between aldehydes and ketones. *Tollens' reagent,* which consists of a solution containing silver ion in aqueous ammonia, is the most visually appealing oxidizing agent for aldehydes. Treatment of an aldehyde with this reagent, in which the Ag^+ ion (present as $[Ag(NH_3)_2]^+$) is the oxidizing agent, rapidly yields the carboxylic acid anion and metallic silver. If the reaction is done in a clean glass container, metallic silver deposits on the inner walls, producing a beautiful shiny mirror (Figure 15.2a). Before modern instrumental methods were available, chemists had to rely on such visible chemical changes to identify chemical compounds.

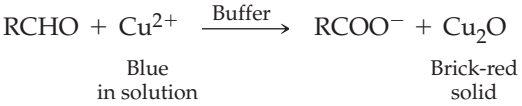
Tollens' test

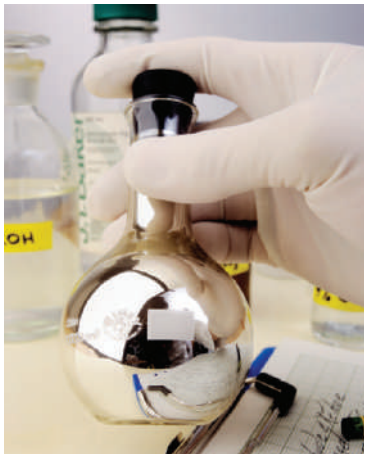


A test with another mild oxidizing agent, known as *Benedict's reagent,* also relies on reduction of a metal ion to produce visible evidence of the presence of aldehydes. The reagent solution contains blue copper(II) ion, which is reduced to give a precipitate of red copper(I) oxide in the reaction with an aldehyde (Figure 15.2b). Unlike the Tollens' test, however, Benedict's reagent does not unequivocally distinguish between ketones and aldehydes, as it will also produce a positive result in the presence of ketones that have an —OH on the carbon next to the carbonyl (*alpha* hydroxy ketones), a common grouping of atoms found in sugars. As with aldehydes, a red copper(I) precipitate is evidence of the presence of these ketones. As a result, a negative Tollens' test and a positive Benedict's test will allow one to distinguish between these two biologically important functional groups.

At one time, Benedict's reagent was extensively used as a test for sugars in the urine, which are primarily aldehydes and *alpha* hydroxy ketones. Today, more specific and more sensitive enzyme-based tests are preferred (see the Chemistry in Action "Diagnosis and Monitoring of Diabetes" on p. 742 in Chapter 22).

Benedict's test





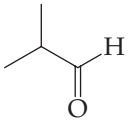
(a)

(b)

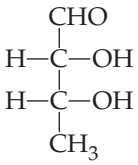
▲ Figure 15.2
The Tollens' and Benedict's tests for aldehydes.
(a) In the Tollens' test, colorless silver ion (Ag^+) is reduced to metallic silver. (b) In the Benedict's test for aldehyde-containing sugars, the blue copper(II) ion (Cu^{2+} tube on left) is reduced to copper(I) to give brick-red copper(I) oxide (Cu_2O, tube on right). Glucose was used to produce the brick-red precipitate on the right. In both tests, an aldehyde is oxidized to the carboxylic acid anion.

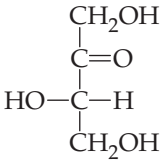
PROBLEM 15.10

Indicate whether the following compounds will give a positive or negative result when treated with (i) Tollens' reagent or (ii) Benedict's reagent.

(a) 

(b) Cyclohexanone

(c) 

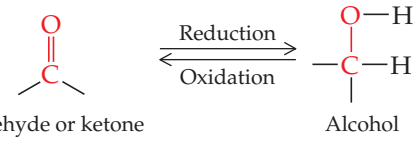
(d) 

15.6 Reduction of Aldehydes and Ketones

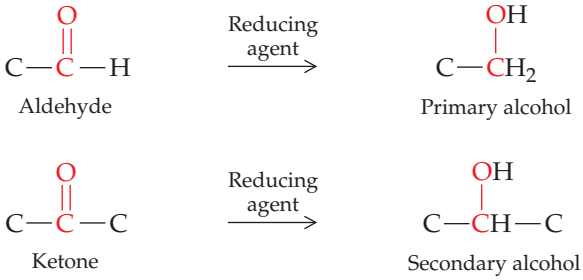
Learning Objective:

- Identify the products of the reduction of aldehydes and ketones.

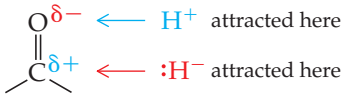
The reduction of a carbonyl group occurs with the addition of hydrogen across the double bond to produce an —OH group, a reaction that is the reverse of the oxidation of an alcohol.



Aldehydes are reduced to primary alcohols, and ketones are reduced to secondary alcohols.

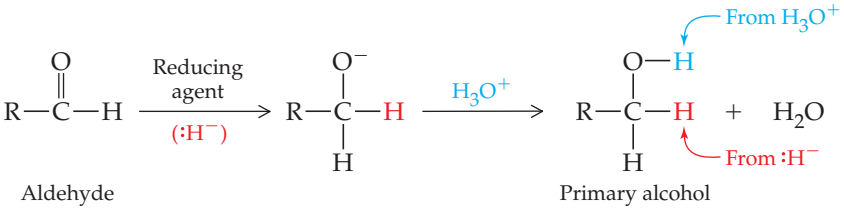


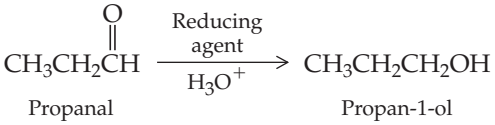
These reductions occur by formation of a bond to the carbonyl carbon atom by a hydride ion ($:H^-$) accompanied by bonding of a hydrogen ion (H^+) to the carbonyl oxygen atom. The reductions make good sense when you think about the polarity of the carbonyl group. The carbonyl-group carbon has a partial positive charge because electrons are drawn away by the electronegative oxygen atom, so the negatively charged hydride ion is drawn to this carbon atom. Because the oxygen atom has a partial negative charge, the positively charged hydrogen atom is attracted there.



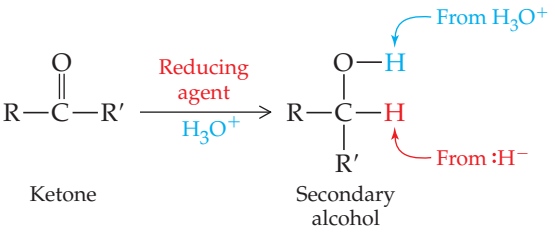
Note that a hydride ion ($:H^-$) has a lone pair of valence electrons. Both electrons are used to form a covalent bond to the carbonyl carbon. This change leaves a negative charge on the carbonyl oxygen. Aqueous acid is then added, H^+ bonds to the oxygen, and a neutral alcohol results. Thus, the two new hydrogen atoms in the alcohol product come from different sources.

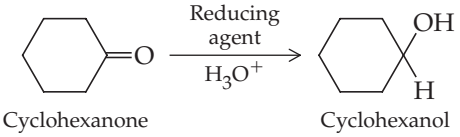
Reduction of an aldehyde





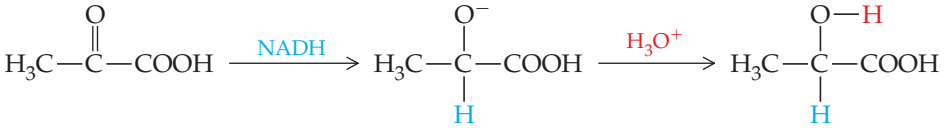
Reduction of a ketone





In biological systems, the reducing agent for a carbonyl group is often the coenzyme nicotinamide adenine dinucleotide (abbreviated as NAD), which cycles between reacting as a reducing agent (NADH) and an oxidizing agent (NAD^+) by the loss and gain of a hydride ion ($:H^-$). The biochemical reduction of pyruvic acid, a ketone-containing acid that plays a pivotal role in energy production, utilizes NADH. The reaction occurs in active skeletal muscles. Vigorous exercise causes a buildup of the reduction product, lactic acid, which can irritate muscles and cause discomfort and soreness.

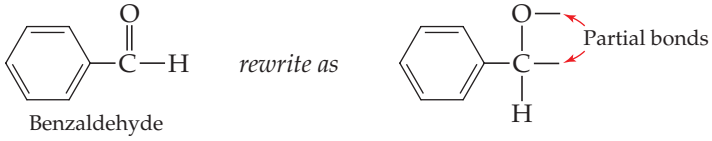
The reduction of aldehydes and ketones to alcohols is an important reaction in living cells, and NADH is the common source of the hydride ion. It donates H^- to an aldehyde or ketone to yield an anion, which then picks up H^+ from surrounding aqueous fluids. The major role of NADH as a biochemical reducing agent is introduced in Section 21.7 and the transformation of pyruvate to lactate will be discussed in Section 22.5.



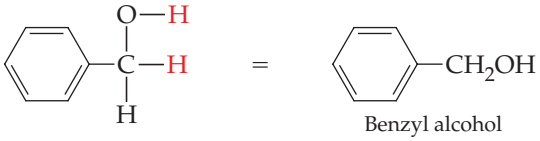
Worked Example 15.2 Writing the Products of a Carbonyl Reduction

What product would you obtain by reduction of benzaldehyde?

ANALYSIS First, draw the structure of the starting material, showing the double bond in the carbonyl group. Then rewrite the structure showing only a single bond between C and O, along with partial bonds to both C and O.



Finally, attach hydrogen atoms to the two partial bonds and rewrite the product.



SOLUTION

The product obtained is benzyl alcohol.

PROBLEM 15.11

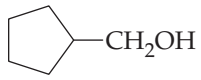
Draw line structures of the following compounds and the product you would obtain from the reduction of each.

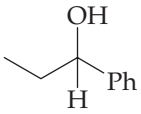
(a) Isopropyl methyl ketone **(b)** *p*-Hydroxybenzaldehyde

(c) 2-Methylcyclopentanone

PROBLEM 15.12

What ketones or aldehydes might be reduced to yield the following alcohols?

(a) 

(b) 

(c) $HOCH_2—CH_2—CH_2OH$

15.7 Addition of Alcohols: Hemiacetals and Acetals

Learning Objectives:

- Identify the differences between hemiacetals, hemiketals, acetals, and ketals.
- Predict the products of hemiacetal, hemiketal, acetal, and ketal formation and their hydrolysis.

Hemiacetal and Hemiketal Formation

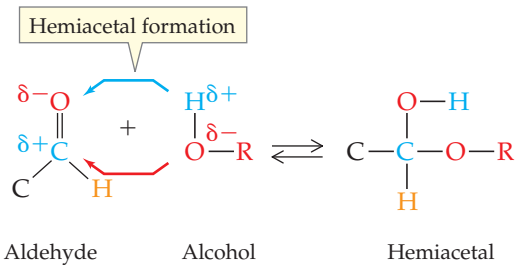
In Section 13.6, we discussed the addition of water to a carbon–carbon double bond to form alcohols. Similarly, aldehydes and ketones also undergo **addition reactions** in which an alcohol combines with the carbonyl carbon and oxygen. When this occurs with an aldehyde, the initial addition products are known as *hemiacetals*. **Hemiacetals** have both an alcohol-like —OH group and an ether-like —OR group bonded to what was once the carbonyl carbon atom of the aldehyde, forming a new chiral carbon. The H from the alcohol bonds to the carbonyl-group oxygen, and the OR from the alcohol bonds to the carbonyl-group carbon. When this reaction occurs with ketones, the initial addition products are known as **hemiketals.**

Addition reaction, aldehydes and ketones Addition of an alcohol or other compound to the carbon double bond to give a carbon–oxygen single bond.

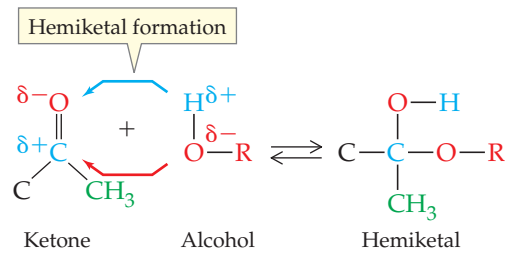
Hemiacetal A compound with both an alcohol-like —OH group and an ether-like —OR group bonded to the carbon atom that was at one time the aldehyde carbonyl carbon.

Hemiketal A compound with both an alcohol-like —OH group and an ether-like —OR group bonded to the carbon atom that was at one time the ketone carbonyl carbon.

Recall the concept of a chiral carbon was discussed in Section 14.10.



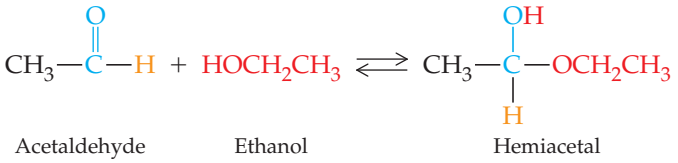
Aldehyde Alcohol Hemiacetal

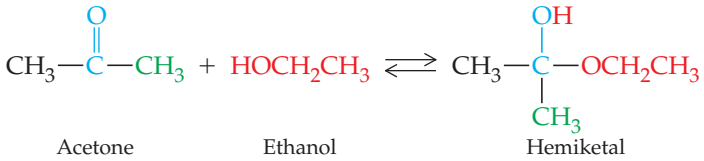


Ketone Alcohol Hemiketal

- *The negatively polarized alcohol oxygen atom adds to the positively polarized carbonyl carbon* (similar to what happens in reduction of the carbonyl group). Almost all carbonyl-group reactions follow this same polarity pattern.
- *The reaction is reversible.* Hemiacetals and hemiketals rapidly revert back to aldehydes or ketones by loss of alcohol and establish an equilibrium with the aldehyde or ketone.

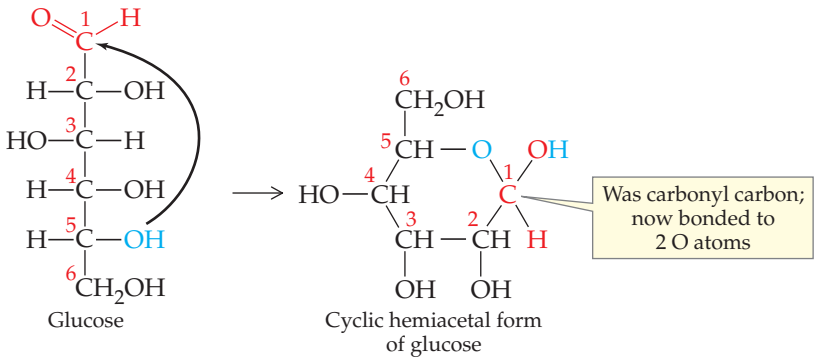
Ethanol (CH_3CH_2OH) forms a hemiacetal with acetaldehyde and a hemiketal with acetone as follows:

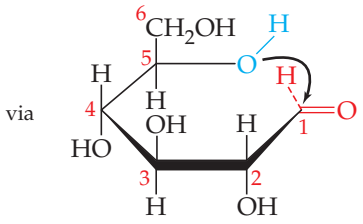




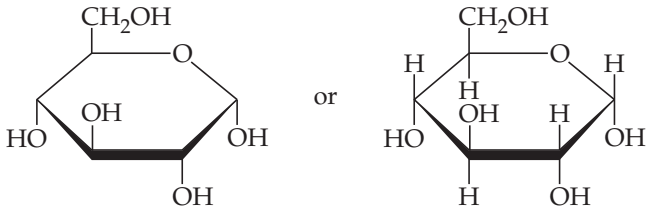
(For a more detailed look at how hemiacetals and acetals are formed, see Mastering Reactions: Carbonyl Additions on p. 527.)

In practice, hemiacetals and hemiketals are often too unstable to be isolated. When equilibrium is reached, very little of the hemi-species is present. A major exception occurs when the alcohol —OH and carbonyl —C═O functional groups that react are part of the *same* molecule. For thermodynamic reasons, the resulting *cyclic* hemiacetals or hemiketals are more stable than the noncyclic hemi-species. Because of their greater stability, most simple sugars exist mainly in the cyclic hemiacetal or hemiketal form, as shown next for glucose, rather than in the open-chain form shown below. This occurs when the carbohydrate "folds up" on itself, allowing the internal hemiacetal or hemiketal to form, again shown next for glucose.





The cyclic form of glucose is customarily written as



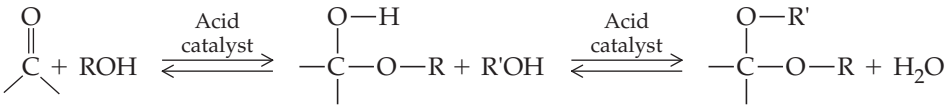
In Section 20.4, we will see the concept of anomers: cyclic isomers of a carbohydrate that differ in the spatial orientation of the —OH on what was originally the carbon of the C=O. This carbon will be called the anomeric carbon (see Problem 15.8).

Acetal and Ketal Formation

If a small amount of acid catalyst is added to the reaction of an alcohol with an aldehyde or ketone, the hemi-species initially formed is converted into an *acetal* or a *ketal* in a substitution reaction. An **acetal** is a compound that has *two* ether-like —OR groups bonded to what was the carbonyl carbon atom of an aldehyde (the two —OR groups can be different). A **ketal** is a compound that has *two* ether-like —OR groups bonded to what was the carbonyl carbon atom of a ketone.

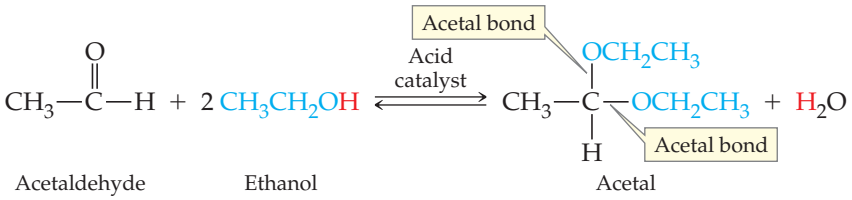
Acetal A compound that has two ether-like —OR groups bonded to the same carbon atom of what was once an aldehyde.

Ketal A compound that has two ether-like —OR groups bonded to the same carbon atom of what was once a ketone.

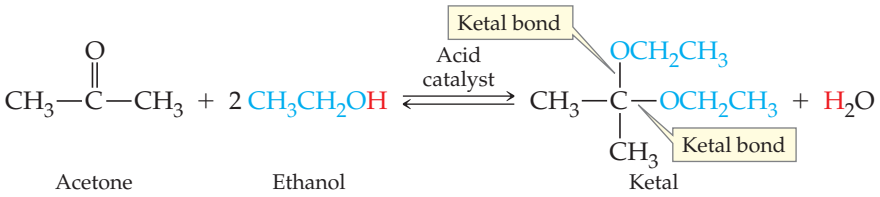


Aldehyde or ketone — Hemiacetal or hemiketal — Acetal or ketal

For example,



Acetaldehyde — Ethanol — Acetal

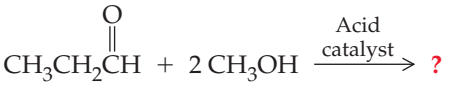


Acetone — Ethanol — Ketal

It is important to note that the current set of IUPAC guidelines discourages the use of the hemiketal and ketal labels and instead favors the use of hemiacetal and acetal for the products formed upon addition of alcohols to *both* aldehydes and ketones, thereby recognizing them more as functional groups than as specific addition products. While we will make a distinction in this chapter between the products obtained when alcohols add to an aldehyde versus a ketone, keep in mind that the reaction is identical in both cases.

Worked Example 15.3 Predicting the Products of Hemiacetal and Acetal Formation

Write the structure of the intermediate hemiacetal and the acetal final product formed in the following reaction:



—continued on next page

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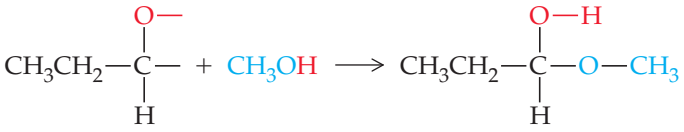
ANALYSIS First, rewrite the structure showing only a single bond between C and O, along with partial bonds to both C and O.

Next, add 1 molecule of the alcohol (CH_3OH in this case) by attaching —H to the oxygen partial bond and —OCH_3 to the carbon partial bond. This yields the hemiacetal intermediate.

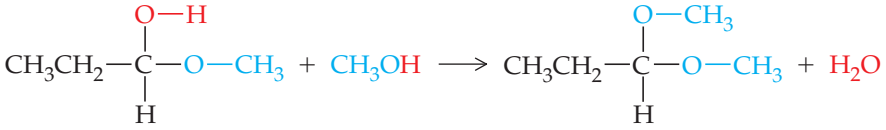


Hemiacetal

Finally, replace the —OH group of the hemiacetal with an —OCH_3 from a second molecule of alcohol.

SOLUTION

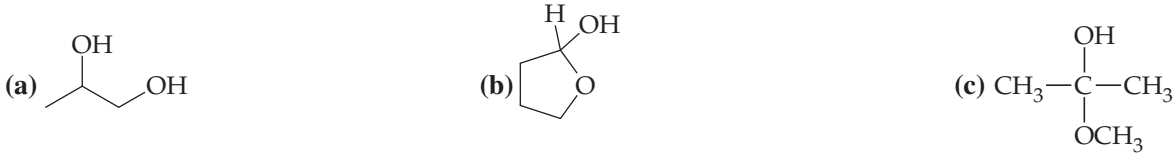
The reaction produces acetal and water.



Acetal

Worked Example 15.4 Identification of Hemiacetals and Hemiketals

Which of the following compounds are hemiacetals and which are hemiketals?



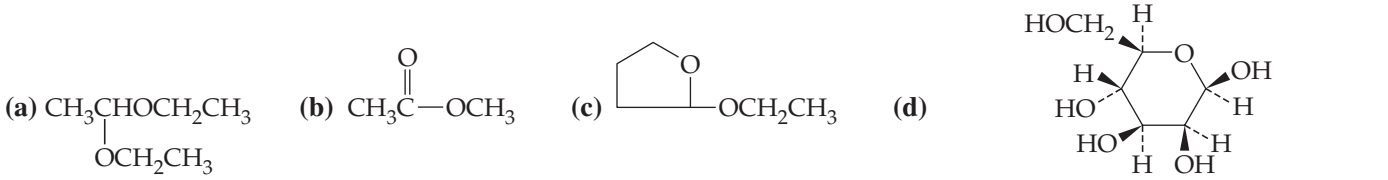
ANALYSIS To identify a hemiacetal or a hemiketal, look for a carbon atom with single bonds to two oxygen atoms, with one being an —OH group and one an —OR group. Note that the O of the —OR group can be part of a ring. If the two remaining groups are carbons, it is a hemiketal; if one is a carbon and the other a hydrogen, it is a hemiacetal.

SOLUTION

Compound (a) contains two O atoms, but they are bonded to *different* C atoms; it is not a hemiacetal; rather it is a diol. Compound (b) has one ring C atom bonded to two oxygen atoms, one in the substituent —OH group and one bonded to the rest of the ring, which is the R group; the other two groups bonded to that carbon are a H and another C; it is a cyclic hemiacetal. Compound (c) also contains a C atom bonded to one —OH group and one —OR group, but here the other two bonded groups are carbons, so (c) is a hemiketal.

Worked Example 15.5 Identification of Acetals and Ketals

Which of the following compounds are acetals and ketals?



Mannose
(a sugar found attached to proteins in humans)

ANALYSIS As in identifying hemiacetals and hemiketals, look for a carbon atom that has single bonds to two oxygen atoms, but in this case both of them will be —OR groups. Note that the O of the —OR group can be part of a ring. If the two remaining bonded groups are carbons, it is a ketal; if one is a carbon and the other a hydrogen, it is an acetal.

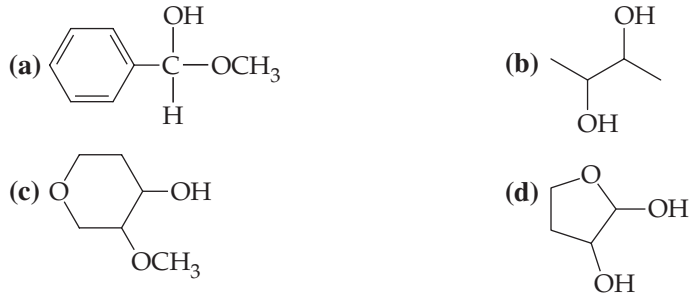
SOLUTION

In (a), the central carbon atom is bonded to one $-CH_3$, one —H, and *two* $-OCH_2CH_3$ groups, so the compound is an acetal. Compound (b) does have a carbon atom bonded to two oxygen atoms, but one of the bonds is a double bond rather than a single bond, so this is not an acetal (it is, in fact, an ester; Chapter 17). Compound (c) has an oxygen atom in a ring, making it also part of an —OR group, where R is the ring. Since one of the carbons connected to the O in the ring is also connected to an $-OCH_2CH_3$ group, compound (c) is an acetal. Compound (d) is a sugar known as mannose; it too has an oxygen atom in a ring, making it part of an —OR group, where R is the ring. Since one of the carbons connected to the O in the ring is also connected to a H and an OH, compound (d) is a hemiacetal.

It should be noted that cyclic systems of these types are the most difficult to recognize, yet they will be the ones you will see most often as you progress through biochemistry, so the more practice you get at recognizing these, the better! Anytime you see an oxygen in a ring, always look at the carbons attached to either side of it to see if one of them has another oxygen attached. If one of them does, you have a cyclic hemiacetal, hemiketal, acetal, or ketal.

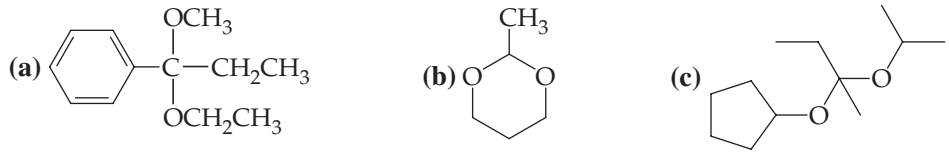
PROBLEM 15.13

For each compound shown next, determine whether it is a hemiacetal, a hemiketal, or neither.



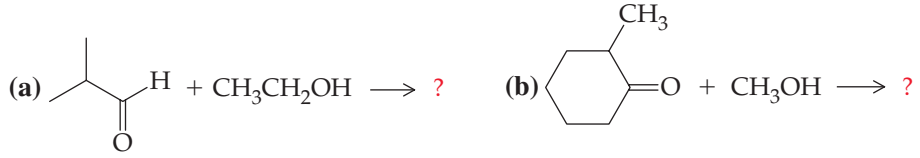
PROBLEM 15.14

Determine whether the following compounds are acetals or ketals. Draw the structure of the aldehyde or ketone it came from.



PROBLEM 15.15

Draw the structures of the hemiacetals or hemiketals formed in these reactions:

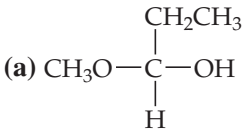


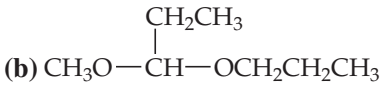
PROBLEM 15.16

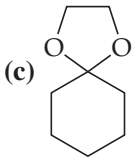
Draw the structure of each acetal or ketal final product formed in the reactions shown in Problem 15.15 if an excess of alcohol was used.

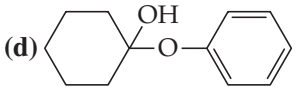
PROBLEM 15.17

For each compound shown next, determine whether it is a hemiacetal, a hemiketal, an acetal, or a ketal.



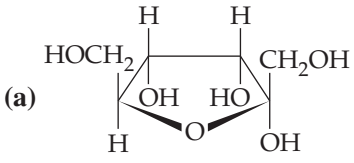




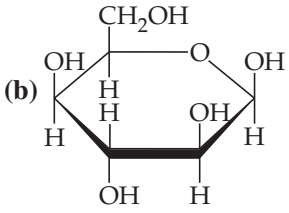


PROBLEM 15.18

Sugars (or carbohydrates, Chapter 20) form cyclic hemiacetals and hemiketals very readily; the carbon that is part of the hemiacetal or hemiketal linkage (and originally came from the C═O) is known as the *anomeric carbon* (Section 20.4). For each of the following, determine whether it is a hemiacetal or a hemiketal, and put a star on the anomeric carbon for each.



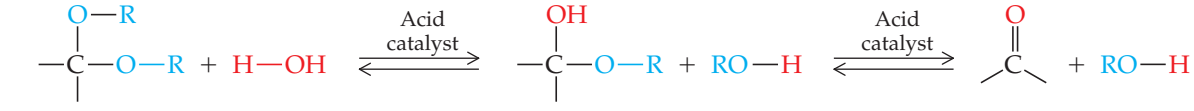
Tagatose



Idose

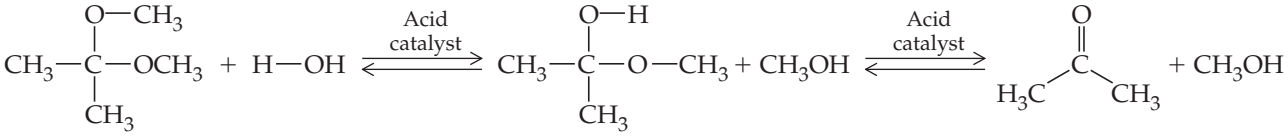
Acetal and Ketal Hydrolysis

Because acetal and ketal formation are equilibrium reactions, the extent to which the reaction proceeds in either direction can be controlled by changing the reaction conditions. Remember that water is one of the products formed during their formation; therefore, the aldehyde or ketone from which an acetal or ketal is formed can be regenerated by reversing the reaction. As a result, reversal simply requires an acid catalyst and a large quantity of water to drive the reaction back toward the aldehyde or ketone (Le Châtelier's principle, Section 7.9).



Acetal or Ketal | Hemiacetal or hemiketal | Aldehyde or ketone | Alcohol

For example,



The reaction shown earlier is an example of **hydrolysis** (*Greek*: "to split with water"), a reaction in which a bond or bonds are broken and the —H and —OH of water add to the atoms of the broken bond or bonds. With either an acetal or ketal, the first step is formation of the hemi-species as the water breaks one of the C—OR bonds and a C—OH bond is formed in its place. The carbonyl group is then formed as the bond to the H of the C—OH and the hemi-species C—OR bond is broken. The result is the ketone or aldehyde from which the acetal or ketal was made plus two molecules of the alcohol RO—H. A simple way for you to show the steps of this reaction is presented in Worked Example 15.6.

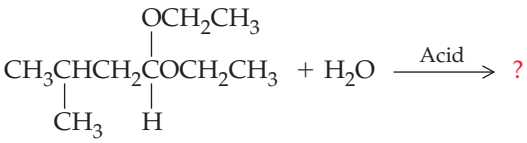
It should be noted that although acetals, ketals, hemiketals, and hemiacetals react with water in the presence of acid, they are unreactive under basic conditions (pH > 7), which is important since physiological pH is slightly greater than seven.

Hydrolysis A reaction in which a bond or bonds are broken and the H— and —OH of water add to the atoms of the broken bond or bonds.

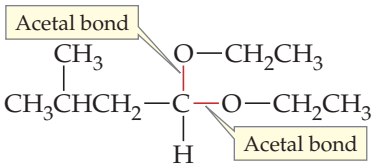
Consider for a moment that biochemical reactions take place in an environment where water molecules are always available, along with enzyme catalysts precisely suited to the necessary reactions. In this environment, it is not surprising that hydrolysis reactions play an important role. During digestion, hydrolysis breaks bonds in carbohydrates (Section 22.1), triacylglycerols (Section 24.1), and proteins (Section 25.1).

Worked Example 15.6 Writing the Products Obtained from Acetal Hydrolysis

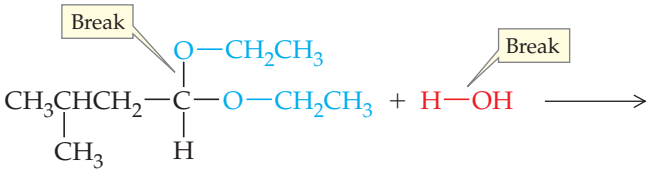
Write the structure of the aldehyde or ketone that forms by hydrolysis of the following acetal:



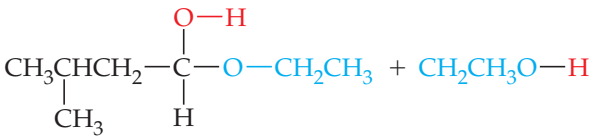
ANALYSIS The products are the aldehyde or ketone plus two molecules of the alcohol from which the acetal could have been formed. First, identify the two C—O acetal bonds, redrawing the structure if necessary.



Next, break the H—OH bond and one of the acetal C—OR bonds (in this case, it does not matter which one); move the water OH to the acetal carbon to form the hemiacetal and the water H to the OR to form one molecule of HOR.



Acetal

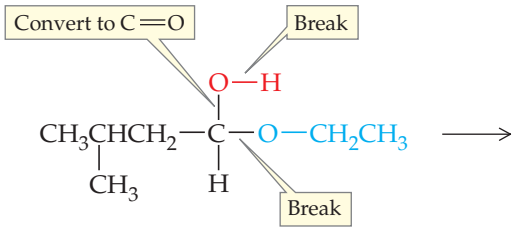


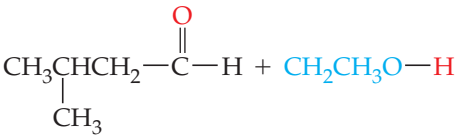
Hemiacetal

Remove the H and OR groups from the hemiacetal, and change the C—O single bond to a C=O double bond to give carbon the four bonds it must have. Combine the H and OR you removed from the second alcohol molecule.

—*continued on next page*

—continued from previous page





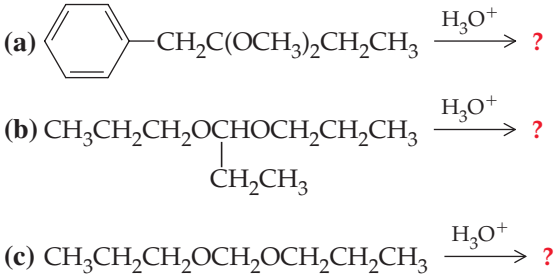
3-Methylbutanal

SOLUTION

In this example, the product is an aldehyde. The procedure is identical if you start with a ketal rather than an acetal.

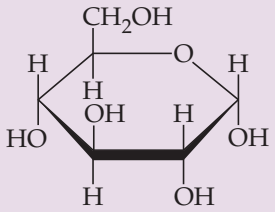
PROBLEM 15.19

What aldehydes or ketones result from the following hydrolysis reactions? What alcohol is formed in each case? It may help to redraw these in line structure format.

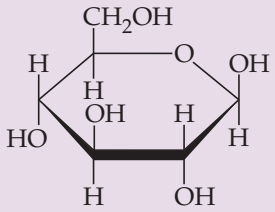


HANDS-ON CHEMISTRY 15.1

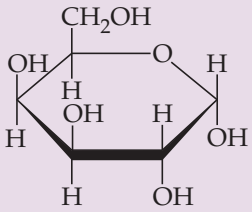
One of the more complex groups of molecules you will have to recognize and deal with are the carbohydrates (Chapter 20), which exist almost exclusively in their hemiacetal and hemiketal form. In this exercise, you are going to get a feel for them by building models of glucose, galactose, and fructose (the heavy ring bonds are meant to look like they are coming out toward you).



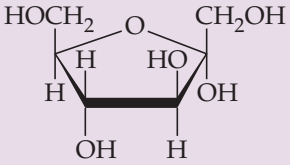
alpha-Glucose
(α-Glucose)



beta-Glucose
(β-Glucose)



alpha-Galactose
(α-Galactose)



alpha-Fructose
(α-Fructose)

You will be using the methods and techniques outlined in Hands-On Chemistry 13.1 (p. 444). For this exercise, you will be building what are known as *Haworth representations* of the molecules; that is to say that you will build the molecules as if the ring were flat (this is perfectly fine for the comparisons we will be doing here). Throughout this exercise, remember that carbon is tetravalent (four bonds); you will approximate the OH groups using a single gumdrop.

Building Blocks Needed for This Exercise—for this exercise, you will need the following (this will build four structures):

One box of toothpicks—round is best but any will do.

Nineteen carbon gumdrops—use either black or some other dark color, as long as they are different colors than those needed for other structures.

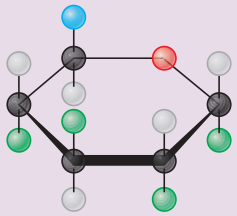
Four ring oxygen gumdrops—use red or orange. These will be used only when an oxygen is in a ring.

Fifteen "OH" gumdrops—use blue or green. You will use these to represent the OH groups that are attached to the ring.

Sixteen hydrogen gumdrops—use white or clear. You will use these to represent a H when it is attached to a ring carbon.

Five "CH_2OH" gumdrops—rather than building each CH_2OH unit needed, you will represent these using a single gumdrop. Use any color other than the ones you used earlier. We will use these to represent the OH groups.

Make the ring flat and all groups coming off of a ring carbon perpendicular to the ring. Based on this, your model of *alpha*-glucose should look like the following:



Once you have these assembled, you can begin. Be prepared to use more toothpicks and/or gumdrops if needed. You may want to take pictures of each model you make with your phone for review later.

a. Start by assembling *alpha*-glucose. How many chiral carbons does it have? (Review Section 14.10 if necessary.) Identify the hemiacetal carbon in this molecule.

b. Now, assemble *beta*-glucose. How many chiral carbons does it have? (Review Section 14.10 if necessary.) Identify the hemiacetal carbon in this molecule.

c. Now, compare *alpha*-glucose to *beta*-glucose. Are they mirror images? Use a small hand mirror to check if you are not sure. You should find that they are NOT mirror images; what carbon(s) have different configurations (orientation in space) in the two molecules? Two molecules with more than one chiral carbon that have the same configuration on all carbons EXCEPT the hemiacetal or hemiketal carbon one are known as *anomers,* and the hemiacetal or hemiketal carbon is said to be the *anomeric carbon*. Notice the spatial location of the OH on the anomeric carbon when compared to the CH_2OH attached to the ring. In carbohydrate chemistry, when these groups are on the same side of the ring they are said to be *beta;* when on opposite sides, they are said to be *alpha*.

d. Now, build *alpha*-galactose; how many chiral carbons does it have? Compare it to *alpha*-glucose; which carbon(s) have different configurations? Are these two molecules anomers? Two molecules with more than one chiral carbon that have the same configuration on all non-hemiacetal or hemiketal carbons EXCEPT one are known as *epimers.* An anomer is a special type of epimer.

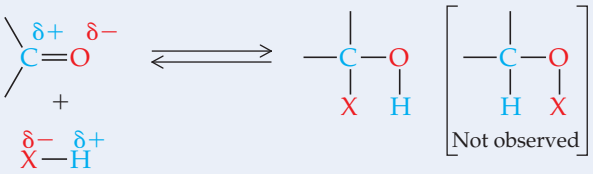
e. (Optional) Build the model of *alpha*-fructose. How many chiral carbons does it have? Can you identify the anomeric carbon? See if you can deduce what the structure of *beta*-fructose might look like.

MASTERING REACTIONS

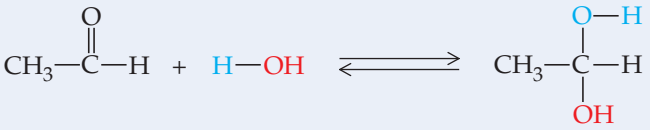
Carbonyl Additions

In Chapter 13, we learned how additions to carbon–carbon (C═C) double bonds occur (see Mastering Reactions: How Addition Reactions Occur on p. 456). We were able to predict the products by examining the initially formed intermediate (the carbocation) and evaluating its stability. This was necessary because there is no inherent preference for attack at one carbon over the other in an alkene. Now consider the carbon–oxygen double bond (C═O) of a carbonyl. A carbonyl has a natural polarity, and because it is also a double bond, its reactions should be similar to those of a C═C. Let's look closer at these additions.

A carbonyl is a polarized double bond (Section 15.1), such that the carbon carries a partial positive charge δ^+ and the oxygen carries a partial negative charge δ^-. As a result, there will always be a preference for how a similarly polarized reagent will add.



Thus, the electron-poor end (δ^+) of the reagent will *always* attach to the O of the carbonyl and the electron-rich end (δ^-) to the C. This process is also a true equilibrium and is governed by Le Châtelier's principle. So, in the presence of water one might expect the following to occur:



Carbonyl hydrate

The carbonyl hydrate formed is similar to the alcohol obtained when water adds across a C═C; unlike an alcohol, however, most carbonyl hydrates are impossible to isolate. The reason for this stems from Le Châtelier's principle: One must remove water to isolate the carbonyl hydrate, but the very act of doing so pushes the equilibrium back to the starting material side, the C═O. This points out an important difference in the two reactions: unlike alkenes, only a few addition products of carbonyls are stable enough to be isolated. Here, we will focus on the two most important reactions: addition of HCN and addition of alcohols (here, we concern ourselves exclusively with ketones and aldehydes; in Chapter 17, we will examine what happens if the C═O is part of a carboxyl group).

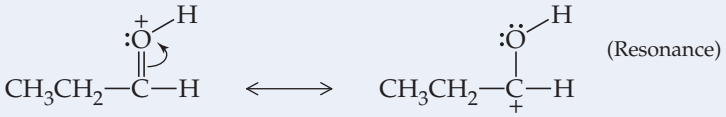
The mechanism for addition of methanol to propionaldehyde is shown next; it begins in the same manner as for a C═C. A trace

(*continued*)

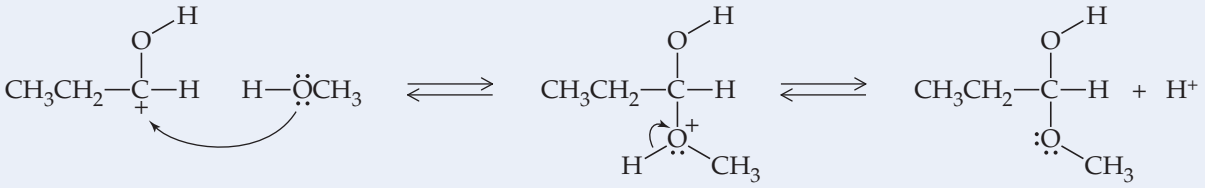
catalytic amount of acid protonates the carbonyl (Step 1), which is then activated toward addition; this is necessary as the carbonyl, while more reactive than a C=C, is still not quite reactive enough for the addition to occur to any great extent on its own.

Step 1

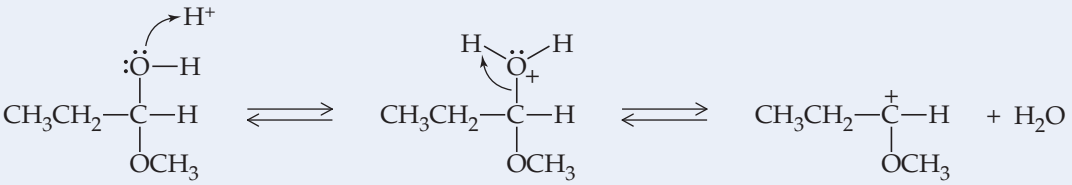
Step 2

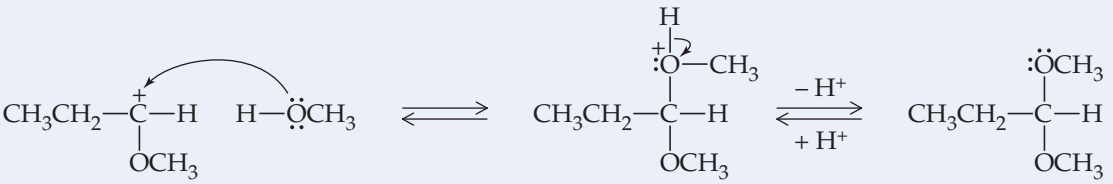


Step 3



Acetal Formation





The amount of H^+ necessary is so small that it can simply come from anywhere. The protonated carbonyl is in resonance with the species in which the positive charge has migrated from the O to the C (Step 2), thus providing an ideal intermediate to which the alcohol can add. Addition of methanol followed by loss of H^+ provides the hemiacetal (Step 3). As long as there is an excess of alcohol, the equilibrium should favor the formation of the hemiacetal.

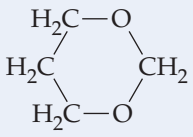
Although only a trace of acid (if any) is needed for formation of the hemiacetal, the presence of H^+ is absolutely necessary for further conversion to the acetal. Protonation of the —OH of the hemiacetal, followed by loss of water and subsequent attack by another alcohol molecule will provide, after loss of H^+, the acetal.

Notice here that water is one of the products formed; as long as the amount of water is much less than the amount of alcohol present, the equilibrium will favor the acetal. In fact, if the acid is neutralized at the end of the reaction (by addition of base), the acetal can be easily isolated, as both acid and water are necessary for the equilibrium to reverse direction.

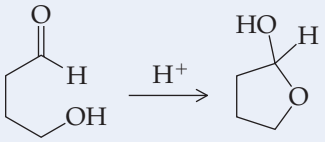
The mechanism of the hydrolysis of an acetal is simply the reverse of the processes shown earlier; by addition of both H^+ and H_2O the equilibrium can be made to proceed in the direction that favors the ketone or aldehyde and alcohol-starting materials.

MR Problem 15.1 Hydrates are formed when water, rather than an alcohol, adds across the carbonyl carbon. Chloral hydrate, a potent sedative and component in "knockout" drops, is formed by reacting trichloroacetaldehyde with water in a reaction analogous to hemiacetal formation. Draw the formula of chloral hydrate.

MR Problem 15.2 Provide the mechanism for the hydrolysis of the acetal shown next. (Hint: Apply all the steps given in the mechanism for the formation of the acetal in reverse.)



MR Problem 15.3 Cyclic hemiacetals form easily and have enhanced stability due to their compactness. Provide the mechanism for the following reaction:



CHEMISTRY IN ACTION

When Is Toxicity Beneficial?

We rely on medicines throughout our life, but almost all medicines have side effects, toxicity being one of them. Are there any times that toxicity is a good thing?

In its broadest meaning, the term *drug* refers to any chemical agent, other than food, that affects living organisms and is usually reserved for substances that prevent or treat disease. By contrast, a *poison* or *toxic substance* is any chemical agent that harms living organisms. As a result, the categories "drugs" and "toxin" are not mutually exclusive. Often a substance that cures disease or alleviates symptoms in low concentrations will cause injury or death when taken in larger amounts. Perhaps the most significant class of medicines that have to be toxic to carry out their designed purpose are the drugs used to treat cancer.

The treatment of cancers with chemical agents (chemotherapy or chemo) has long been both a frustrating and rewarding experience in medicine. Since most drugs used to treat cancer affect only cells that are actively reproducing, and since cancer cells grow and multiply much more rapidly than most normal cells in the body, these rogue cells will usually be much more strongly affected by these drugs than "normal" cells. However, the fact remains that chemo drugs will also kill normal cells just as readily as cancer cells.

Drugs used in chemotherapy can be classified into five general categories: 1) *alkylating agents* (chemicals that directly damage deoxyribonucleic acid (DNA), preventing its reproduction), 2) *antimetabolites* (agents that substitute for the normal building blocks of DNA and ribonucleic acid (RNA)), 3) *antitumor antibiotics* (drugs that alter the DNA inside cancer cells), 4) *topoisomerase inhibitors* (compounds that interfere with enzymes called topoisomerases, which help separate the strands of DNA for replication), and 5) *mitotic inhibitors,* the newest class of chemo drugs that prevent cell division by interfering with the protein called tubulin, which is used to form microtubules. Microtubules are very long, cable-like proteins that are assembled when needed to move organelles in a cell around; they are necessary to move and separate chromosomes and other components when a cell undergoes division (mitosis). Because cancer cells grow and spread by nonstop mitotic division, they are more sensitive to inhibition of mitosis than normal cells. If cell growth can be stopped, then one of two things can happen: the cell will eventually die or undergo internal repair. In either case, the cancer cell is stopped dead in its tracks.

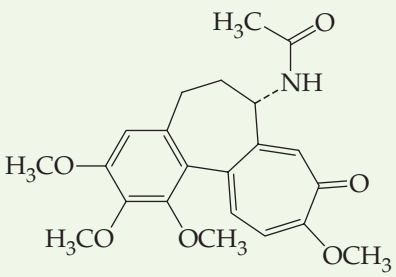
▲ The beautiful autumn crocus; one of the most endangered plants in the world and the most lethal, it contains colchicine, a toxin for which there is no antidote.

Almost all known mitotic inhibitors are intricate organic molecules that contain a wide variety of functional groups, with some containing the ketone function. Originally isolated from plants, these compounds inhibit mitosis. One example is colchicine. Originally isolated from the autumn crocus, colchicine is known to interfere with mitosis; however, it was dropped from further study due to its extremely toxic nature. Scientists studying tubulin discovered a colchicine-binding site and reasoned that synthetic analogs with lower overall toxicity might be possible; however, out of this work, two colchicine-binding site inhibitors (CBSIs) were discovered (Phenstatin and BCN-105P) and are currently being investigated for the treatment of solid tumors.

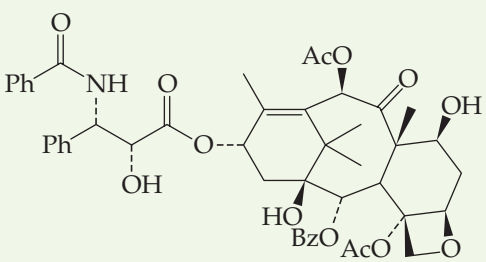
Another promising mitotic inhibitor that also contains a ketone is paclitaxel (also known as Taxol), which we first learned about at the beginning of the chapter. Isolated from the bark of the Pacific Yew tree, this complex, highly oxygenated molecule has shown great promise in the treatment of a number of solid tumor cancers including ovarian, breast, lung, bladder, and melanoma, as well as Kaposi's sarcoma, the cancer most often associated with patients suffering from acquired immunodeficiency syndrome (AIDS). While paclitaxel has drawbacks associated with it (including hair loss, lowering of white blood cell count, gastrointestinal problems, high blood pressure, depression, muscle cramps, and headache), it is considered so important that it has been placed on the World Health Organization's List of Essential Medicines, a list of the most important medications needed in for good, basic health.

CIA Problem 15.3 What are the five classes of chemotherapy drugs?

CIA Problem 15.4 (a) What are mirotubules? (b) Why would drugs that target microtubules make good chemo medicines?



Colchicine



Taxol

CIA Problem 15.5 Tetrodotoxin, found in the puffer fish, has been investigated for use in treatment of moderate to severe cancer pain. This extremely toxic compound is lethal to humans when injected in doses of 8 μg or more per kilogram of body weight. If an average adult male weighs 90 kg, how much tetrodotoxin is needed to kill him?

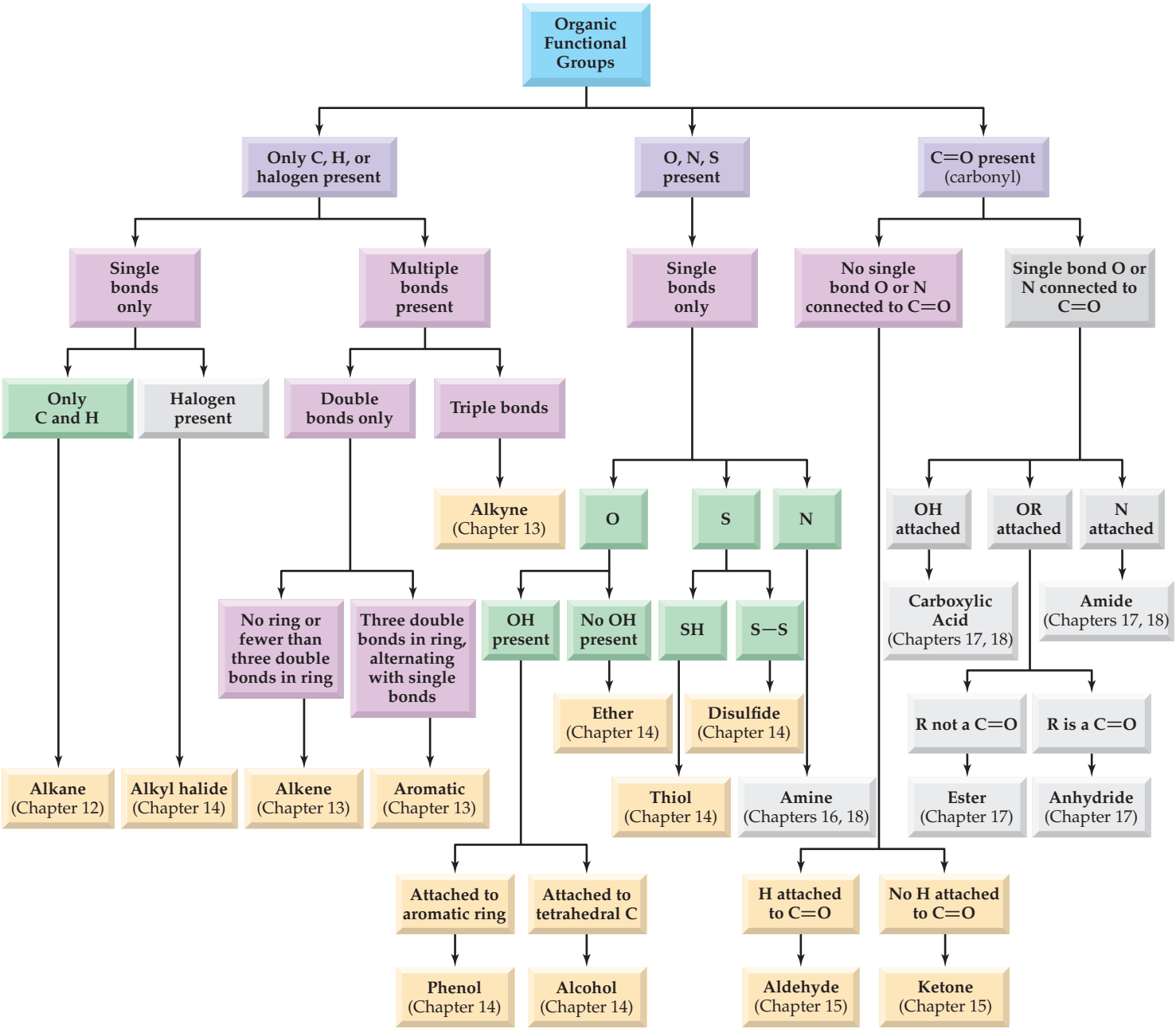
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Identify the carbonyl group and describe its polarity and shape.** The *carbonyl group* is a carbon atom connected by a double bond to an oxygen atom, C═O. Because of the electronegativity difference between carbon and oxygen, the C═O group is polar, with a partial negative charge on oxygen and a partial positive charge on carbon. The oxygen and the two substituents on the carbonyl-group carbon atom form a trigonal planar *(see Problems 20, 27–29, 48, 49, and 66)*.
- **Name and draw simple aldehydes and ketones given a structure or a name.** The simplest *aldehydes* and *ketones* are known by common names (formaldehyde, acetaldehyde, benzaldehyde, and acetone). Aldehydes are named systematically by replacing the final *-e* in an alkane name with *-al* and when necessary numbering the chain starting with 1 at the —CHO group. Ketones are named systematically by adding *-one* to the alkane name for saturated ketones and numbering starting with 1 at the end nearer the C═O group. In ketones, the location of the carbonyl group is indicated by placing the number of its carbon between the alkane name and *-one*. Some common names of ketones identify each alkyl group separately *(see Problems 26, 27, 29–35, 50, 54–57, and 63)*.
- **Describe the polarity, hydrogen bonding, and water solubility of aldehydes and ketones.** Aldehyde and ketone molecules are moderately polar, do not hydrogen bond with each other, but can accept hydrogen bonds from water molecules. Those with less than four to five carbons are water-soluble, and the ketones are excellent solvents. In general, aldehydes and ketones are higher boiling than alkanes but lower boiling than alcohols of similar molar mass. Many aldehydes and ketones have distinctive, sometimes pleasant odors *(see Problems 20, 22, 52, 53, 61, and 62)*.
- **Identify common aldehydes and ketones and their uses.** Aldehydes and ketones are present in many plants, where they contribute to their aromas; many are used as food flavorings. Such natural aldehydes and ketones are widely used in perfumes and flavorings. Formaldehyde (an irritating and toxic substance) is used in polymers, is present in smog-laden air, and is produced biochemically from ingested methanol. Acetone is a widely used solvent and is a by-product of food breakdown during uncontrolled diabetes and starvation. Many sugars (*carbohydrates*) are aldehydes or ketones *(see Problems 45, 49, 52, and 53)*.
- **Identify the products formed from the oxidation of aldehydes (and see that ketones do not oxidize in the same way).** Mild oxidizing agents convert aldehydes to carboxylic acids but have no effect on simple ketones. Tollens' reagent is used to indicate the presence of an aldehyde, while Benedict's reagent will give a positive test result for both aldehydes and *alpha* hydroxy ketones *(see Problems 21, 38, 40, 41, 52, 58, and 60)*.
- **Identify the products of the reduction of aldehydes and ketones.** Reducing agents, such as the hydride ion (H^-), add to the C of the C═O group in an aldehyde or ketone, while the accompanying hydrogen ion (H^+) adds to the O. Aldehydes produce primary alcohols, whereas ketones produce secondary alcohols. In biological systems, the reducing agent for a carbonyl group is often the coenzyme NAD, which cycles between reacting as a reducing agent (NADH) and an oxidizing agent (NAD^+) by the loss and gain of a hydride ion ($:H^-$) *(see Problems 20, 39, and 58)*.
- **Identify the differences between hemiacetals, hemiketals, acetals, and ketals.** Aldehydes establish equilibria with alcohols to form hemiacetals or acetals, whereas ketones do the same to form hemiketals and ketals. *Hemiacetals* and *hemiketals* have an —OH and an —OR on a tetravalent carbon; in a hemiacetal the other two groups attached are a C and a H, whereas in a hemiketal the other two groups are both C *(see Problems 23, 25, 36, 42–44, and 47)*.
- **Predict the products of hemiacetal, hemiketal, acetal, and ketal formation and their hydrolysis.** The relatively unstable *hemiacetals and hemiketals*, which have an —OH and an —OR on what was the carbonyl carbon, result from addition of one alcohol molecule (which provides the —OR group) to the C═O bond. The more stable *acetals and ketals*, which have two —OR groups on what was the carbonyl carbon, form by the addition of a second alcohol molecule to a hemiacetal or hemiketal. The aldehyde or ketone C═O bond can be regenerated from an acetal or ketal by treatment with an acid catalyst and a large quantity of water, with the —OR groups being converted back into the alcohols they came from (ROH). This is an example of a *hydrolysis* reaction *(see Problems 23, 24, 36, 37, 42–47, 59, 64, and 65)*.

KEY WORDS

Acetal, *p. 521*
Addition reaction, aldehydes and ketones, *p. 519*
Aldehyde, *p. 509*
Carbonyl compound, *p. 509*
Carbonyl group, *p. 509*
Hemiacetal, *p. 519*
Hemiketal, *p. 519*
Hydrolysis, *p. 525*
Ketal, *p. 521*
Ketone, *p. 509*

CONCEPT MAP: ORGANIC CHEMISTRY FAMILIES

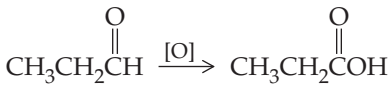


▲ **Figure 15.3** **Functional Group Concept Map.** This is the same concept map we saw at the end of Chapters 12–14, except the functional groups discussed in this chapter, aldehydes and ketones, have now been colorized.

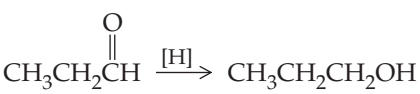
SUMMARY OF REACTIONS

1. Reactions of aldehydes

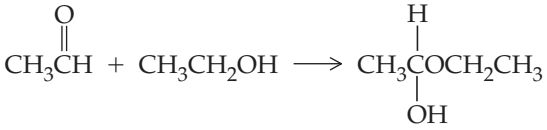
(a) Oxidation to yield a carboxylic acid (Section 15.5).

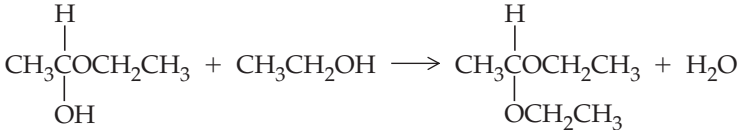


(b) Reduction to yield a primary alcohol (Section 15.6).



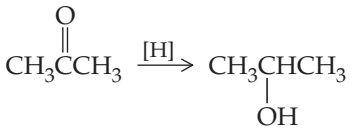
(c) Addition of alcohol to yield a hemiacetal or acetal (Section 15.7).



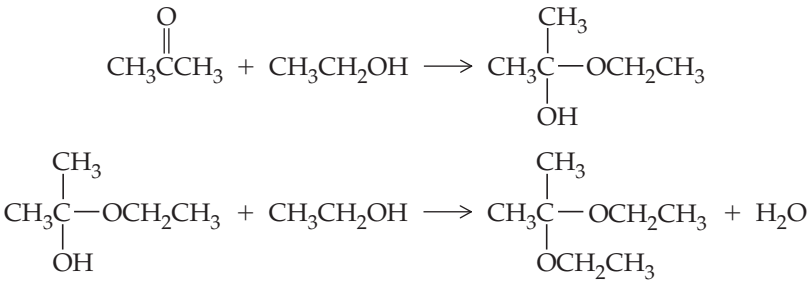


2. Reactions of ketones

(a) Reduction to yield a secondary alcohol (Section 15.6).

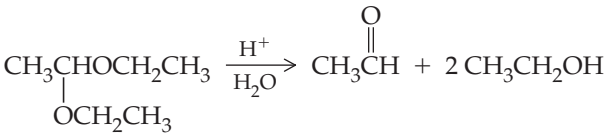


(b) Addition of an alcohol to yield a hemiketal or ketal (Section 15.7).



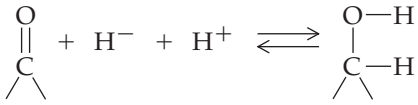
3. Reaction of acetals and ketals

Hydrolysis to regenerate an aldehyde or ketone (Section 15.7).



UNDERSTANDING KEY CONCEPTS

15.20 The carbonyl group can be reduced by addition of a hydride ion (H^-) and a proton (H^+). Removal of H^- and H^+ from an alcohol results in a carbonyl group.

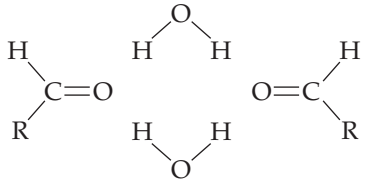


(a) To which atom of the carbonyl is the hydride ion added and why?

(b) In the reaction, indicate which direction represents reduction and which represents oxidation.

15.21 A fundamental difference between aldehydes and ketones is that one can be oxidized to carboxylic acids but the other cannot. Which is which? Give an example of a test to differentiate aldehydes from ketones.

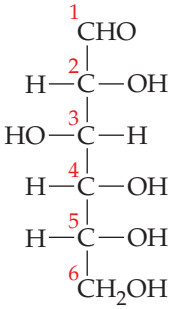
15.22 In the following diagram, indicate with dashed lines where hydrogen bonds would form. Explain why you chose these atoms to hydrogen bond.



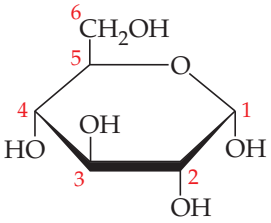
15.23 **(a)** Describe what happens in the reaction of an aldehyde with an alcohol.

(b) Copy the following structures and use lines to show where new bonds are formed. Cross out bonds that no longer exist as the aldehyde and alcohol react to form a hemiacetal.

15.24 Glucose is the major sugar in mammalian blood. We often see it represented as either the "free aldehyde" or the cyclic hemiacetal forms shown here. Of the two forms of glucose, the cyclic hemiacetal is the preferred form found in blood. Can you suggest two reasons why?



"Free aldehyde"



Cyclic hemiacetal

15.25 Describe the structural difference between a ketal and an acetal. Draw one of each to demonstrate your point.

ADDITIONAL PROBLEMS

(Note: For the following, the term "alpha" (α) refers to the carbon directly attached to the carbonyl group and "beta" (β) to the carbon two away from the carbonyl group.)

ALDEHYDES AND KETONES (SECTIONS 15.1 AND 15.2)

15.26 Draw a structure for a compound that meets each of the following descriptions:

(a) A 6-carbon cyclic ketone with a methyl group on the beta carbon

(b) An aldehyde with four carbons

(c) An *alpha*-bromoaldehyde, C_4H_7BrO

(d) A *beta*-hydroxyketone, $C_4H_8O_2$

15.27 Draw a structure for a compound that meets each of the following descriptions:

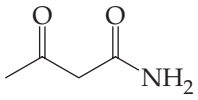
(a) A 5-carbon cyclic ketone. What is the approximate C—O bond angle in this ketone?

(b) An 8-carbon ketone with six carbons as its longest chain

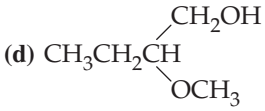
(c) A *beta*-ketoaldehyde, $C_6H_{10}O_2$

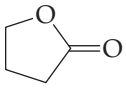
(d) A cyclic *alpha*-hydroxyketone, $C_5H_8O_2$

15.28 Indicate which compounds contain aldehyde or ketone carbonyl groups.

(a) $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_3$ **(b)** 

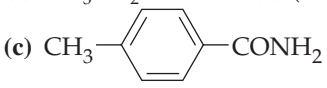
(c) $CH_3CH_2—O—CH_2—CHO$

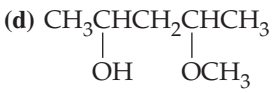
(d) 

(e)  **(f)** 

15.29 Redraw each of the following in line structure format. Indicate which compounds have an aldehyde carbonyl group, a ketone carbonyl group, or neither.

(a) CH_3CH_2CHO **(b)** $(CH_3)_2C(OH)CH_2CH_2CH_3$

(c) 

(d)  **(e)** $CH_3CH_2COCH_2CH_3$

15.30 Draw structures corresponding to the following aldehyde and ketone names:

(a) 3-Methylpentanal

(b) 4-Chloro-2-hydroxybutanal

(c) *p*-Methylbenzaldehyde

(d) 2-Ethylcycloheptanone

(e) Cyclopropyl methyl ketone

(f) Methyl phenyl ketone (also known as acetophenone)

15.31 Draw structures corresponding to the following aldehyde and ketone names:

(a) 4-Hydroxy-2,2,4-trimethylheptanal

(b) 4-Ethyl-2-isopropylhexanal

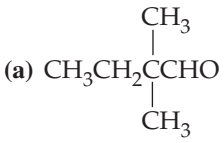
(c) *p*-Bromobenzaldehyde

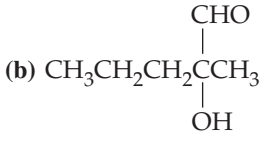
(d) 2,4-Dihydroxycyclohexanone

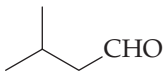
(e) 1,1,1-Trichloropentan-3-one

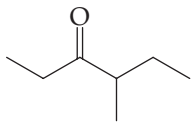
(f) 2-Methylhexan-3-one

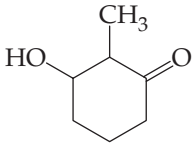
15.32 Give systematic names for the following aldehydes and ketones:

(a) 

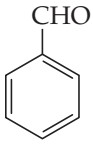
(b) 

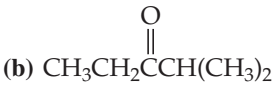
(c) 

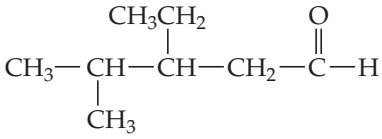
(d) 

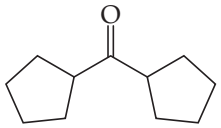
(e) 

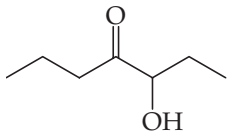
15.33 Give IUPAC names for the following aldehydes and ketones:

(a) 

(b) 

(c) 

(d) 

(e) 

15.34 The following names are incorrect. What is wrong with each?

(a) Pentan-1-one

(b) 4-Methylpentan-3-one

(c) Butan-3-one

15.35 The following names are incorrect. What is wrong with each?

(a) Cyclohexanal **(b)** 2-Butanal

(c) 1-Methylpentan-1-one

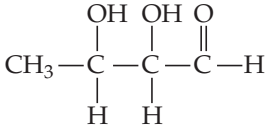
REACTIONS OF ALDEHYDES AND KETONES (SECTIONS 15.5–15.7)

15.36 Draw the structure of the compound obtained when one mole of methanol reacts with one mole of butanal in the presence of an acid catalyst.

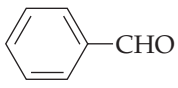
15.37 Draw the structure of the compound obtained when two moles of methanol reacts with one mole of methyl ethyl ketone in the presence of an acid catalyst.

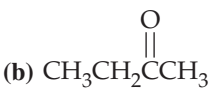
15.38 Which of the following compounds will react with Tollens' reagent? With Benedict's reagent?

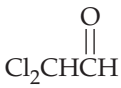
(a) Cyclopentanone **(b)** Hexanal

(c) 

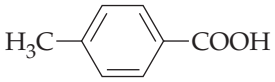
15.39 Draw the structures of the products formed when the following compounds react with a reducing agent.

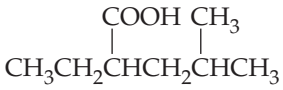
(a) 

(b) 

(c) 

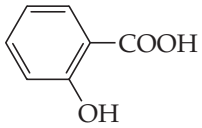
15.40 Draw the structures of the aldehydes that might be oxidized to yield the following carboxylic acids:

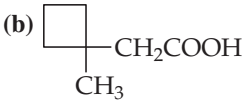
(a) 

(b) 

(c) $CH_3CH{=}CHCOOH$

15.41 Draw the structures of the aldehydes that might be oxidized to yield the following carboxylic acids:

(a) 

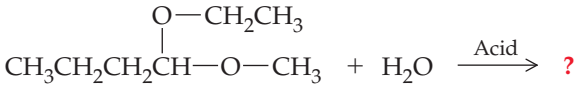
(b) 

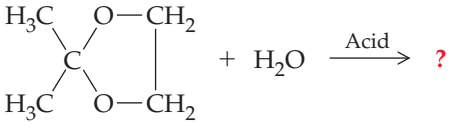
(c) $CH_3CH{=}CHCH_2COOH$

15.42 Write the structures of the hemiacetal or hemiketal that result from reactions (a) and (b). Label each product as a hemiacetal or hemiketal. Write the structures of the complete hydrolysis products of the acetal or ketal in (c) and (d).

(a) Butan-2-one + Propan-1-ol ⟶ ?

(b) Butanal + Isopropanol ⟶ ?

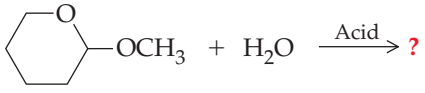
(c) 

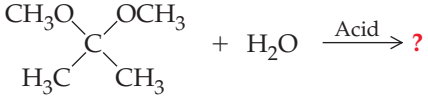
(d) 

15.43 Write the structures of the hemiacetal or hemiketal that result from reactions (a) and (b). Write the structures of the complete hydrolysis products of the acetal or ketal in (c) and (d).

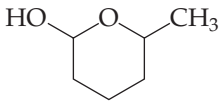
(a) Acetone + Ethanol ⟶ ?

(b) Hexanal + Butan-2-ol ⟶ ?

(c) 

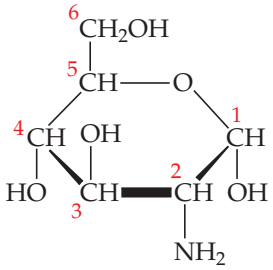
(d) 

15.44 Cyclic hemiacetals commonly form if a molecule has both an alcohol group and a carbonyl group elsewhere in the same molecule, especially if they are four or five carbons apart. What is the structure of the hydroxy aldehyde from which this hemiacetal might form?

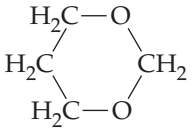


Cyclic hemiacetal

15.45 Glucosamine is found in the shells of lobsters; it exists largely in the cyclic hemiacetal form shown here. Draw the structure of glucosamine in its open-chain hydroxy aldehyde form (the hemiacetal carbon is labeled 1).



15.46 What two products result from the complete hydrolysis of this cyclic acetal?

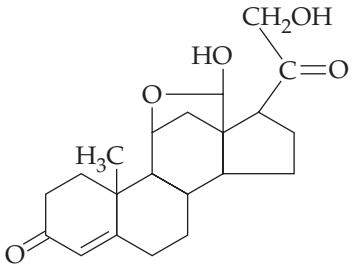


15.47 Acetals and ketals are usually made by reaction of an aldehyde or ketone with two molecules of a monoalcohol. If an aldehyde or ketone reacts with one molecule of a dialcohol, however, a cyclic acetal or ketal results.

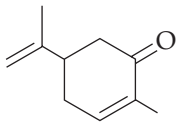
(a) Draw the structure of the hemiketal formed when the —OH labeled in red reacts with cyclopentanone;

(b) Draw the cyclic ketal formed when the hemiketal from part (a) reacts with the —OH labeled in blue.

15.48 Aldosterone is a key steroid involved in controlling the sodium–potassium balance in the body. Identify the functional groups in aldosterone.



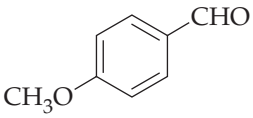
15.49 The compound carvone is responsible for the odor of spearmint. Identify the functional groups in carvone.



Carvone

CONCEPTUAL PROBLEMS

15.50 Name the following compound, which is used in the fragrance industry.



15.51 Can the alcohol $(CH_3)_3COH$ be formed by the reduction of an aldehyde or ketone? Why or why not?

15.52 Many flavorings and perfumes are partially based on fragrant ketones, with far fewer being based on fragrant aldehydes. Why do you think ketones are used more frequently than aldehydes? See Section 15.5 for a clue.

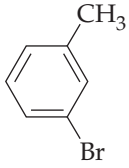
15.53 One problem with burning some plastics is the release of formaldehyde. What are some of the physiological effects of exposure to formaldehyde?

15.54 Name the following compounds using IUPAC nomenclature:

(a) $CH_3CH_2\overset{\overset{O}{\|}}{C}CH(CH_3)_2$

(b) $CH_3CH_2CH_2CH{=}CH_2$

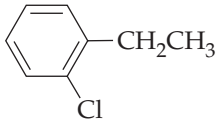
(c)



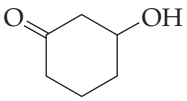
(d) $(CH_3)_3CCH_2\overset{\overset{O}{\|}}{C}CH_2CH_3$

15.55 Name the following compounds:

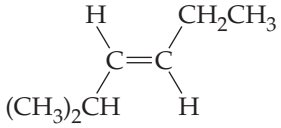
(a)



(b)



(c)



(be sure to include *cis* or *trans* in the name)

(d) $(CH_3)_2CH{-}\overset{\overset{O}{\|}}{C}{-}H$

15.56 Draw the structural formulas of the following compounds:

(a) 2,4-Dinitroacetophenone

(b) 2,4-Dihydroxycyclopentanone

(c) 2-Methoxy-2-methylpropane

(d) 2,3,4-Trimethylpentan-3-ol

15.57 Draw the structural formulas of the following compounds:

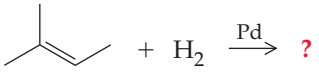
(a) 2,3-Dimethylpentanal

(b) 1,3-Dibromopropanone

(c) 4-hydroxy-4-methylhexan-2-one

15.58 Complete the following equations (refer to "Summary of Reactions" in Chapters 13 and 14 if necessary):

(a)



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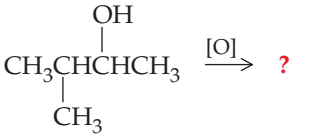

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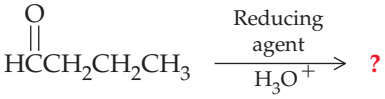
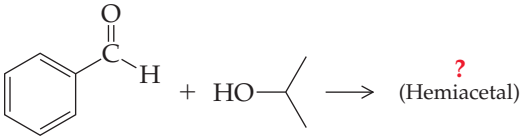
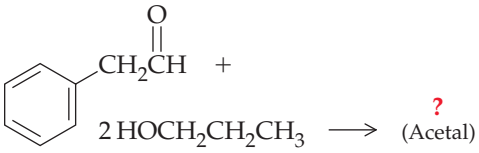


(d)

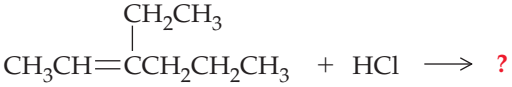


15.59 Complete the following equations:

(a)



(b)



(c)

15.60 How could you differentiate between hexan-3-ol and hexanal using a simple chemical test?

15.61 The liquids butan-1-ol and butanal have similar molar masses. Which is expected to have the higher boiling point? Explain your choices.

15.62 Butan-2-one has a solubility of 26 g/100 mL of H_2O, but heptan-2-one, which is found in clove and cinnamon bark oils, is only very slightly soluble in water. Explain the difference in solubility of these two ketones.

GROUP PROBLEMS

15.63 Draw all the ketones you can with a chemical formula of $C_8H_{16}O$, whose longest chain is eight carbons. Name each using both its IUPAC and common name.

15.64 In Problem 15.24, you were given the structure of the free aldehyde form of glucose. Try to draw the two cyclic hemiacetal forms of glucose you would get if (a) the OH on C4 formed the ring and (b) the OH on C3 formed the ring.

15.65 Using the ketone structural form of fructose (Section 20.1), draw the hemiketal you would get if (a) the OH on C4 formed the ring and (b) if the OH on C6 formed the ring.

15.66 In the Chemistry in Action "Enediyne Antibiotics: A Newly Emerging Class of Antitumor Agents" in Chapter 13, you were given the structure of Diynemicin A. Identify all of the functional groups present in this molecule.

16

Amines

CONTENTS

CONCEPTS TO REVIEW

A. Lewis Structures (Section 4.7)

B. Polar Covalent Bonds (Section 4.9)

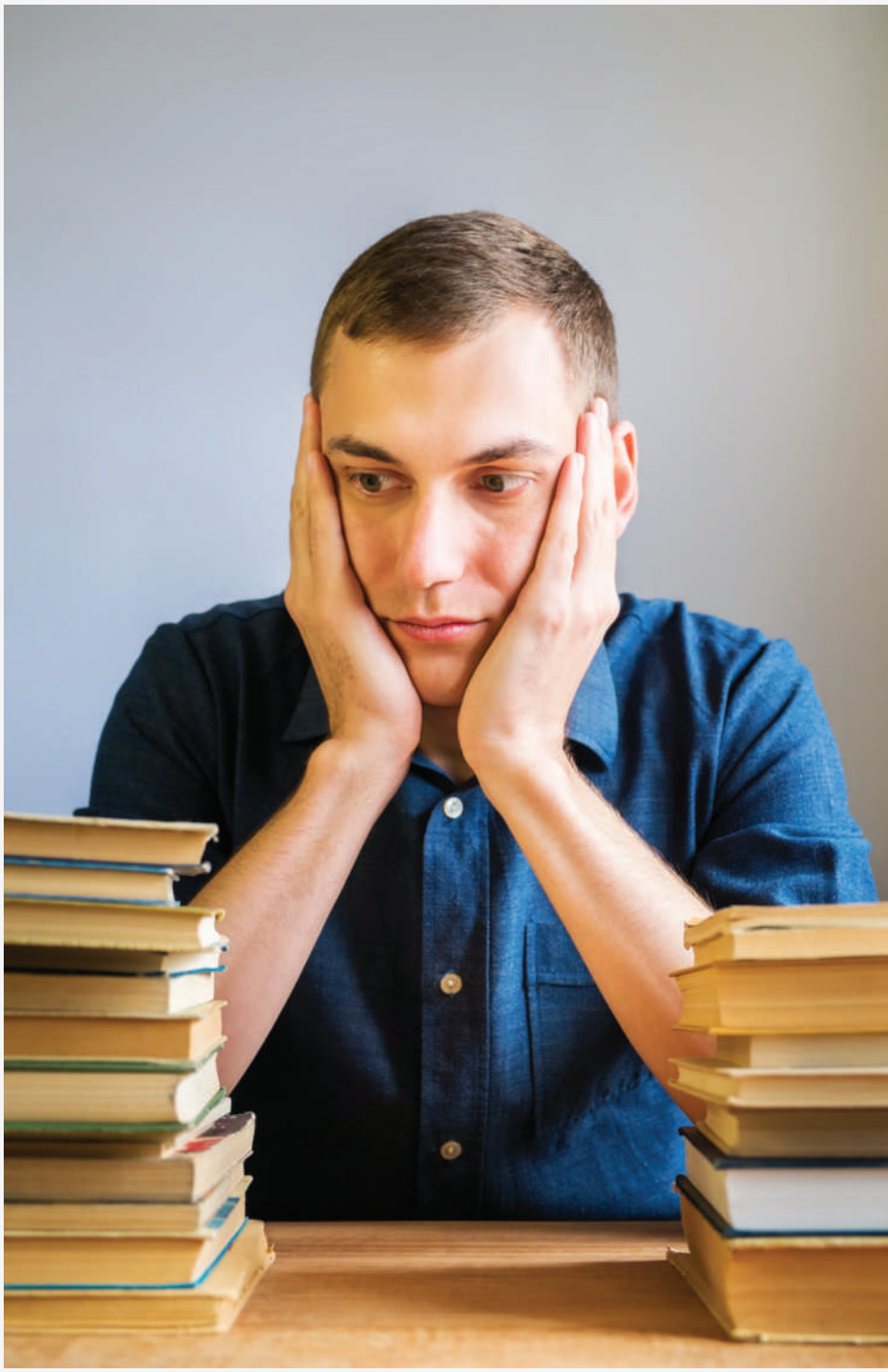
C. Acids and Bases (Sections 5.4, 10.1, 10.2, and 10.8)

D. Hydrogen Bonds (Section 8.2)

E. Acid Dissociation Constants (Sections 10.3–10.5)

F. Functional Groups (Section 12.2)

G. Naming Alkanes (Section 12.6)



▲ Sometimes the stress of our day-to-day life can be overwhelming. When anxiety becomes uncontrollable, medications can help.

The brain is the organ we know the least about, yet it controls essentially every aspect of who and what we are. Packed away and isolated from the rest of your body, it has an extraordinary set of defenses in place to keep it protected (see the Chemistry in Action "The Blood–Brain Barrier" in Chapter 29). But things can go wrong: seizures, strokes, anxiety, and depression to name but a few. Anxiety is something that all of us face at multiple times during our life; most of the time we can combat it through exercise, meditation, and other

natural remedies such as chamomile tea or lemon balm. For an extreme case of anxiety, therapy may be indicated; but what if our anxiety is so great that these methods do not work? When this is the case, medical intervention is called for. Luckily, medications exist for just such a condition. These drugs, which are molecules that effect how signals are transmitted in the brain, can have both good and bad properties of their own. Benzodiazepines can provide immediate relief but carry the possibility of addiction; Serotonin reuptake inhibitors do not carry the problem of being addictive but are not usually able to provide immediate relief. What do all of these drugs have in common? They are all amines. We will examine these closer in the Chemistry in Action "Calming a Stormy Mind: Amines as Anti-Anxiety Medications" at the end of this chapter.

From a biochemical standpoint, many of the molecules that carry chemical messages (such as the neurotransmitters, Chapter 28) are relatively simple amines with extraordinary powers. Histamine, the compound that initiates hay fever and other allergic reactions, is an amine; you have experienced its power first-hand if you have ever had an insect bite. In addition, many of the drugs that have been developed to mimic or to control the activity of histamine—the antihistamines present in cold and allergy medications—are amines. The amino group ($-NH_2$) is important in the formation and stability of proteins, and heterocyclic amines play a crucial part in the function of DNA and RNA. These are but a few examples of the roles played by amines.

16.1 Classifying Amines

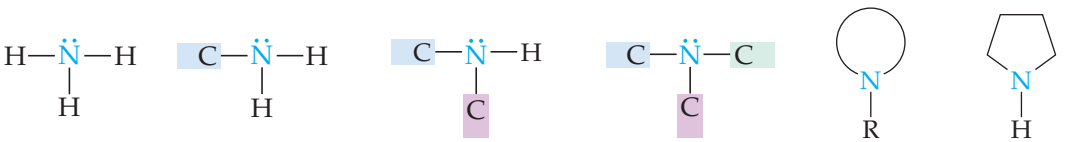
LOOKING AHEAD We will explore the function of amines in proteins and DNA in Chapters 18 and 25, respectively.

Learning Objective:

- Identify and classify an amine as primary, secondary, or tertiary.

Amines contain one or more organic groups bonded to nitrogen; they have the general formulas RNH_2, R_2NH, and R_3N. In the same way that alcohols and ethers can be thought of as organic derivatives of water, amines are organic derivatives of ammonia (NH_3). In general, they are classified as *primary* (1°), *secondary* (2°), or *tertiary* (3°), according to how many organic groups are individually bound *directly* to the nitrogen atom. The organic groups (represented below by colored rectangles) may be large or small, they may be the same or different, or they may be connected to one another through a ring.

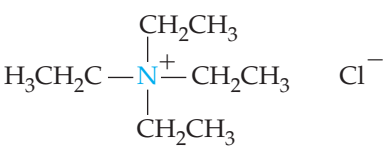
Amine A compound that has one or more organic groups bonded to nitrogen: primary, RNH_2; secondary, R_2NH; or tertiary, R_3N.

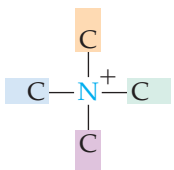


Ammonia	A primary amine (RNH_2)	A secondary amine (R_2NH)	A tertiary amine (R_3N)	A cyclic amine	Pyrrolidine
NH_3	$CH_3CH_2NH_2$	$(CH_3CH_2)_2NH$	$(CH_3CH_2)_3N$		

Note that each amine nitrogen atom has a lone pair of electrons. The lone pair, although not always shown, is always there for a nitrogen that has three groups bonded to it and is responsible in large part for the chemistry of amines. When a fourth group bonds to the nitrogen, it does so through this lone pair; the product is a **quaternary ammonium ion** (Section 16.6), which has a permanent positive charge and forms ionic compounds with anions [for example, $(CH_3CH_2)_4N^+Cl^-$]:

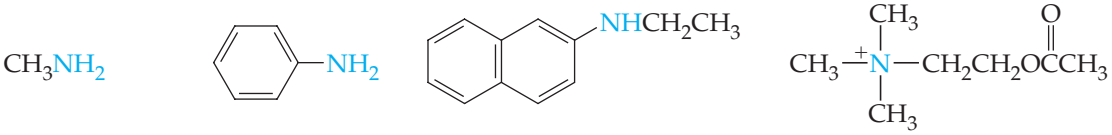
Quaternary ammonium ion A positive ion with four organic groups bonded to the nitrogen atom (R_4N^+).





A quaternary ammonium ion (R_4N^+)

The groups bonded to the amine nitrogen atom may be alkyl or aryl (aromatic) groups and may or may not contain other functional groups. For example:



Methanamine (a primary alkyl amine) | Aniline (a primary aromatic amine) | *N*-Ethylnaphthylamine (a secondary aromatic amine) | Acetylcholine, a neurotransmitter (a quaternary ammonium ion)

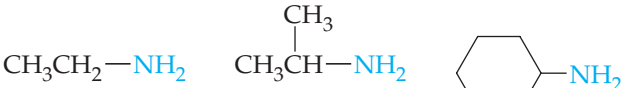
16.2 Naming and Drawing Amines

Learning Objective:

- Name a simple amine given its structure or draw an amine given its name.

Primary alkyl amines (RNH_2) are named by identifying the alkyl group attached to nitrogen and adding the suffix *-amine* to the alkyl group name.

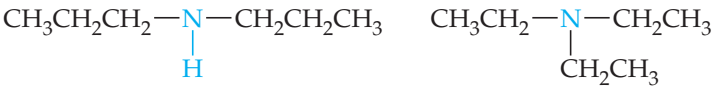
Some examples of naming primary amines



Ethanamine | Isopropylamine | Cyclohexylamine

Simple, nonheterocyclic secondary (R_2NH) and tertiary (R_3N) amines (those possessing two or three identical groups on the nitrogen, respectively) are named by adding the appropriate prefix, *di-* or *tri-*, to the alkyl group name along with the suffix *-amine*.

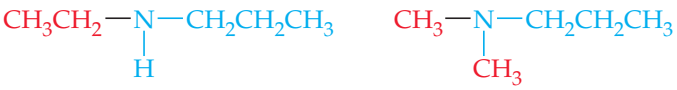
Some examples of naming simple 2° and 3° amines



Dipropylamine | Triethylamine

When the R groups in secondary or tertiary amines are different, the compounds are named as *N*-substituted derivatives of a primary amine. The parent compound chosen as the primary amine based on the R group containing the longest carbon chain; all other groups are considered to be *N*-substituents (*N* because they are attached directly to nitrogen). The following compounds, for example, are named as propylamines because the propyl group in each is the largest alkyl group:

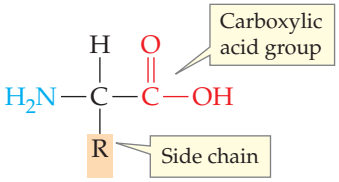
Some examples of naming more complex 2° and 3° amines



N-Ethylpropylamine | *N*,*N*-Dimethylpropylamine

Heteroyclic amines (Section 16.3) are an important family of amines in which the nitrogen is part of the ring structure; the nomenclature of these compounds is too complicated to discuss here and will be addressed as needed.

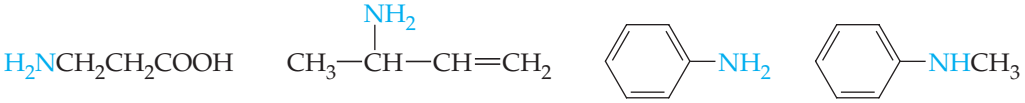
Proteins are polymers of α-amino acids, in which the $-NH_2$ group of one amino acid is linked through the carboxyl of a second via an amide bond. All amino acids contain both the amino functional group, $-NH_2$, and the carboxylic acid functional group, $-COOH$ (in addition to whatever functional groups are part of the side chain). The chemistry of carboxylic acids, esters, and amides is discussed in Chapter 17. The amino acids and their combination to form proteins are covered in Chapter 18.



An amino acid

Amino group The —NH_2 functional group.

The —NH_2 functional group is an **amino group,** and when this group is a substituent, *amino-* is used as a prefix in the name of the compound (for example, when the compound has a C═O present, Chapters 15 and 17). Aromatic amines are an exception to this rule and are primarily known by their historical, or common, names. The simplest aromatic amine is known by its common name aniline, and derivatives of it are named as anilines:



3-Aminopropanoic acid | 3-Aminobut-1-ene | Aniline | *N*-Methylaniline

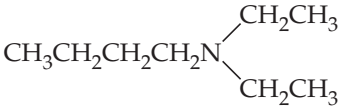
Worked Example 16.1 Drawing and Classifying Amines from Their Names

Write the structure of *N,N*-diethylbutylamine and identify it as a primary, secondary, or tertiary amine.

ANALYSIS Look for terms within the name that provide clues about the parent compound and its substituents. For example, the word "butyl" immediately preceding the *-amine* suffix indicates that butylamine, the 4-carbon alkyl amine, is the parent compound. The *N,N* indicates that two other groups are bonded to the amino nitrogen, and the *diethyl* indicates they are both ethyl groups.

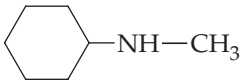
SOLUTION

The structure shows that three alkyl groups are bonded to the N atom, so this must be a tertiary amine.



Worked Example 16.2 Naming and Classifying an Amine from Its Structure

Name the following compound. Is it a primary, secondary, or tertiary amine?



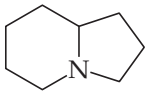
ANALYSIS Determine how many organic groups are attached to the nitrogen. We can see that two carbon groups are bonded to the nitrogen. Since the cyclohexyl group is the largest alkyl group bonded to N, the compound is named as a cyclohexylamine. One methyl group is bonded to the nitrogen; we indicate this with the prefix *N*.

SOLUTION

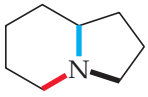
The name is *N*-methylcyclohexylamine. Because the compound has two groups bonded to N, it is a secondary amine.

Worked Example 16.3 Classifying a Cyclic Amine from Its Structure

The following heterocyclic amine is named octahydroindolizine. Is it a primary, secondary, or tertiary amine?



ANALYSIS Start by looking at the nitrogen; we can see that it is attached to three different carbons (as indicated by red, blue, and black bond lines). Even when the nitrogen is part of a ring, an amine will be classified by the number of organic groups that are bonded to it.



SOLUTION

In this molecule, three individual carbon groups are bound to N; it therefore is a tertiary amine.

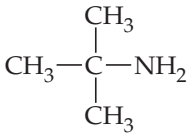
PROBLEM 16.1

Identify the following compounds as primary, secondary, or tertiary amines.

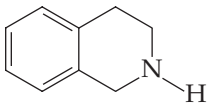
(a) $CH_3(CH_2)_4CH_2NH_2$

(b) $CH_3CH_2CH_2NHCH(CH_3)_2$

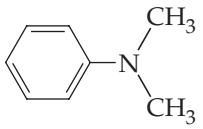
(c)



(d)



(e)

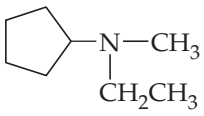


PROBLEM 16.2

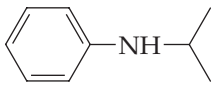
What are the names of these amines?

(a) $(CH_3CH_2CH_2)_2NH$

(b)



(c)



PROBLEM 16.3

Draw structures corresponding to the following names:

(a) Octylamine

(b) *N*-Methylpentylamine

(c) *N*-Ethylaniline

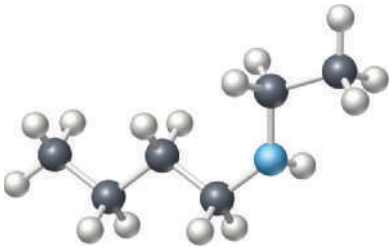
(d) 4-Aminobutan-2-ol

PROBLEM 16.4

Classify the amines in Problem 16.3 (a)–(c) as primary, secondary, or tertiary.

KEY CONCEPT PROBLEM 16.5

Draw the structure of the tetramethylammonium ion. Why does this species have a permanent positive charge? (See Sections 16.1 and 16.6.)



KEY CONCEPT PROBLEM 16.6

Draw the condensed and line formula of the molecule in the margin. Is it a primary, secondary, or tertiary amine? Why?

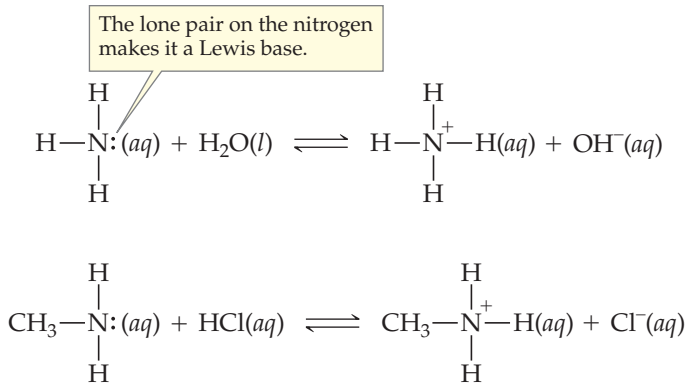
16.3 Properties of Amines

Learning Objective:

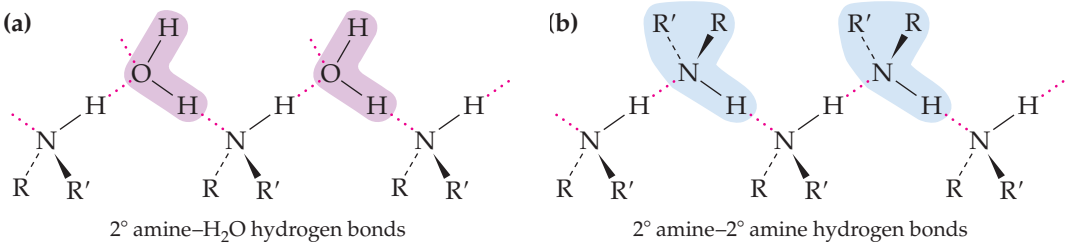
- Describe amine properties such as hydrogen bonding, solubility, boiling point, and basicity.

Lewis base A compound containing an unshared pair of electrons (an amine, for example).

The lone electron pair on the nitrogen in amines, like the lone electron pair in ammonia, causes amines to act as either weak Brønsted–Lowry bases or as **Lewis bases,** by forming a bond with an H^+ ion from an acid or water (see Sections 10.1 and 16.5).



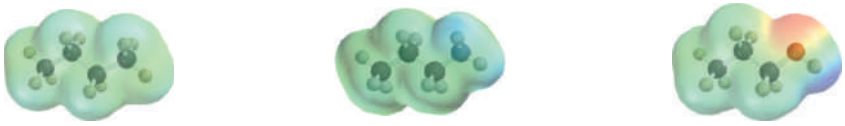
In primary and secondary amines, hydrogen bonds can form between the lone pair on the very electronegative nitrogen atom and the slightly positive hydrogen atom on another primary or secondary amine. All amines (primary, secondary, and tertiary) can form hydrogen bonds with water (Figure 16.1).



▲ **Figure 16.1**
Hydrogen bonding of a secondary amine.
Hydrogen bonding (shown by red dots) between (a) a secondary amine and water; and (b) two secondary amines.

Because of their ability to engage in hydrogen bonding, primary and secondary amines have higher boiling points than alkanes of similar size. Amines are, in general, lower boiling than alcohols of similar size due to the fact that hydrogen bonds amines form with one another are weaker than those found in alcohols. Primary and secondary amines can hydrogen bond with each other and as a result have higher boiling points than expected; however, tertiary amine molecules have no hydrogen atoms attached to nitrogen and therefore cannot hydrogen-bond with each other. As a result, they are much lower boiling than alcohols or primary or secondary amines of similar molecular mass. All amines, however, can hydrogen-bond to water molecules through the lone electron pair on their nitrogen atoms, so amines with up to about six carbon atoms have appreciable solubility in water.

CONCEPTS TO REVIEW Remember that, in the absence of hydrogen bonding, boiling points of molecules increase with increasing molecular mass; see Figure 12.4.



$CH_3CH_2CH_2CH_3$	$CH_3CH_2CH_2NH_2$	$CH_3CH_2CH_2OH$
Butane, bp 0 °C (273 K) Mol. mass = 58	Propylamine, bp 48 °C (321 K) Mol. mass = 59	Propanol, bp 97 °C (37 K) Mol. mass = 60

Many volatile amines have strong odors. Some smell like ammonia and others like stale fish or decaying meat. The protein in flesh contains amine groups, and the smaller, volatile amines produced during decay and protein breakdown are responsible for the odor of rotten meat. One such amine, 1,5-diaminopentane, is commonly known as cadaverine.

Many amines cause physiological responses. The simpler amines (such as methyl amine, diethyl amine, or triethylamine) are irritating to the skin, eyes, and mucous

membranes and are toxic by ingestion. Some of the more complex amines from plants (such as the alkaloids) can be very poisonous, while others exhibit powerful analgesic (pain relieving) properties (see Section 16.6). All living organisms contain a wide variety of amines, and many useful drugs are amines (see the Chemistry in Action "Calming a Stormy Mind: Amines as Anti-Anxiety Medications" and Hands-On Chemistry 16.1).

Summary: Properties of Amines

- Primary and secondary amines can hydrogen-bond with each other and thus are higher boiling than alkanes but lower boiling than alcohols, due to weaker hydrogen bonds.
- Tertiary amines are lower boiling than secondary or primary amines because hydrogen bonding between tertiary amines is not possible.
- Methanamine, ethanamine, dimethylamine, and trimethylamine are gases; all other simple amines are liquids.
- Volatile amines usually have unpleasant odors.
- Simple amines (those with less than four carbons) are water-soluble due to their ability to hydrogen bonding with water.
- Amines are weak Brønsted–Lowry/Lewis bases (Section 16.5).
- Many amines are physiologically active, and many are toxic.

PROBLEM 16.7

Arrange the following compounds in order of increasing boiling point. Explain why you placed them in that order.

(a) $CH_3-\underset{\displaystyle CH_3}{\overset{|}{N}}-CH_2CH_3$ **(b)** $CH_3CH_2CH_2CH_2OH$ **(c)** $CH_3CH_2CH_2CH_2NH_2$

PROBLEM 16.8

Draw the structures of (a) ethanamine and (b) trimethylamine. Use dashed lines to show how they would form hydrogen bonds to water molecules.

HANDS-ON CHEMISTRY 16.1

The amine functional group is part of a great many compounds you come in contact with on a daily basis. To see how prevalent the amine functional group is in medicine, let's take a look at some of the top 200 drugs of 2015, many of which you have probably heard about, and see what functional groups are present. You will need to have an internet connection to fully carry out this activity.

a. Let's begin by looking at some antibiotics you may be familiar with. Look up the structures of the following four antibiotics: Amoxicillin, Doxycycline, Ciprofloxacin, and Metronidazole. What is each typically prescribed for? Draw their line structure and identify as many functional groups as you can in them (use Table 12.1 to help you). Which of these have the amino functional group present? Classify each amine nitrogen you find as primary, secondary, or tertiary.

b. As of September 2014, the top 10 selling prescription drugs by trade name were as follows:

1. Crestor 2. Synthroid 3. Nexium 4. Ventolin 5. Advair
6. Lantus 7. Vyvanse 8. Lyrica 9. Spiriva 10. Diovan

Look up the structures of each and answer the following questions for each:

1. What is its generic name?
2. What medical condition is it used to treat?
3. Does it contain an amine? If so, classify it.
4. What other functional groups are present in each? (Refer to Table 12.1 if needed.)

c. After completing parts a and b, what can you say about the importance of the amino function in medications that are used everyday?

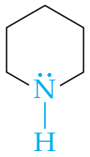
16.4 Heterocyclic Nitrogen Compounds

Learning Objective:

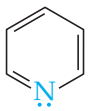
- Identify a heterocyclic amine.

In many nitrogen-containing compounds, the nitrogen atom is in a ring with carbon atoms. Compounds that contain atoms other than carbon in the ring are known as **heterocycles.** Heterocyclic nitrogen compounds may be nonaromatic or aromatic. Piperidine, for example, is a saturated heterocyclic amine with a six-membered ring, and pyridine is an aromatic heterocyclic amine that, like other aromatic compounds, is often represented on paper as a ring with alternating double and single bonds.

Heterocycle A ring that contains nitrogen or some other atom in addition to carbon.

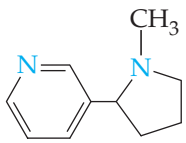


Piperidine
(a saturated cyclic amine)

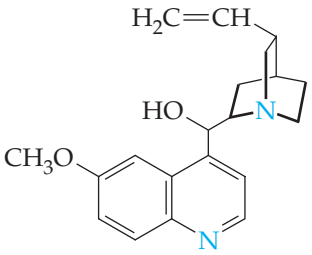


Pyridine
(an aromatic amine)

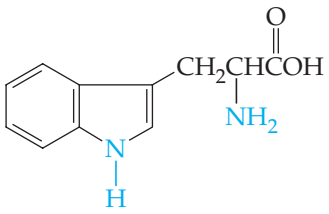
Table 16.1 gives the names and structures of several heterocyclic nitrogen compounds. Because the names of these compounds are historical in origin, they are seemingly random at first sight (for example, the word "purine" was devised by the German chemist Emil Fischer, being a shortened form of "pure urine," alluding to how it was first synthesized). You need not memorize these names and structures, but you should take note that such rings are very common in many natural compounds found in plants and animals. For example, nicotine, from tobacco leaves, contains one pyridine ring and one pyrrolidine ring; quinine, an antimalarial drug isolated from the bark of the South American *Cinchona* tree, contains a quinoline ring system plus a nitrogen ring with a 2-carbon bridge across it. The amino acid tryptophan contains an indole ring system in addition to its amino group.



Nicotine
from tobacco
(an insecticide; an active ingredient in cigarette smoke)

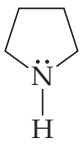


Quinine
from the *Cinchona* tree
(an antimalarial drug)

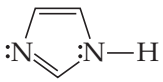


Tryptophan
(an amino acid)

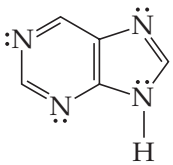
Table 16.1 Some Heterocyclic Nitrogen Compounds



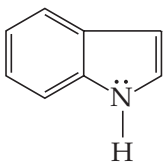
Pyrrolidine
(in nicotine and other alkaloids)



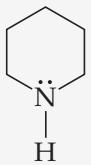
Imidazole
(in histamine)



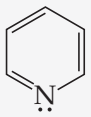
Purine
(nitrogen ring system in DNA; present in anticancer drugs)



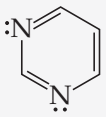
Indole
(in many alkaloids and drugs)



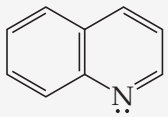
Piperidine
(in many drugs)



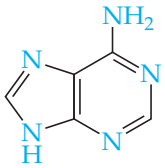
Pyridine
(in many drugs)



Pyrimidine
(nitrogen ring present in DNA and in some B vitamins)



Quinoline
(in antibacterial agents)



Adenine

Adenine, a nitrogen-containing cyclic compound, is one of the four amines that compose the "bases" in DNA that code for genetic traits, as well as being present in ATP (Section 21.5).

Hydrogen bonding that occurs between hydrogen atoms on nitrogens and oxygens and the oxygen or nitrogen atoms of other groups within a molecule helps to determine the shape of many biomolecules. Such attractions contribute to the complex shapes into which large protein molecules are folded (Section 18.8). Hydrogen bonding of amine groups also plays a crucial role in the helical structure of the molecule that carries hereditary information—deoxyribonucleic acid, DNA (Section 26.4).

PROBLEM 16.9

Provide compounds that fit the following descriptions:

(a) Two amines that are gases at room temperature

(b) A heterocyclic amine

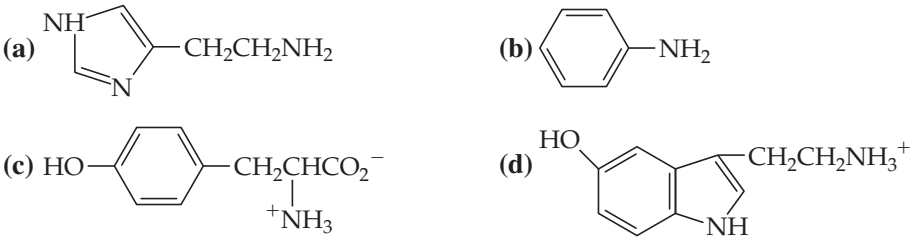
(c) A compound with an amine group on an aromatic ring

PROBLEM 16.10

Consult Table 16.1 and write the molecular formulas for pyrimidine and purine.

PROBLEM 16.11

Which of the following compounds are heterocyclic nitrogen compounds?



16.5 Basicity of Amines

Learning Objective:

- Identify and draw the products formed when an amine reacts with acid.

Ammonium ion A positive ion formed by addition of hydrogen to ammonia or an amine (may be primary, secondary, or tertiary).

Just like ammonia, aqueous solutions of amines are weakly basic because of the formation of OH^- and R_3NH^+ ions in water. Consider the following equilibria of the neutral amines and their **ammonium ions:**

$$CH_3CH_2NH_2 + H_2O \rightleftharpoons CH_3CH_2NH_3^+ + OH^-$$
$$(CH_3CH_2)_2NH + H_2O \rightleftharpoons (CH_3CH_2)_2NH_2^+ + OH^-$$
$$(CH_3CH_2)_3N + H_2O \rightleftharpoons (CH_3CH_2)_3NH^+ + OH^-$$

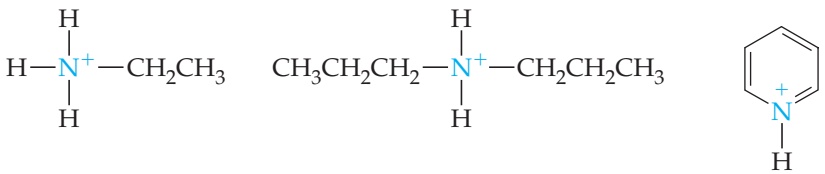
The concepts of equilibrium, and its reversibility, were discussed in Chapters 7 and 10.

Notice that these are reversible reactions; ammonium ions can react as acids in the presence of bases to regenerate the amines. This equilibrium is found to exist in solutions with pH values as high as 8.

Ammonium ions are also formed when amines react with the hydronium ion in acidic solutions:

$$CH_3CH_2NH_2 + H_3O^+ \rightleftharpoons CH_3CH_2NH_3^+ + H_2O$$
$$(CH_3CH_2)_2NH + H_3O^+ \rightleftharpoons (CH_3CH_2)_2NH_2^+ + H_2O$$
$$(CH_3CH_2)_3N + H_3O^+ \rightleftharpoons (CH_3CH_2)_3NH^+ + H_2O$$

The positive ions formed by addition of H^+ to alkylamines are named by replacing the ending *-amine* with *-ammonium*. To name the ions of heterocyclic amines, the amine name is modified by replacing the *-e* with *-ium*. For example:



Ethylammonium ion (from ethanamine)

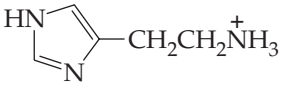
Dipropylammonium ion (from dipropylamine)

Pyridinium ion (from pyridine)

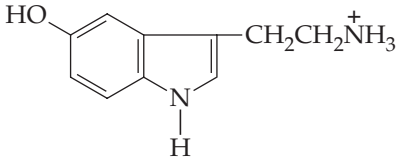
As long as at least one group attached to the nitrogen is a hydrogen, ammonium ions are weakly acidic and will react with bases, such as hydroxide, to regenerate the amine:

$$CH_3CH_2NH_3^+ + OH^- \rightleftharpoons CH_3CH_2NH_2 + H_2O$$
$$(CH_3CH_2)_2NH_2^+ + OH^- \rightleftharpoons (CH_3CH_2)_2NH + H_2O$$
$$(CH_3CH_2)_3NH^+ + OH^- \rightleftharpoons (CH_3CH_2)_3N + H_2O$$

As a result of the aqueous equilibria shown, amines exist as ammonium ions in the water environment of blood and other body fluids, which have a typical pH value of 7.4; for this reason, they are written as ions in the context of biochemistry. For example, histamine and serotonin (both neurotransmitters, Section 28.7) are represented as follows:



Histamine
(causes allergic reaction)



Serotonin
(a neurotransmitter active in the brain)

In general, nonaromatic amines (such as $CH_3CH_2NH_2$ or piperidine, Table 16.2) are slightly stronger bases than ammonia, and aromatic amines (such as aniline or pyridine, Table 16.2) are weaker bases than ammonia:

Basicity: Nonaromatic amines > Ammonia > Aromatic amines

Worked Example 16.4 Amines as Bases in Water

Write balanced equations for the reaction of ammonia with water and for the reaction of ethanamine with water. Label each species in your equations as either an acid or a base.

ANALYSIS Determine which species is the base and which is the acid. Remember that the base will accept a hydrogen ion from the acid. Review the definitions for a Brønsted–Lowry base (Section 10.1) and a Lewis base (Section 16.3).

SOLUTION

Like ammonia, amines have a lone pair of electrons on the nitrogen atom. Because ammonia is a base that reacts with water to accept a hydrogen ion (which bonds to the lone pair), it is reasonable to expect that amines are bases that react in a similar manner.

$$\underset{\textit{Base}}{NH_3} + \underset{\textit{Acid}}{H_2O} \rightleftharpoons \underset{\textit{Acid}}{NH_4^+} + \underset{\textit{Base}}{OH^-}$$

$$\underset{\textit{Base}}{CH_3CH_2NH_2} + \underset{\textit{Acid}}{H_2O} \rightleftharpoons \underset{\textit{Acid}}{CH_3CH_2NH_3^+} + \underset{\textit{Base}}{OH^-}$$

Notice that in both cases, water acts as an acid because it donates a hydrogen ion to the nitrogen.

PROBLEM 16.12

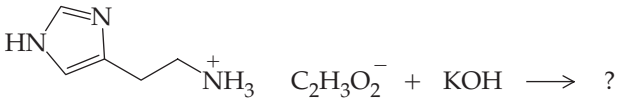
Write an equation for the acid-base equilibrium of:

(a) Pyrrolidine and water **(b)** Pyridine and water

Label each species in the equilibrium as either an acid or a base.

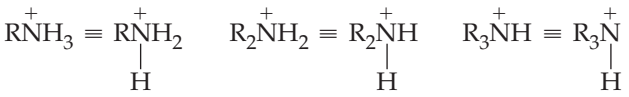
Worked Example 16.5 Ammonium Ions as Acids in Water

Histamine will react with acids (such as acetic acid) to form ammonium salts, which themselves are weak acids. When treated with KOH, the free amine is regenerated. Write a balanced equation for the reaction of histamine acetate with potassium hydroxide:

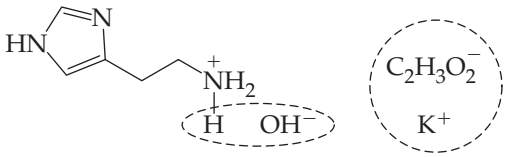


Histamine acetate

ANALYSIS The ammonium ion is a weak acid and will react with a base to give the amine, water, and the salt of the anion that was originally paired with the ammonium ion. It is also important to remember that a nitrogen with both a positive charge and at least one hydrogen can be written as follows:

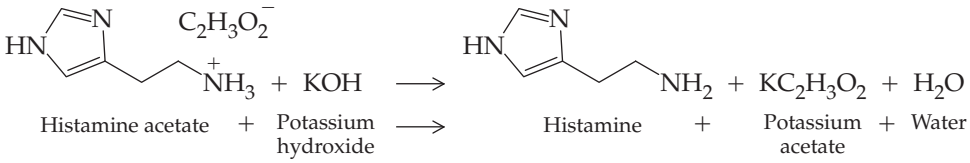


Since the H on the positively charged nitrogen is acidic, the KOH will react as follows:



SOLUTION

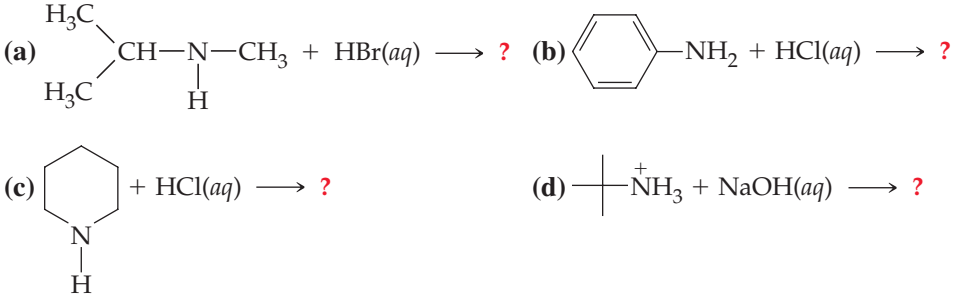
The balanced overall reaction can be written as such:



Histamine acetate + Potassium hydroxide ⟶ Histamine + Potassium acetate + Water

PROBLEM 16.13

Complete the following equations:



PROBLEM 16.14

Name the organic ions produced in reactions (a)–(c) in Problem 16.13.

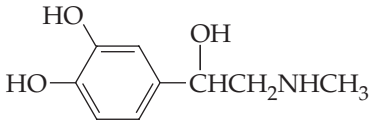
PROBLEM 16.15

Which is the stronger base in each pair?

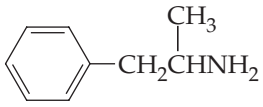
(a) Ammonia or ethanamine **(b)** Triethylamine or pyridine

PROBLEM 16.16

When each of the following biologically active amines is placed into the body, they immediately pick up an H^+ to form an ammonium ion. Draw the structures of the ammonium ions formed by the following amines:



Epinephrine
(a biochemical messenger)



Amphetamine
(a CNS stimulant and drug of abuse)

16.6 Amine Salts

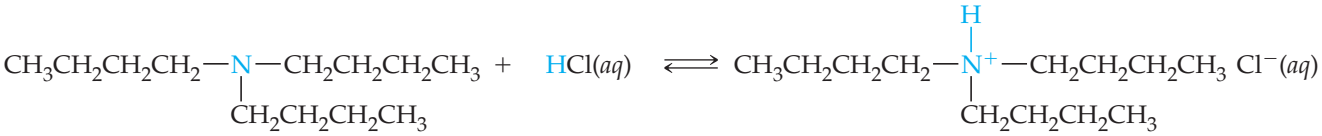
Learning Objective:

- Identify a quaternary ammonium ion and describe its properties.

An **ammonium salt** (also known as an *amine salt*) is composed of a cation and an anion and is named by combining the ion names. For example, in methylammonium chloride $(CH_3NH_3^+Cl^-)$, the methylammonium ion, $CH_3NH_3^+$, is the cation and the chloride ion is the anion.

Ammonium salt An ionic compound composed of an ammonium cation and an anion; an amine salt.

Ammonium salts are generally odorless, white, crystalline solids that are much more water-soluble than neutral amines because they are ionic (see the Chemistry in Action "Medications, Body Fluids, and the 'Solubility Switch'" on p. 580). For example:



Tributylamine
(water-insoluble)

Hydrochloric
acid

Tributylammonium chloride
(water-soluble)

In medicinal chemistry, amine salt formulas are quite often written and named by combining the structures and names of the amine and the acid used to form its salt. By this system, methylammonium chloride is written $CH_3NH_2 \cdot HCl$ and named methanamine hydrochloride (this will be a convention you will see more as you study the biochemistry sections of this book). This system is often used with drugs that are amine salts. For example, diphenhydramine is one of a family of antihistamines available in over-the-counter medications. Antihistamines of this type are oily liquids and difficult to formulate as such, so they are converted to amine salts for formulation into medications (see the Chemistry in Action "Medications, Body Fluids, and the 'Solubility Switch,'" Chapter 17).

$$(CH_6H_5)_2CHOCH_2CH_2N(CH_3)_2 \cdot HCl$$

or

$$(C_6H_5)_2CHOCH_2CH_2CH_2NH(CH_3)_2^+Cl^-$$

Diphenhydramine hydrochloride
(Benadryl), an antihistamine

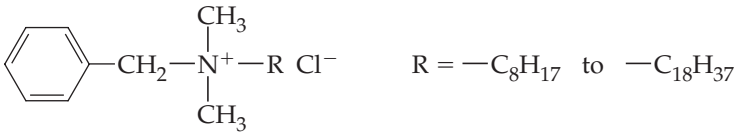
▲ Over-the-counter ammonium salts. The active ingredient in each of these over-the-counter medications is an ammonium salt.

Quaternary ammonium salt An ionic compound composed of a quaternary ammonium ion and an anion.

If a free amine is needed, it is easily regenerated from an amine salt by treatment with a base:

$$CH_3NH_3^+Cl^-(aq) + NaOH(aq) \longrightarrow CH_3NH_2(aq) + NaCl(aq) + H_2O(l)$$

Quaternary ammonium ions have four organic groups bonded to the nitrogen atom, and this bonding gives the nitrogen a permanent positive charge. With no H atom that can be removed by a base and no lone pair on the nitrogen that can bond to H^+, ammonium ions are neither acidic nor basic, and their structures in solution are unaffected by changes in pH. Their salts are known as **quaternary ammonium salts.** One commonly encountered quaternary ammonium salt has the following structure, where R represents a range of C_8 to C_{18} alkyl groups:



Benzalkonium chloride
(an antiseptic and disinfectant)

These benzalkonium chlorides have both antimicrobial and detergent properties. As dilute solutions, they are used in surgical scrubs and for sterile storage of instruments; concentrated solutions, however, are harmful to body tissues.

PROBLEM 16.17

Write the structures of the following compounds:

(a) Butyldiethylammonium bromide
(b) Tetrabutylammonium hydroxide
(c) Propylammonium iodide
(d) Isopropylmethylammonium chloride

PROBLEM 16.18

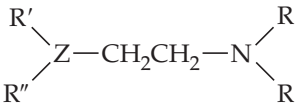
Identify each compound in Problem 16.17 as the salt of a primary, secondary, tertiary, or quaternary amine.

PROBLEM 16.19

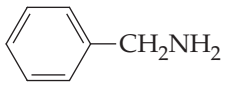
Write an equation for the formation of the free amine from butylammonium chloride by reaction with aqueous OH^-.

PROBLEM 16.20

The general structure of an antihistamine is shown in the margin. Does Benadryl (p. 547) have that general structure? Explain your comparison of the two structures.



Z = N, C, C — O



Benzylamine

PROBLEM 16.21

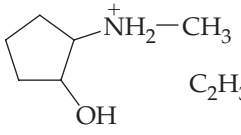
Write the structure of benzylamine hydrochloride in two different ways, and name the hydrochloride as an ammonium salt.

PROBLEM 16.22

Provide the products expected from the following reactions:

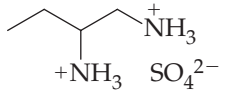
(a) $(CH_3CH_2)_3\overset{+}{N}H\ Br^- + LiOH \longrightarrow$?

(b)



$C_2H_3O_2^- + NaOH \longrightarrow$?

(c)



$SO_4^{2-} + 2\ KOH \longrightarrow$?

16.7 Amines in Plants: Alkaloids

Learning Objective:

- Describe the sources of alkaloids, name some examples, and tell how their properties are typical of amines.

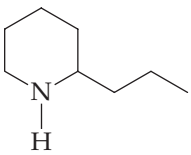
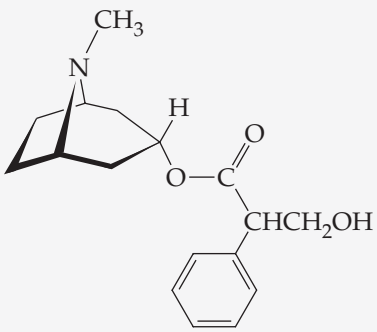
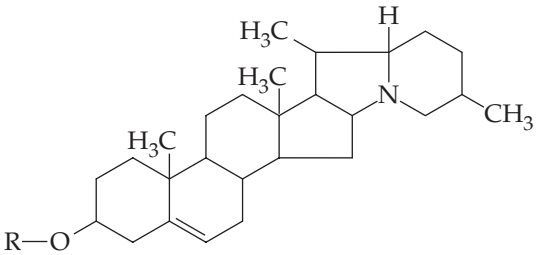
The roots, leaves, and fruits of flowering plants are a rich source of nitrogen compounds. These compounds, once called "vegetable alkali" because their water solutions are basic, are now referred to as **alkaloids.**

Alkaloid A naturally occurring, nitrogen-containing compound isolated from a plant; usually basic, bitter, and often poisonous.

The molecular structures of many thousands of alkaloids have been determined, with many having important medical uses. Most are bitter-tasting, physiologically active, structurally complex, and toxic to human beings and other animals in sufficiently high doses. One hypothesis is that the bitterness and poisonous nature of alkaloids probably evolved to protect plants from being devoured by animals. Not all alkaloids are known for their poisonous nature, however; most people are familiar with the physiological activity of two alkaloids—caffeine and nicotine (p. 543), which are stimulants. Quinine (p. 543) was for a long time the only drug available for treating malaria (caused by a parasitic protozoan); it is still used as a standard for bitterness: even a micromolar solution (μM; 1×10^{-6} mol/L) tastes bitter. Other alkaloids are notable as pain relievers *(analgesics),* as sleep inducers, and for the euphoric states they can create. The opiates (named because they are naturally occurring alkaloids found in the opium poppy *[Papaver somniferum]*) have been known since ancient times. About 20 alkaloids are present in the poppy, including morphine and codeine. The alkaloids themselves are oily liquids, and not very soluble in water; in contrast, their ammonium salts tend to be crystalline solids that are freely soluble in water.

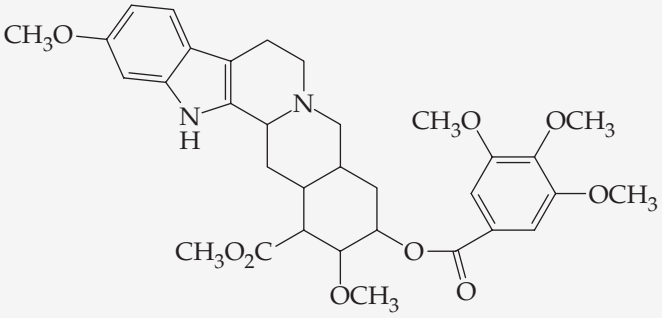
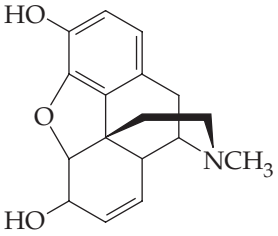
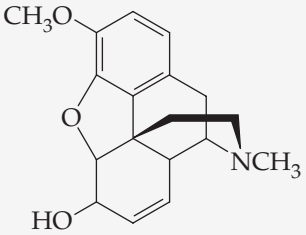
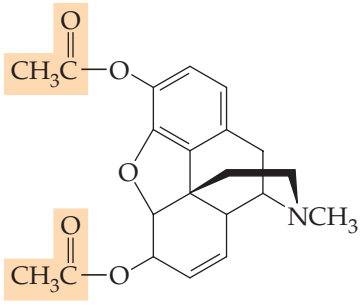
Table 16.2 lists some of the more historically common alkaloids along with their properties and uses.

Table 16.2 Some Alkaloids and Their Properties

Name	Structure	Properties and Uses
Coniine		• Extracted from poison hemlock *(Conium maculatum).* • Toxic to humans and all classes of livestock. • Fatal at levels below 0.1 g; death is caused by respiratory paralysis • Used to carry out death sentences in ancient Greece (most famously Socrates).
Atropine		• Toxic substance in the herb known as *deadly nightshade* or *belladonna (Atropa belladonna).* • Acts on the central nervous system. • In appropriately low dosage, used medically to reduce cramping of the digestive tract and in the treatment of slow heart rate (bradycardia). • Used as a treatment against nerve gases, such as Sarin.
Solanine	 R = three sugar molecules	• More potent poison than atropine. • Found in tiny amounts in potatoes just under the skin and contributes to their characteristic flavor. • Amounts increase in potatoes upon exposure to light and is the reason you must peel green potatoes deeply (the green is due to chlorophyll, which is not toxic, and acts as a warning). • Has fungicidal and pesticidal properties. • Possesses sedative and anticonvulsant properties, and has been used as a treatment for asthma, with questionable effectiveness.

(Continued)

Table 16.2 (*Continued*)

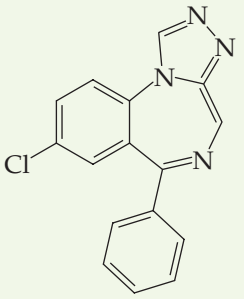
Name	Structure	Properties and Uses
Reserpine		• An indole alkaloid isolated from the dried root of *Rauwolfia serpentina* (Indian snakeroot). • Used for centuries in India for the treatment of insanity, as well as fever and snakebites. • Historically used medically for the control of high blood pressure, it revolutionized treatment of a previously untreatable and life-threatening condition. • Rarely used today in humans due to the development of better drugs for hypertension. • Used as a long-acting tranquilizer to subdue excitable or difficult horses.
Morphine		• The most abundant opiate found in opium; is believed to be historically the first active ingredient, natural plant alkaloid ever isolated. • Originally named after the Greek god of dreams, Morpheus, due to its tendency to cause sleep. • Acts directly on the central nervous system (CNS) to relieve pain; medically used to treat both acute and chronic pain. • Has a high potential for addiction due to rapid development of both tolerance to its analgesic effects and psychological dependence.
Codeine (3-methyl-morphine)		• The second-most abundant alkaloid in opium, it is a naturally occurring methylated morphine. • Used to treat mild to moderate pain and to relieve coughing; also used to suppress premature labor contractions. • Often used in combination with other pain relievers such as acetaminophen, aspirin, or ibuprofen, providing greater pain relief than either compound alone.
Heroin (diacetyl-morphine)		• A synthetic opiate, it is prepared by acetylation of the —OH groups of morphine (highlighted in orange). • Developed chiefly as a nonaddictive morphine substitute for cough suppressants; since proven to be false. • When injected, it is two to four times more potent than morphine with a faster onset of action. • The higher potency and speed of action are due to its ability to very rapidly cross the blood–brain barrier (the acetyl groups render it much more fat soluble than morphine itself) where it is deacetylated ultimately to morphine. • Used as a legal, medically prescribed drug for pain, as a cough suppressant and as an antidiarrhea drug. • Highly addictive, making its illegal, recreational use a real problem in society.

CHEMISTRY IN ACTION

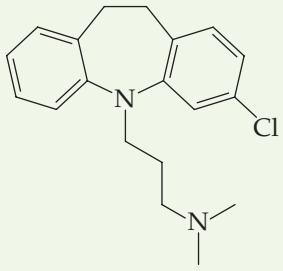
Calming a Stormy Mind: Amines as Anti-Anxiety Medications

Anxiety. We all experience it at one time or another in our daily life, whether getting to an appointment on time, taking a test, a job interview, or just meeting your date for the first time. For most of us, it is a fleeting condition: we deal with it and move on with our lives. When stress in our life is more persistent, like applying to nursing or graduate school, or raising a family, many people find ways to lessen the effects of anxiety through exercise, meditation, or other methods to relieve stress. But what if you cannot find a way to deal with your anxiety? In 2015, the United States alone has approximately 40 million people with anxiety disorders, many of whom feel their anxiety is so severe they cannot eat, sleep, work, or function normally. Prolonged anxiety can lead to depression, so its treatment is a real medical concern.

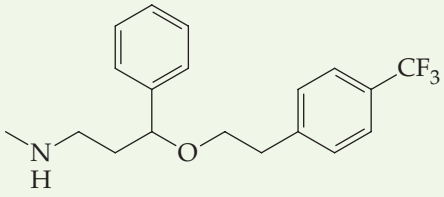
Medications to treat anxiety (anxiolytics) include alprazolam (Xanax), clomipramine (Anafanil), fluoxetine (Prozac), and sertraline (Zoloft), which are but a few anxiolytics regularly prescribed for the treatment of obsessive-compulsive disorder (OCD), social anxiety disorder, and panic attacks. What all of these drugs have in common is that they are heterocyclic amines that also contain aromatic rings with halogens present on them.



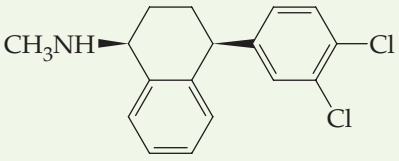
Alprazolam



Clomipramine



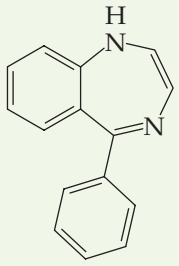
Fluoxetine



Sertraline

The mode of action of these anti-anxiety drugs depends on what brain receptors they target. For example, alprazolam and clomipramine target gamma-aminobutyric acid (GABA) receptors in the brain, increasing feelings of relaxation. These two molecules belong to a class known as the benzodiazapines (BZDs), a name that reflects the core structure found in all BZDs.

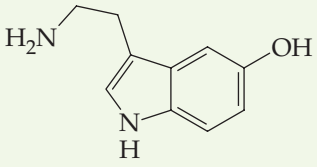
Benzodiazapines are regarded as the most effective class of medications for reducing anxiety, as they can in many cases be used on an "as needed" basis; the most famous member of this class being diazepam (Valium). For short-term use, they are considered the drug of choice, but their effectiveness comes with a high risk of both tolerance (higher and higher doses needed over time to achieve a desired effect) and addiction. Long-term regular use also has an associated risk of the development of dementia and permanent memory impairment. To overcome these side effects, new classes of anxiolytics were needed.



Benzodiazepine core structure

A second group of anti-anxiety medications belong to what are known as the selective serotonin reuptake inhibitors, or SSRIs. Fluoxetine and sertraline are examples of this class of anxiolytic.

SSRIs are believed to increase levels of the neurotransmitter serotonin by inhibiting its reuptake, making more of this important neurotransmitter available. Serotonin in the brain plays an important role in many behaviors, including sleep, appetite, and mood. Serotonin is believed to be a contributor to feelings of well-being and happiness, so when levels drop, it is thought that mood swings follow; the SSRIs can alleviate these. Unlike the BZDs, however, they cannot be used as needed but rather require a breaking in period to reach effective levels, sometimes taking two to eight weeks for the full, positive effects of the medication to be seen. Since they have not been shown to be addictive, and tolerance has a slower onset, they are more effective as a long-term option. In addition, the SSRIs have been found to be safe to take with almost all other medicines, another important aspect of a long-term drug. But even the SSRIs are not the answer for all; they can be poorly tolerated in many patients, as well as producing significant unwanted side effects such as weight gain, sleepiness or insomnia, and headaches. Still, the benefits of these amazing amines in almost all cases outweigh the drawbacks. Current research into this area is still going at full speed; as we get better at understanding what biochemical mechanisms are at work in anxiety and depression, new, safer, and more effective medications to treat these conditions will undoubtedly become available.



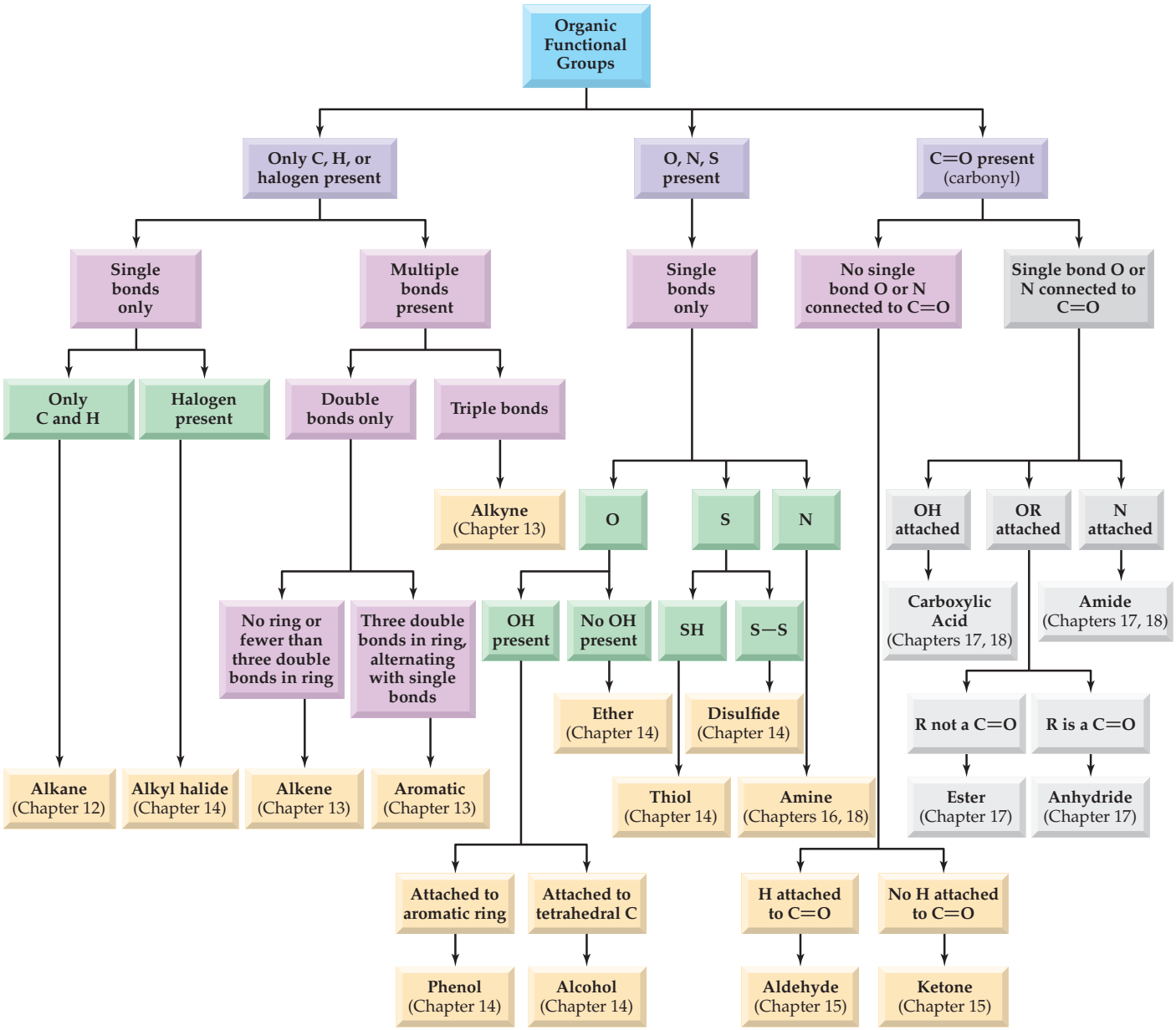
Serotonin

CIA Problem 16.1 A medication used to treat anxiety disorders is generally called what?

CIA Problem 16.2 What are the benefits of the benzodiazapines? What are the side effects?

CIA Problem 16.3 What are the benefits of the SSRIs as compared to the benzodiazapines? Their side effects?

CONCEPT MAP: ORGANIC CHEMISTRY FAMILIES



▲ **Figure 16.2 Functional Group Concept Map.** This is the same concept map we saw at the end of Chapters 12–15, except the functional groups discussed in this chapter, aldehydes and ketones, have now been colorized.

SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Identify and classify an amine as primary, secondary, or tertiary.** *Amines* are classified as *primary*, *secondary*, or *tertiary*, depending on whether they have one, two, or three organic groups individually bonded to nitrogen. These amines can all accept hydrogen ion (H^+) to form *ammonium ions*, which have four bonds to the nitrogen, which bears a single positive charge. Ions with four organic groups bonded to nitrogen are known as *quaternary ammonium ions (see Problems 23, 31, 32, 35, and 36).*
- **Name a simple amine given its structure or draw an amine given its name.** Primary amine names have *-amine* added to the alkyl group name, and secondary and tertiary amines with identical R groups have *di-* and *tri-* prefixes. When the R groups are different, amines are named as *N-substituted derivatives* of the amine with the largest R group. Ions derived from amines are named by replacing *-amine* in the name with *-ammonium.* The structure of a simple amine is drawn by starting with the nitrogen and placing alkyl groups on as called for. The $-NH_2$ group when found as a substituent in a molecule is called an *amino group (see Problems 29–32, 35, 36, 45, 46, 52, and 58).*
- **Describe amine properties such as hydrogen bonding, solubility, boiling point, and basicity.** Amines have an unshared electron pair on nitrogen that is available to allow it to behave as a base (and accept a proton) or to be used for hydrogen bonding. Primary and secondary amine molecules hydrogen-bond to each other, but tertiary amine molecules cannot do so. Thus, the general order of boiling points for molecules of comparable size is

Hydrocarbons < Tertiary amines < Primary and secondary amines < Alcohols

All amines can, however, hydrogen-bond to other molecules containing OH and NH groups, and for this reason small amine molecules

are water-soluble. Many amines are physiologically active. Volatile amines have strong, unpleasant odors *(see Problems 23–25, 27, 33, 34, 49, 50, 54, and 57).*

- **Identify a heterocyclic amine.** In *heterocyclic amines*, the nitrogen of the amine group is bonded to two carbon atoms that are part of a ring. The ring can be aromatic or nonaromatic. Nonaromatic, heterocyclic amines are about as basic as regular amines. If the nitrogen is part of an aromatic ring, its lone pair of electrons becomes part of the aromatic system, making it less basic than a nonaromatic amine. Heterocyclic amines tend to have names that are historical in origin *(see Problems 48 and 55–57).*
- **Identify and draw the products formed when an amine reacts with acid.** Amines are weak bases and establish equilibria with water by accepting H^+ to form ammonium ions (RNH_3^+, $R_2NH_2^+$, R_3NH^+) and hydroxide ions (OH^-). They react directly with acids to form ammonium ions, which are water soluble. Ammonium ions react as acids (proton donors) in the presence of a base; when that base is hydroxide, water is formed and the uncharged amine is regenerated *(see Problems 28, 39–42, 44, and 53).*
- **Identify a quaternary ammonium ion and describe its properties.** *Quaternary ammonium ions* (R_4N^+) are ions that form when all four bonds to the nitrogen are to carbons. Quaternary ammonium ions have a permanent positive charge since they have no lone electron pair; because of this, they are not bases, nor can they form hydrogen bonds. They are not acids, because all bonds to nitrogen are to carbons and not hydrogens. Due to their fixed positive charge, they are water soluble *(see Problems 28, 35, 36, 39, 40, 43–45, and 49).*
- **Describe the sources of alkaloids, name some examples, and tell how their properties are typical of amines.** *Alkaloids* are naturally occurring nitrogen compounds found in plants. Quinine, morphine, and atropine are three examples of alkaloids. All alkaloids are amines and, therefore, basic. Most possess a bitter taste. Like other amines, many are physiologically active, notably as poisons or analgesics *(see Problems 38, 48, 51, and 55).*

KEY WORDS

Alkaloid, *p. 549*
Amine (primary, secondary, tertiary), *p. 537*
Amino group, *p. 539*
Ammonium ion, *p. 544*
Ammonium salt, *p. 547*
Heterocycle, *p. 543*
Lewis base, *p. 540*
Quaternary ammonium ion, *p. 537*
Quaternary ammonium salt, *p. 548*

SUMMARY OF REACTIONS

1. Reactions of amines (Section 16.4)

(a) Acid-base reaction with water:

$$CH_3CH_2NH_2 + H_2O \rightleftharpoons CH_3CH_2NH_3^+ + OH^-$$

(b) Acid-base reaction with a strong acid to yield an ammonium ion:

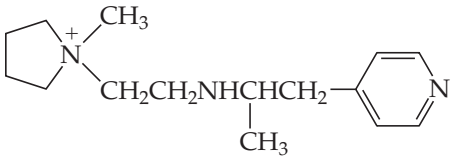
$$CH_3CH_2NH_2 + H_3O^+ \longrightarrow CH_3CH_2NH_3^+ + H_2O$$

2. Reaction of ammonium ion (Section 16.4) or amine salt (Section 16.5) Acid-base reaction of primary, secondary, or tertiary amine salt (or ion) with a base to regenerate the amine:

$$CH_3CH_2NH_3^+Cl^- + NaOH \longrightarrow CH_3CH_2NH_2 + NaCl + H_2O$$

UNDERSTANDING KEY CONCEPTS

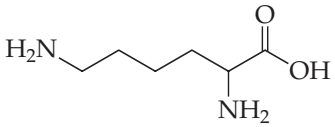
16.23



(a) For the compound above, identify each nitrogen as either a primary, secondary, tertiary, quaternary, or aromatic amine.

(b) Which amine group(s) would be able to provide a hydrogen bond? Which could accept a hydrogen bond?

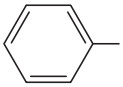
16.24 The structure of the amino acid lysine (in its uncharged form) is shown below.

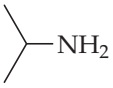


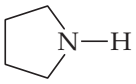
(a) Which amine groups would be able to participate in hydrogen bonding?

(b) Is lysine likely to be water-soluble? Explain.

16.25 Draw structures to illustrate hydrogen bonding (similar to those on p. 541) between the following compounds.

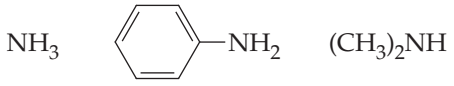
(a) Four  molecules

(b) Two  and two H_2O

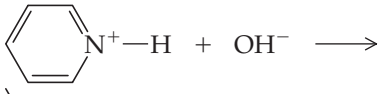
(c) Two CH_3NH_2 and two 

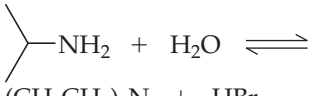
16.26 Explain what bonds must be made or broken and where the electrons go when the hydrogen-bonded water between the two amines shown on page 541 reacts to form an amine, ammonium ion, and OH^-.

16.27 Which of these amines is the strongest base? The weakest? (See Section 16.4.)

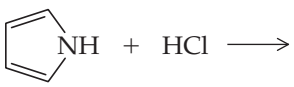


16.28 Complete the following equations:

(a) 

(b) 

(c) $(CH_3CH_2)_3N + HBr \longrightarrow$

(d) 

ADDITIONAL PROBLEMS

AMINES AND AMMONIUM SALTS (SECTIONS 16.1–16.3)

16.29 Draw the structures corresponding to the following names:

(a) *N*-Methylcyclohexylamine

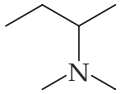
(b) Dipropylamine **(c)** Pentylamine

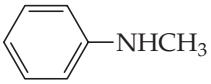
16.30 Draw the structures corresponding to the following names:

(a) *N*-Methylpentylamine

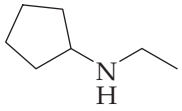
(b) *N*-Ethylcyclobutylamine **(c)** *p*-Propylaniline

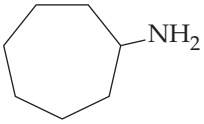
16.31 Name the following amines, and classify them as primary, secondary, or tertiary:

(a) 

(b) 

16.32 Name the following amines, and identify them as primary, secondary, or tertiary:

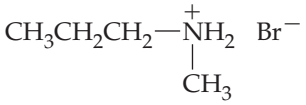
(a) 

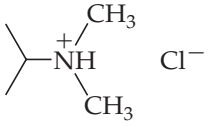
(b) 

16.33 Is water a weaker or stronger base than ammonia?

16.34 Which is a stronger base, diethyl ether or diethylamine?

16.35 Give names or structures for the following ammonium salts. Indicate whether each is the ammonium salt of a primary, secondary, or tertiary amine.

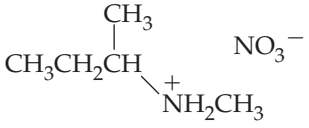
(a) 

(b) 

(c) *N*-Propylbutylammonium bromide

(d) Cyclobutylammonium bromide

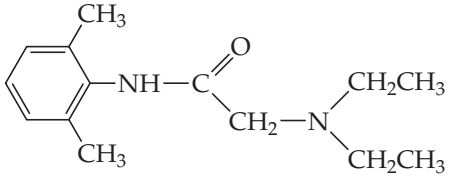
16.36 Give names or structures for the following ammonium salts. Indicate whether each is the ammonium salt of a primary, secondary, or tertiary amine.

(a) 

(b) Pyridinium chloride

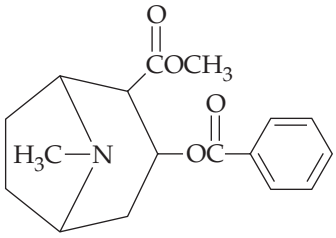
(c) *N*-Butyl-*N*-isopropylhexylammonium chloride

16.37 The compound lidocaine is used medically as a local anesthetic. Identify the functional groups present in lidocaine (refer to Section 12.2).



Lidocaine

16.38 Identify the functional groups in cocaine (refer to Section 12.2).



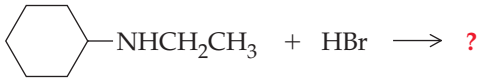
Cocaine

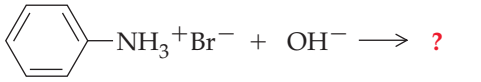
16.39 Draw the structures of the ammonium ions formed when the amines in Problem 16.29 are treated with acid.

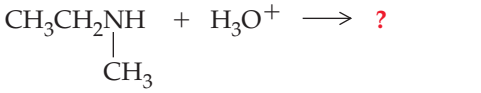
16.40 Draw the structures of the ammonium ions formed when the amines in Problem 16.30 are treated with acid.

REACTIONS OF AMINES (SECTIONS 16.3, 16.5, 16.6)

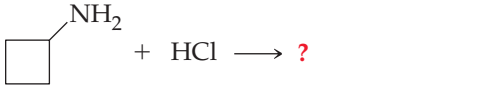
16.41 Complete the following equations (hint: remember that a nitrogen with three groups bound to it has a lone pair and one with four does not; see Worked Examples 16.4 and 16.5 for help):

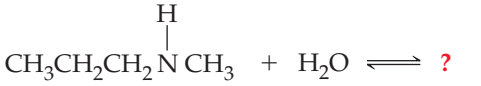
(a) 

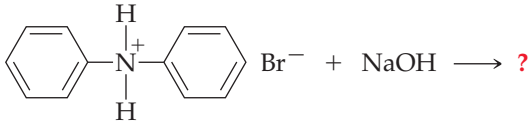
(b) 

(c) 

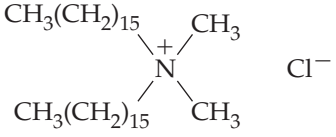
16.42 Complete the following equations. (Hint: Remember that a nitrogen with three groups bound to it has a lone pair and one with four does not; see Worked Examples 16.4 and 16.5 for help.)

(a) 

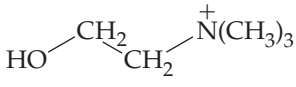
(b) 

(c) 

16.43 Many hair conditioners contain an ammonium salt such as the following to help prevent "fly-away" hair. These ions will react with neither acid nor base. Provide a reason why.



16.44 Choline has the following structure. Do you think that this substance reacts with aqueous hydrochloric acid? If so, what is the product? If not, why not?



CONCEPTUAL PROBLEMS

16.45 Propose structures for amines that fit these descriptions:

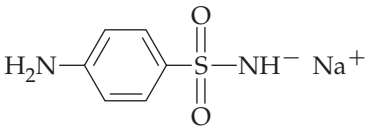
(a) A secondary amine with formula $C_5H_{13}N$

(b) A tertiary amine with formula $C_6H_{13}N$

(c) A cyclic quaternary amine that has the formula $C_6H_{14}N^+$

16.46 *para*-Aminobenzoic acid (PABA) is a common ingredient in sunscreens. Draw the structure of PABA (refer to Table 13.2).

16.47 PABA (Problem 16.46) is used by certain bacteria as a starting material from which folic acid (a necessary vitamin, Table 19.3) is made. Sulfa drugs such as sodium sulfanilamide work because they resemble PABA. The bacteria try to metabolize the sulfa drug, fail to do so, and die due to lack of folic acid.

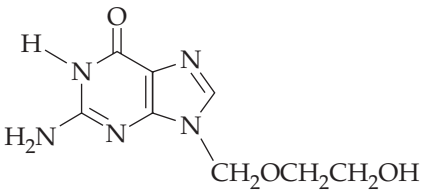


Sodium sulfanilamide

(a) Describe how this structure is similar to that of PABA.

(b) Why do you think the sodium salt, rather than the neutral compound, is used as the drug?

16.48 Acyclovir is an antiviral drug used to treat herpes infections. It has the following structure:

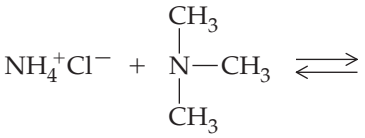


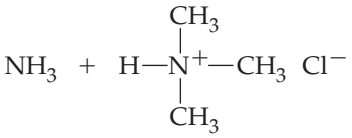
Acyclovir

(a) What heterocyclic base (Table 16.1) is the parent of this compound?

(b) Label the other functional groups present.

16.49 Which is the stronger base, trimethylamine or ammonia? In which direction will the following reaction proceed?

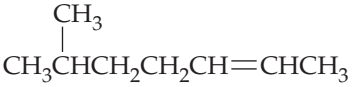


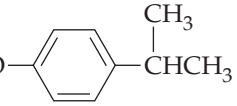


16.50 How do amines differ from analogous alcohols in (a) odor, (b) basicity, and (c) boiling point?

16.51 Name at least two undesirable characteristics are often associated with alkaloids.

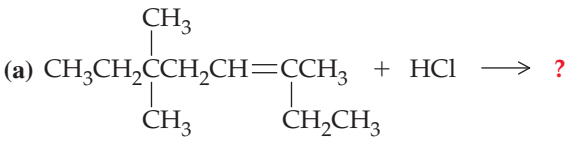
16.52 Name the following compounds:

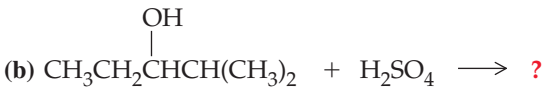
(a) 

(b) 

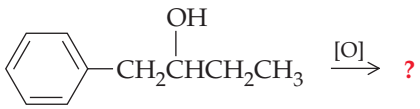
(c) $(CH_3CH_2CH_2CH_2)_2NH$

16.53 Complete the following equations (Hint: Answers may include concepts learned from previous organic chapters):

(a) 

(b) 

(c) $2\ CH_3CH_2SH \xrightarrow{[O]}$?

(d) 

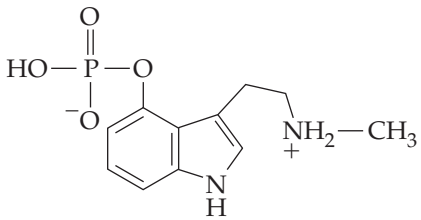
(e) $(CH_3)_3N + H_2O \rightleftharpoons$?

(f) $(CH_3)_3N + HCl \longrightarrow$?

(g) $(CH_3)_3NH^+ + OH^- \longrightarrow$?

16.54 Hexylamine and triethylamine have the same molar mass. The boiling point of hexylamine is 129 °C (402 K), whereas that of triethylamine is only 89 °C (362 K). Explain these observations.

16.55 Baeocystin is a hallucinogenic compound that is isolated from the mushroom *Psilocybe baeocystis* and has the structure shown below. What heterocyclic base (Table 16.1) is the parent of this compound?



Baeocystin

16.56 Why is cyclohexylamine not considered to be a heterocyclic nitrogen compound?

16.57 Benzene and pyridine are both single-ring, aromatic compounds. Benzene is a neutral compound that is insoluble in water. Pyridine, with a similar molar mass, is basic and completely miscible with water. Explain these phenomena.

16.58 Name the organic reactants in Problem 16.41.

GROUP PROBLEMS

16.59 1-Propylamine, propan-1-ol, acetic acid, and butane have about the same molar masses. Which would you expect to have the (a) highest boiling point, (b) lowest boiling point, (c) least solubility in water, and (d) least chemical reactivity? Have each member of your group chose a part to answer, and then discuss with each other why those answers were chosen.

16.60 Which of the two amines, decylamine or ethanamine, would you expect to be more soluble in water and why?

16.61 Lemon juice, which contains citric acid, is traditionally recommended for removing the odor associated with cleaning fish. What functional group is responsible for a "fishy" odor, and why does lemon juice work to remove the odor? If possible, test this at home using a piece of fish.

17

Carboxylic Acids and Their Derivatives

CONTENTS

CONCEPTS TO REVIEW

A. Electronegativity and Molecular Polarity (Sections 5.8 and 5.9)

B. Hydrogen Bonds (Section 8.2)

C. Acid-Base Chemistry (Sections 10.1–10.6 and 10.14)

D. Functional Groups (Section 12.2)

E. Naming Alkanes (Section 12.6)

F. Types of Organic Reactions (Section 13.5)

▲ Many pain relievers utilize the carboxylic acid functional group as a solubility switch, aiding in their ability to be effective analgesiscs.

We humans are composed of about 60–65% water, so it is safe to say that biochemically we live and function in an aqueous environment. Yet, the vast majority of the organic molecules you have seen to date have little to no solubility in water. So how are molecules that are not soluble in water used in an aqueous environment? This is a particularly important question when those organic molecules are medicines. To accomplish this, nature

has ingeniously used the idea of incorporating a "solubility switch" into many of the biomolecules found. A solubility switch is simply a group present in a molecule that can turn it from being insoluble to soluble and back again as needed. The two most common functional groups that allow this to be achieved are amines (Chapter 16) and carboxylic acids, which we will discuss in this chapter. In a basic environment a carboxylic acid will be converted into a carboxylate ion, making it soluble. This strategy has been used by chemists to make medicines soluble in bodily fluids, allowing them to be transported from their entry point in the body to their site of action. Common carboxylic acid-containing drugs such as naproxen (Aleve) utilize this strategy. We will examine the idea of the solubility switch in the Chemistry in Action "Medications, Body Fluids, and the 'Solubility Switch'" found at the end of this chapter.

The last group of carbonyl compounds to be discussed are the *carboxylic acids* and their *derivatives*—the *esters* and *amides*. Esters of phosphoric acid are introduced here as well because of their major role in biochemistry and their chemical similarity to carboxylic acids and esters.

17.1 Carboxylic Acids and Their Derivatives: Properties and Names

Learning Objectives:

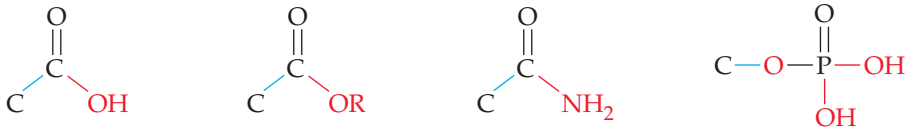
- Compare and contrast the structures, reactions, hydrogen bonding, water solubility, boiling points, and acidity or basicity of carboxylic acids, esters, and amides.
- Name simple carboxylic acids, esters, and amides given a structure and write a structure given a name.

Carboxylic acids have an —OH group bonded to the carbonyl carbon atom. In their derivatives, the —OH group is replaced by other groups. **Esters** have an —OR′ group bonded to the carbonyl carbon atom. **Amides** have an $-NH_2$, —NHR′, or $-NR'_2$ group bonded to the carbonyl carbon atom. Finally, there are the esters of phosphoric acid; these are important in the chemistry of a number of biomolecules, especially deoxyribonucleic acid (DNA) (Chapter 28).

Carboxylic acid A compound that has a carbonyl group bonded to an —OH group, RCOOH.

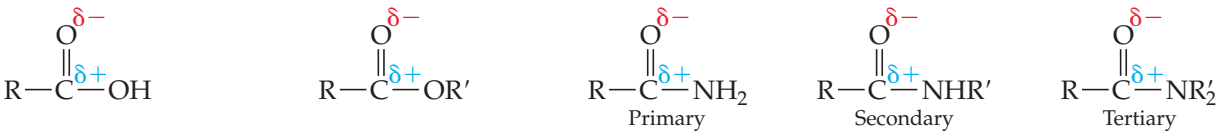
Ester A compound that has a carbonyl group bonded to an —OR′ group, RCOOR′.

Amide A compound that has a carbonyl group bonded to a nitrogen-atom group, $RCONR'_2$, where the R′ groups may be alkyl groups or hydrogen atoms.



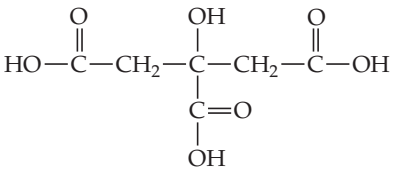
Carboxylic acid | Ester | Amide | Phosphoric acid ester

Since carboxylic acids, esters, and amides all contain a carbonyl carbon atom (C═O) bonded either to an oxygen or to a nitrogen, they are all polar. Their structural similarities also account for many similarities in the properties of these compounds. As a result, they all boil at a higher temperature than comparable alkanes. Carboxylic acids and amides that have a H on the nitrogen can also take part in hydrogen bonding, which plays a prominent role in their chemical, physical, and biochemical properties.



Carboxylic acid (RCOOH or RCO_2H) | Ester (RCOOR′ or RCO_2R') | Amides (Primary, Secondary, Tertiary) ($RCONH_2$, RCONHR′, $RCONR'_2$)

Carboxylic acids occur throughout the plant and animal kingdoms; two of the most common you will regularly come across are acetic acid and citric acid. Acetic acid is the primary organic component of vinegar, which is simply a solution of 4–8% (v/v) acetic

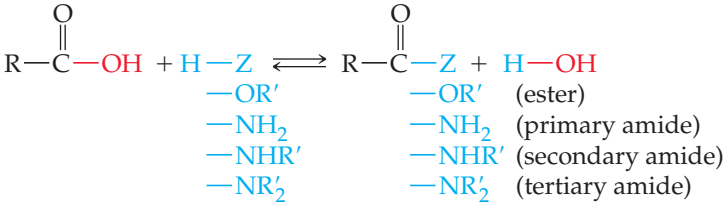


Citric acid

LOOKING AHEAD Citric acid lends its name to the *citric acid cycle*, part of the major biochemical pathway that leads directly to the generation of energy. Citric acid is the product of the first reaction of an eight-reaction cycle, which is presented in Section 21.8.

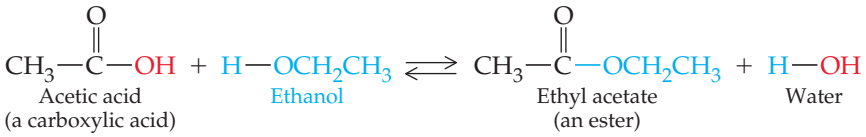
acid in water (with various flavoring agents). Arising from the fermentation of fruit in the presence of excess oxygen, the production of "boutique" vinegars from various wine varietals has become big business. Citrus fruits owe their tartness to citric acid; for example, lemon juice contains 4–8% (v/v) and orange juice about 1% (v/v) citric acid. Citric acid is what is known as a tricarboxylic acid, since it has three carboxylic acid groups in it. Produced by almost all plants and animals during metabolism, its normal concentration in human blood is about 2 mg/100 mL. Citrates (a term used to describe mixtures of citric acid and its salts) are commonly used to add tartness to candies and soft drinks and react with hydrogen carbonate ion to produce the fizz in Alka-Seltzer; they are also used extensively in pharmaceuticals and cosmetics.

Because these compounds all contain a carbonyl group attached to an electronegative atom, they all are able to undertake substitution reactions at the carbonyl carbon, unlike ketones and aldehydes. Carboxylic acids and their derivatives commonly undergo **carbonyl-group substitution reactions,** in which a group we represent as —Z replaces (substitutes for) the group bonded to the carbonyl carbon atom:

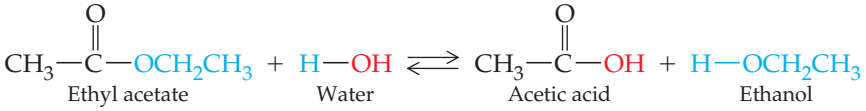


Carbonyl-group substitution reaction A reaction in which a new group replaces (substitutes for) a group attached to a carbonyl-group carbon.

For example, esters are routinely made by such reactions.

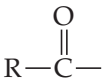


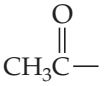
And esters can be converted back to carboxylic acids by reversing the reaction (this is known as hydrolysis).



Acyl group An RC═O group.

Acyl groups





Acetyl (Ac)

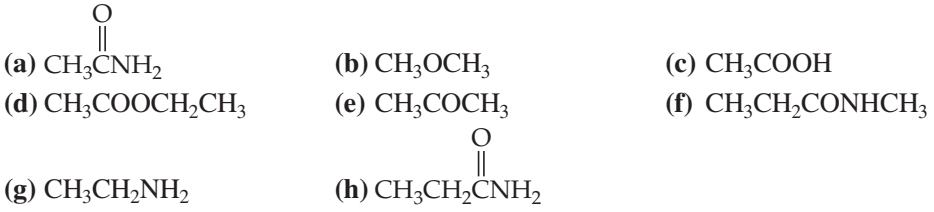
Benzoyl (Bz)

The portion of the carboxylic acid that does not change during a carbonyl-group substitution reaction is known as an **acyl group.**

In biochemistry, carbonyl-group substitution reactions are called *acyl transfer reactions* and play an important role in the metabolism of a variety of biomolecules.

PROBLEM 17.1

Identify the following molecules as a carboxylic acid, an amide, an ester, or none of these.



Carboxylic Acids

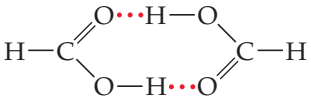
The most significant property of carboxylic acids is their behavior as weak acids. They surrender the hydrogen of the **carboxyl group,** —COOH, to bases and establish an acid-base equilibrium in aqueous solution (a property further discussed in Section 17.3). The common carboxylic acids share the concentration-dependent corrosive properties of all acids but are not generally hazardous to human health.

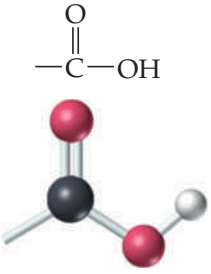
Carboxyl group The —COOH functional group.

Like alcohols, carboxylic acids form hydrogen bonds with each other so that even formic acid (HCOOH), the simplest carboxylic acid, is a liquid at room temperature with a boiling point of 101 °C (374 K).

CONCEPTS TO REVIEW Recall that acid–base equilibria were discussed in Sections 10.1–10.3.

Carboxylic acids pair up by hydrogen bonding, as illustrated for formic acid.





Carboxyl group

Acids with saturated, straight-chain R groups of up to nine carbon atoms are volatile liquids with strong, pungent, and usually unpleasant odors; those with up to four carbons are water-soluble. Acids with R groups larger than nine carbons are waxy, odorless solids. In general, as the carbon chain length gets longer, the melting and boiling points increase; this is especially true for boiling points, where each carbon that is added increases the boiling temperature by 20–25 °C (293–298 K). Their water solubility decreases as the size of the hydrophobic, alkane-like R group increases relative to the size of the water-soluble —COOH portion.

Recall that the relationship between the size of the hydrophobic portion of an organic molecule and its solubility was discussed in Section 14.3.

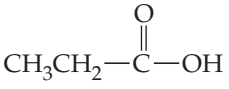
Nomenclature

Since we have now introduced all of the main functional groups found in organic chemistry, we need to learn how to name compounds that contain more than one functional group. Within the International Union of Pure and Applied Chemistry (IUPAC) nomenclature scheme, a hierarchy exists when more than one functional group is present; that is, the priority of the functional group determines how the compound is named. That priority, from most important to least, is as follows:

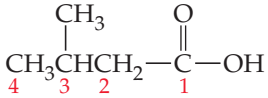
Carboxylic Acids>Esters>Amides>Aldehydes>Ketones>Alcohols>Thiols>Amines>Ethers>Alkenes>Alkynes>Alkyl Halides>Alkanes.

So, a molecule that contains both an alcohol and a carboxylic acid is named as a carboxylic acid, and a molecule that contains an amine and an alcohol would be named as an amine, and so on. Numbering starts with the carbon that is either attached to or part of the functional group. While you will need to know how to name only simple multifunctional compounds, it is important that you are aware of this hierarchy, as it will come up later in biochemistry and will help you to understand why these molecules are named or classified as they are.

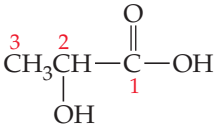
Carboxylic acids are named in the IUPAC system by replacing the final *-e* of the corresponding alkane name with *-oic acid*. The 3-carbon acid is propanoic acid; the straight-chain, 4-carbon acid is butanoic acid; and so on. If alkyl substituents are present, the chain is numbered beginning at the —COOH end, as in 3-methylbutanoic acid; the same goes if a second, lower priority functional group is present as in 2-hydroxypropanoic acid (better known as lactic acid, the acid present in sour milk).



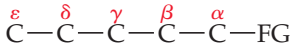
Propanoic acid



3-Methylbutanoic acid

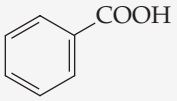
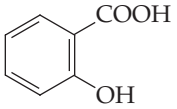


Lactic acid
(2-hydroxypropanoic acid)



Greek indexing system used in common nomenclature. The α carbon is the first C attached to the functional group (FG)

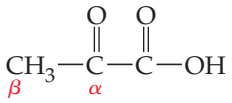
Table 17.1 Some Common Carboxylic Acids

Structure	Common Name
Carboxylic Acids	
HCOOH	Formic
CH_3COOH	Acetic
CH_3CH_2COOH	Propionic
$CH_3CH_2CH_2COOH$	Butyric
$CH_3CH_2CH_2CH_2COOH$	Valeric
$CH_3(CH_2)_{16}COOH$	Stearic
Dicarboxylic Acids	
HOOCCOOH	Oxalic
$HOOCCH_2COOH$	Malonic
$HOOCCH_2CH_2COOH$	Succinic
$HOOCCH_2CH_2CH_2COOH$	Glutaric
Unsaturated Acids	
$H_2C{=}CHCOOH$	Acrylic
$CH_3CH{=}CHCOOH$	Crotonic
Aromatic Acids	
	Benzoic
	Salicylic

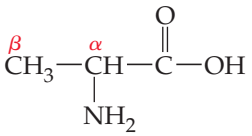
Acetyl group (Ac) A $CH_3—C(=O)—$ group.

Biochemistry is dependent on the continual breakdown of food molecules. Frequently, this process requires transfer of acetyl groups from one molecule to another. Acetyl-group transfer occurs, for example, at the beginning of the citric acid cycle, which is central to the production of life-sustaining energy (Section 21.8).

Unfortunately, the common names of many of the carboxylic acids are used far more often than their IUPAC names, primarily because carboxylic acids were among the first organic compounds to be isolated and purified. Formic acid (from the Latin *formica,* "ant"), acetic acid (from the Latin *acetum,* "sour"), and lactic acid (from *lactis,* "milk") are but three examples. Recognizing the common acid names given in Table 17.1 is important, as they provide the basis for many of the derivatives of these acids. When using common names, the carbon atoms attached to the —COOH group are identified by Greek letters α, β, γ, and so on, rather than numbers. For example, using the common system to name the structure on the left below, the 3-carbon acid is *propionic acid,* and the second C=O group (a *keto* group in common nomenclature) next to the —COOH group is an α-keto group and the compound called an α-keto acid.



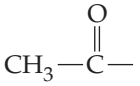
α-Ketopropionic acid (an α-keto acid, Pyruvic acid, a key biochemical intermediate)



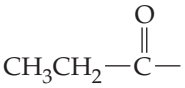
α-Aminopropionic acid (alanine)

In alanine, as in all common amino acids, the $–NH_2$ group is on the α carbon atom (the C next to –COOH).

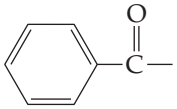
When discussing the acyl group that remains after a carboxylic acid loses its —OH, we replace the *-ic acid* at the end of the acid name with *-oyl*. One very important exception is the acyl group from acetic acid, which is traditionally called an **acetyl group** and is abbreviated Ac.



Acetyl group

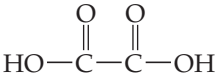


Propanoyl group



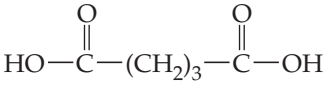
Benzoyl group

Dicarboxylic acids, which contain two —COOH groups, are named systematically by adding the ending *-dioic acid* to the alkane name (the *-e* is retained). Again, the simple dicarboxylic acids are usually referred to by their common names. Oxalic acid (IUPAC name: ethanedioic acid) is found in plants of the genus *Oxalis,* which includes rhubarb and spinach. You will encounter succinic acid, glutaric acid, and several other dicarboxylic acids when we come to the generation of biochemical energy and the citric acid cycle (Section 21.8).



Oxalic acid (ethanedioic acid)

Succinic acid (butanedioic acid)

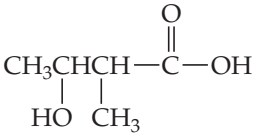


Glutaric acid (pentanedioic acid)

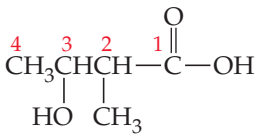
Unsaturated acids (carboxylic acids that contain one or more carbon–carbon double bonds) are named systematically in the IUPAC system with the ending *-enoic*. For example, the simplest unsaturated acid, $H_2C{=}CHCOOH$, is named propenoic acid. It is, however, best known as acrylic acid, which is a raw material for acrylic polymers.

Worked Example 17.1 Naming a Carboxylic Acid

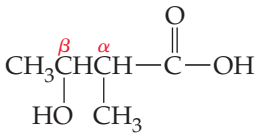
(a) Give the systematic and common names for this compound:



ANALYSIS Because this molecule contains both an alcohol and a carboxylic acid, and the carboxylic acid has the higher priority, it will be named as a carboxylic acid. First identify the longest chain containing the —COOH group and number it starting with the carboxyl-group carbon.



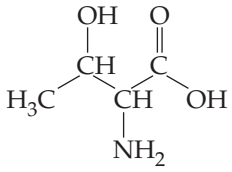
The parent compound is the 4-carbon acid, butanoic acid. It has a methyl group on carbon 2 and a hydroxyl group on carbon 3. From Table 17.1 we see that the common name for the 4-carbon acid is butyric acid. In the common nomenclature scheme, substituents are located by Greek letters rather than numbers.



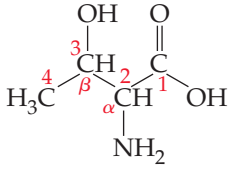
SOLUTION

The IUPAC name of this molecule is 3-hydroxy-2-methylbutanoic acid; the common name of this acid is β-hydroxy-α-methylbutyric acid.

(b) Give the systematic and common names for this compound:



ANALYSIS Because this molecule contains an alcohol, an amine, and a carboxylic acid, and the carboxylic acid has the higher priority, it will be named as a carboxylic acid. Again, identify the longest chain containing the —COOH group and number it starting with the carboxyl-group carbon.



The parent compound is the 4-carbon acid, butanoic acid. It has an $—NH_2$ group (amino) on carbon 2 and a hydroxyl group on carbon 3. The common name for the 4-carbon acid is butyric acid.

SOLUTION

The IUPAC name of this molecule is 3-hydroxy-2-aminobutanoic acid; the common name of this acid is β-hydroxy-α-aminobutyric acid. It is an amino acid that is commonly known as threonine (Chapter 18).

PROBLEM 17.2

Draw the structures of the following acids:

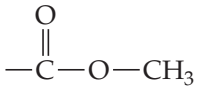
(a) 2-Ethyl-3-hydroxyhexanoic acid **(b)** *m*-Nitrobenzoic acid

PROBLEM 17.3

Write both the complete structural formula of succinic acid (refer to Table 17.1), showing all bonds, and the line-angle structural formula.

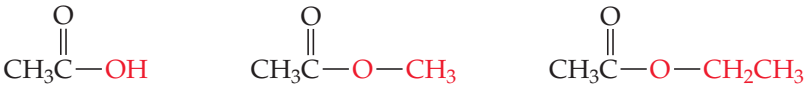
PROBLEM 17.4

Draw and name the acid that is formed by addition of Br_2 to the double bond in acrylic acid (refer to Table 17.1 and Section 13.6).


Ester

Esters

When the —OH of the carboxyl group is converted to the —OR′ of an ester group (—COOR′), the ability of the molecules to hydrogen-bond with each other is lost (although esters can still accept hydrogen bonds from water). Simple esters therefore have lower boiling than the acids from which they are derived.


Acetic acid (bp 118 °C (391 K))

Methyl ester (bp 57 °C (330 K))

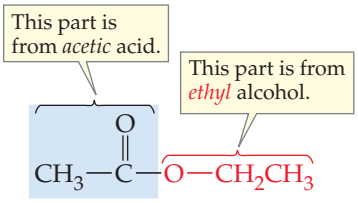
Ethyl ester (bp 77 °C (350 K))

The simple esters are colorless, volatile liquids with pleasant odors, and many of them contribute to the natural fragrance of flowers and ripe fruits. The lower-molecular-mass esters are somewhat soluble in water and are quite flammable. Esters are neither acids nor bases in aqueous solution.

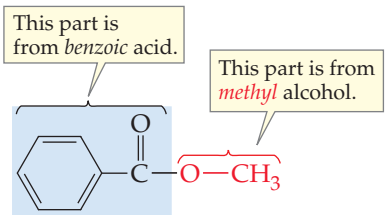
Nomenclature

Ester names consist of two words. The first is the name of the alkyl group R′ in the ester group —COOR′. The second is the name of the parent acid, with the family-name ending *-ic acid* replaced by *-ate*. Note that the order of the two parts of the name is the reverse of the order in which ester condensed formulas are usually written.

Naming an ester

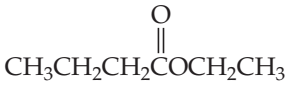


Ethyl acetate



Methyl benzoate

Both common and systematic names are derived in this manner. For example, an ester of a straight-chain, 4-carbon carboxylic acid is named systematically as a butanoate (from butanoic acid) or by its common name as a butyrate (from butyric acid).


Ethyl butyrate (ethyl butanoate)

This ester is used as a food flavoring to give the taste and smell of pineapples.

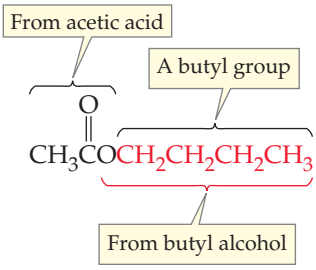
Worked Example 17.2 Writing the Structure of an Ester from Its Name

What is the structure of butyl acetate?

ANALYSIS The two-word name consisting of an alkyl group name followed by an acid name with an *-ate* ending shows that the compound is an ester. The name "acetate" shows that the RCO— part of the molecule is from acetic acid (CH_3COOH). The "butyl" part of the name indicates that a butyl group has replaced H in the carboxyl group.

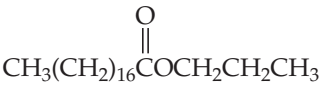
SOLUTION

The structure of butyl acetate is

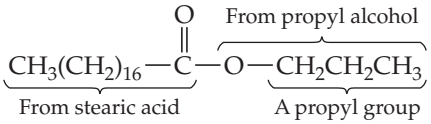


Worked Example 17.3 Naming an Ester from Its Structure

What is the name of this compound?



ANALYSIS The compound has the general formula RCOOR′, so it is an ester. The acyl part of the molecule (RCO—) is from stearic acid (see Table 17.1). The R′ group has three carbon atoms and is therefore a propyl group.



SOLUTION
The compound is propyl stearate.

PROBLEM 17.5

Draw the structures of the following compounds:

(a) Hexyl benzoate **(b)** Methyl formate

(c) Ethyl acrylate (See Table 17.1)

PROBLEM 17.6

Which of the following compounds would you expect to have the highest boiling point and which the lowest boiling point? Explain your answer.

(a) CH_3OCH_3 **(b)** CH_3COOH **(c)** $CH_3CH_2CH_3$

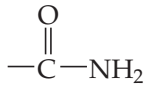
PROBLEM 17.7

In the following pairs of compounds, which would you expect to be more soluble in water? Why?

(a) $C_8H_{17}COOH$ or $CH_3CH_2CH_2COOH$ **(b)** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCOOH$ or $CH_3CH_2COO\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

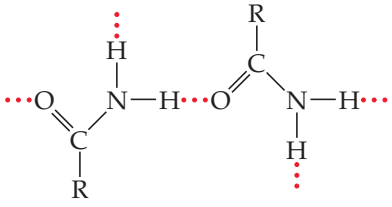
Amides

Compounds with a nitrogen directly attached to the carbonyl carbon atom are *amides*. The nitrogen of an amide may be an $—NH_2$ group or may have one or two R′ groups bonded to it. *Unsubstituted (or primary) amides* ($RCONH_2$) can form multiple hydrogen bonds to other amide molecules and thus have higher melting points and higher boiling points than the acids from which they are derived.



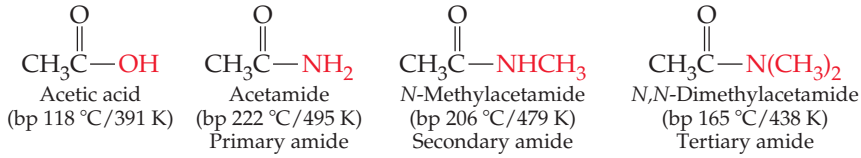
Amide

Hydrogen bonding in $RCNH_2$



(Red dotted line indicates hydrogen bonds.)

Low-molecular-mass unsubstituted amides are solids (except for the simplest amide [formamide, $HCONH_2$, a liquid]) that are soluble in both water (with which they form hydrogen bonds) and organic solvents. *Monosubstituted (or secondary) amides* ($RCONHR'$) can also form hydrogen bonds to each other, but *disubstituted (or tertiary) amides* ($RCONR'_2$) cannot do so and, therefore, have lower boiling points.

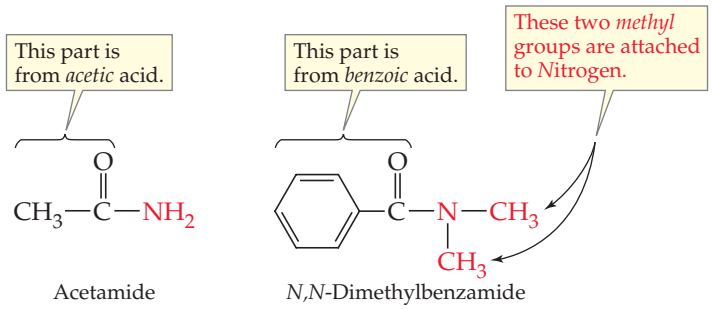


It is important to note the distinction between amines (Chapter 16) and amides. The nitrogen atom is bonded to a carbonyl-group carbon in an amide but *not* in an amine.

The positive end of the carbonyl group attracts the unshared pair of electrons on nitrogen strongly enough to prevent it from acting as a base by accepting a hydrogen atom. As a result, while amines are basic *amides are NOT.*

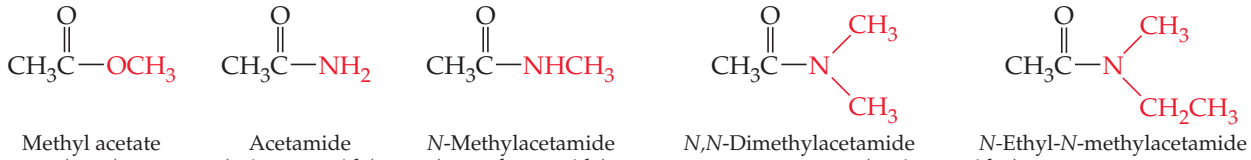
Nomenclature

Primary amides (those with an unsubstituted $—NH_2$ group) are named by replacing the *-ic acid* or *-oic acid* of the corresponding carboxylic acid name with *-amide*. For example, the amide derived from acetic acid is called acetamide. If the nitrogen atom of the amide has alkyl substituents on it, the compound is named by first specifying the alkyl group and then identifying the amide name. The alkyl substituents are preceded by the italicized letter *N* to identify them as being attached directly to nitrogen.



SUMMARY: To review, some derivatives of acetic acid are shown here.

Carbonyl derivatives of acetic acid



Properties of Carboxylic Acids, Esters, and Amides

- All undergo carbonyl-group substitution reactions.
- Esters and amides are made from carboxylic acids.
- Esters and amides can be converted back to carboxylic acids.
- Carboxylic acids, primary amides, and secondary amides exhibit strong hydrogen bonding to one another; esters and tertiary amides do not hydrogen bond to one another. All carboxylic acids and their derivatives, however, can still hydrogen bond to water molecules.
- Simple acids and esters are liquids; all primary amides (except formamide) are solids.
- Carboxylic acids are weak acids and produce acidic aqueous solutions.
- Esters and amides are neither acids nor bases (pH neutral).
- Small (low-molecular-mass) amides are water-soluble, while small esters are slightly water-soluble.
- Volatile acids have strong, sharp odors while volatile esters have pleasant, fruity odors. Amides generally are odorless.

In later chapters, you will see that the fundamental bonding connections in proteins are amide bonds (Section 18.2) and those in oils and fats are ester bonds (Section 24.2).

HANDS-ON CHEMISTRY 17.1

Carboxylic acids and their derivatives are important parts of many of the medicines used daily by many people. Similarly to what we did in Hands-On Chemistry 16.1, let's take a look at some of the top 200 drugs of 2015, many of which you have probably heard about and see what functional groups are present. You will need to have an internet connection to fully carry out this activity.

a. Let's begin by looking at an antibiotic you have surely heard of—penicillin. What you may not know is that there are two commonly used forms: penicillin G and penicillin V. Look up the structures of these, draw their line structure, and identify all the carboxylic acid derived functional groups present. How do the two penicillins differ from one another? How are they the same? From a treatment standpoint, what is each used for?

b. As of September 2014, the top 10 selling prescription drugs by trade name were as follows:

1. Crestor 2. Synthroid 3. Nexium 4. Ventolin 5. Advair
6. Lantus 7. Vyvanse 8. Lyrica 9. Spiriva 10. Diovan

Look up the structures of each and answer the following questions for each:

1. Does it contain a carboxylic acid?
2. Does it contain an amide?
3. If it contains an amide, classify it as primary, secondary, or tertiary.

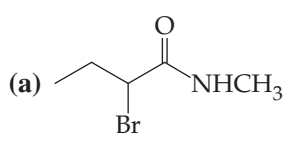
c. Finally, look up the structure of paclitaxel (see the Chemistry in Action "When Is Toxicity Beneficial?" in Chapter 15). Identify all of the ester functional groups present.

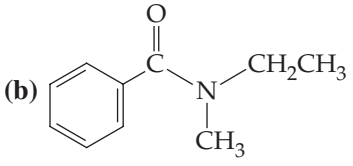
PROBLEM 17.8

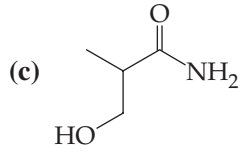
Write both condensed and line structures for (a) the ester formed when butyric acid reacts with cyclopentanol, (b) the amide formed when isopropyl amine is reacted with butyric acid, and (c) the amide formed when diethylamine is reacted with butyric acid. (d) Name the derivatives you created in parts (a)–(c).

PROBLEM 17.9

What are the names of the following compounds?







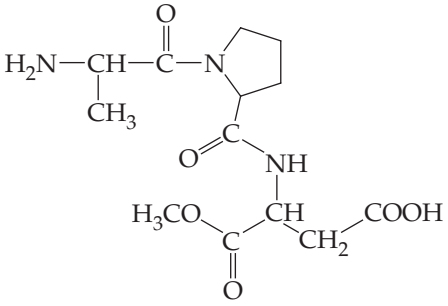
PROBLEM 17.10

Draw structures corresponding to these names:

(a) 4-Methylpentanamide **(b)** *N*-Ethyl-*N*-methylpropanamide

PROBLEM 17.11

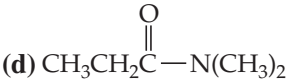
Many important biomolecules are multifunctional; given the molecule shown here, identify the following classes of compounds: (i) α-amino group, (ii) monosubstituted amide, (iii) methyl ester, (iv) carboxylic acid, and (v) disubstituted amide.



PROBLEM 17.12

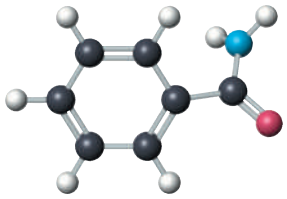
Classify each compound (a)–(f) as one of the following: (i) amide, (ii) ester, or (iii) carboxylic acid.

(a) CH_3COOCH_3 **(b)** RCONHR **(c)** C_6H_5COOH

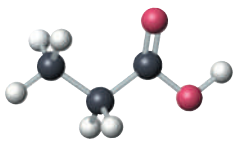
(d)  **(e)** $CH_3CH_2CH_2CONH_2$ **(f)** 

KEY CONCEPT PROBLEM 17.13

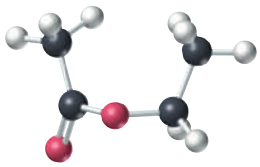
Identify the following molecules as an ester, a carboxylic acid, or an amide, and write both the condensed and line-structural formula for each.



(a)



(b)



(c)

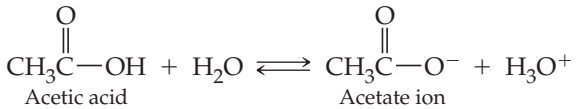
17.2 Acidity of Carboxylic Acids

Learning Objective:

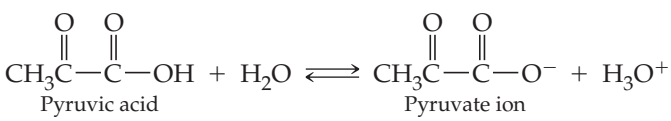
- Describe the acidity of different carboxylic acids and predict the products obtained when they react with strong bases.

Carboxylate anion The anion that results from ionization of a carboxylic acid, $RCOO^-$.

Carboxylic acids are weak acids that establish equilibria in aqueous solution with **carboxylate anions,** $RCOO^-$. The carboxylate anions are named by replacing the *-ic* ending in the carboxylic acid name with *-ate* (giving the same names and endings used in naming esters). At pH 7.4 in body fluids, carboxylic acids exist mainly as their carboxylate anions.



Acetic acid Acetate ion



Pyruvic acid Pyruvate ion

The comparative strength of an acid is measured by its acid dissociation constant (K_a); the smaller the value of K_a, the weaker the acid (Section 10.3). Most organic and biochemists prefer to use pK_a when discussing the acidity of organic and biomolecules; pK_a is defined as minus the log of the K_a ($pK_a = -\log K_a$). With pK_a the *larger and more positive* the number, the *weaker* the acid is; in addition, there is a 10-fold difference in acidity for every 1 pK_a unit.

Recall that this is the same relationship seen for pH values (Section 10.5).

One of the advantages to using pK_a values is that it makes comparing acidities much quicker, since there is no scientific notation involved. Many carboxylic acids have about the same acid strength as acetic acid, as shown by the values in Table 17.2. There are some exceptions, though. Trichloroacetic acid, used to prepare microscope slides, for chemical skin peeling, and to precipitate proteins from body fluids, is a strong acid that must be handled with the same respect as sulfuric acid. Dicarboxylic acids, such as oxalic and glutaric acid, will have two K_a or pK_a values: the first for removal of the first acidic H (K_{a1} and pK_{a1}) and the second for formation of the dianion (K_{a2} and pK_{a2}). Because removal of the second H is 10 to 1000 times harder to accomplish after the first one has been removed, only K_{a1} and pK_{a1} are of any real importance.

Table 17.2 Carboxylic Acid Dissociation Constants and pK_as*

Name	Structure	K_a	pK_a
Trichloroacetic acid	Cl_3CCOOH	2.3×10^{-1}	0.64
Chloroacetic acid	$ClCH_2COOH$	1.4×10^{-3}	2.85
Formic acid	$HCOOH$	1.8×10^{-4}	3.74
Acetic acid	CH_3COOH	1.8×10^{-5}	4.74
Propanoic acid	CH_3CH_2COOH	1.3×10^{-5}	4.89
Hexanoic acid	$CH_3(CH_2)_4COOH$	1.3×10^{-5}	4.89
Benzoic acid	C_6H_5COOH	6.5×10^{-5}	4.19
Acrylic acid	$H_2C{=}CHCOOH$	5.6×10^{-5}	4.25
Oxalic acid	$HOOCCOOH$	5.4×10^{-2}	1.27
	$^-OOCCOOH$	5.2×10^{-5}	4.28
Glutaric acid	$HOOC(CH_2)_3COOH$	4.5×10^{-5}	4.35
	$^-OOC(CH_2)_3COOH$	3.8×10^{-6}	5.42

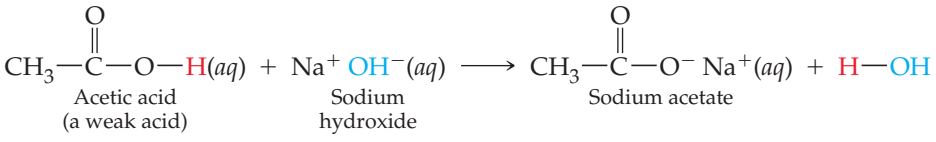
**The acid dissociation constant K_a is the equilibrium constant for the ionization of an acid; the smaller its value, the weaker the acid.*

$$RCOOH + H_2O \rightleftharpoons RCOO^- + H_3O^+ \qquad K_a = \frac{[RCOO^-][H_3O^+]}{[RCOOH]}$$

For pK_a, the larger the value, the weaker the acid.

Carboxylic acids undergo neutralization reactions with bases in the same manner as other acids. With strong bases, such as sodium hydroxide, a carboxylic acid reacts to give water and a **carboxylic acid salt,** as shown here for the formation of sodium acetate. Like all other such aqueous acid–strong base reactions, this reaction proceeds much more favorably in the forward direction than in the reverse direction and is thus written with a single arrow. As for all salts, a carboxylic acid salt is named with cation and anion names. In biological systems, however, where the identity of the cation is unclear or unknown, the ionized form of a carboxylic acid will simply be referred to using only its anion name; for example, the ionized form of citric acid would simply be known as citrate (this is a common practice that you will see used when you study metabolism in Chapters 21, 22, and 25).

Carboxylic acid salt An ionic compound containing a cation and a carboxylate acid anion.

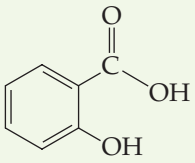
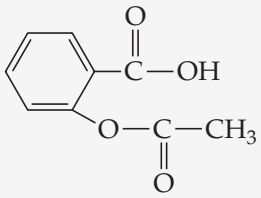
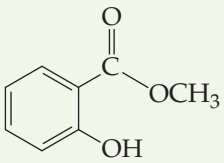
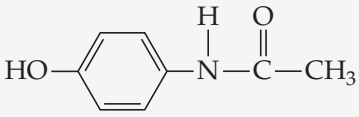


CHEMISTRY IN ACTION

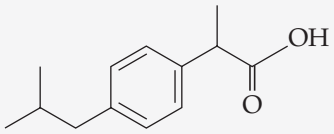
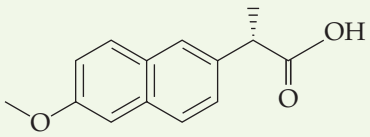
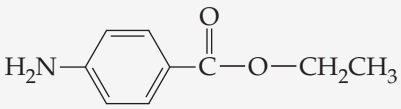
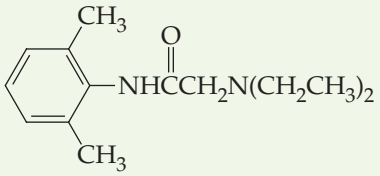
Medicinally Important Carboxylic Acids and Derivatives

Carboxylic acids, esters, and amides have many uses in medicine and living systems. Almost everyone is familiar with aspirin, but you may be surprised to learn that many over-the-counter medications contain one or more carboxyl-containing compounds. The following table lists a few of the most familiar over-the-counter medications that are carboxylic acids or derivatives.

Some Medicinally Important Carboxylic Acids and Derivatives

Name	Structure	Origins and Uses
Salicylic acid		• Found in the bark of the willow tree *(Salix alba)*. • Biosynthesized from the amino acid phenylalanine (Chapter 19). • Found in plants; it has roles in plant development, photosynthesis, and ion transport. • Cherokees used an infusion of willow bark for fever, pain, and other medicinal purposes. • Too insoluble in water and irritating to the stomach to be of widespread use.
Aspirin		• Member of the group of drugs known as salicylates, it was discovered through chemical modifications of salicylic acid. • Undergoes ester hydrolysis in the stomach to give salicylic acid. • Best known for providing pain relief (an *analgesic*), reducing fever (an *antipyretic*), and reducing inflammation (an *anti-inflammatory*). • In recent years, aspirin has been found to inhibit the clumping of blood platelets, protecting against heart attacks caused by blood clots. Small regular doses of aspirin are often recommended for some individuals at risk for heart attack. See Section 23.9 for the chemical action of aspirin. • Undesirable side effects are gastric bleeding and gastrointestinal distress; it also inhibits the action of an enzyme necessary for coagulation of blood cells, causing the time it takes for bleeding to stop to double for several days. • On the WHO Model List of Essential Medicines*.
Methyl salicylate (oil of wintergreen)		• Too poisonous to be of any value as an oral medication. • In low concentration it is used as a fragrance in foods and beverages. • Used as an antiseptic in some mouthwashes. • Therapeutically useful as a *counterirritant*, a substance that relieves internal pain by stimulating nerve endings in the skin. • One of the active ingredients in liniments such as Bengay and Heet.
Acetaminophen		• An alternative to aspirin for pain relief. • Best known by the trade name Tylenol. • Reduces fever but is not an anti-inflammatory agent. • Recommended for use in children over aspirin. • Major advantage is that it does not cause internal bleeding; the pain reliever of choice for individuals prone to bleeding or recovering from surgery or wounds. • Overdoses can cause kidney and liver damage. • On the WHO Model List of Essential Medicines*.

The sodium and potassium salts of carboxylic acids are ionic solids that are usually far more soluble in water than the carboxylic acids themselves; for example, sodium benzoate is about 150 times more soluble in water than benzoic acid. The formation of carboxylic acid salts, as well as the formation of amine salts, is useful in creating water-soluble derivatives of drugs. See the Chemistry in Action "Medications, Body Fluids, and the 'Solubility Switch'" on p. 580.

Name	Structure	Origins and Uses
Ibuprofen		• A nonsteroidal anti-inflammatory drug (NSAID). • Most notably sold as Advil and Motrin. • It is used for relief of symptoms of arthritis, abdominal cramps, fever, and as an analgesic, especially where there is inflammation. • Known to have an effect on blood-clotting times, though this effect is relatively mild and short lived compared with aspirin. • At doses commonly prescribed, it seems to have the lowest incidence of adverse gastrointestinal side effects of all general NSAIDs. On the WHO Model List of Essential Medicines*.
Naproxen		• An NSAID of the same class as ibuprofen. • Known by various trade names, including Aleve and Anaprox. • Commonly used for relief of a wide variety of pain, fever, swelling, and stiffness. • The preferred NSAID for long-term use in people with a high risk of heart attack or stroke due to its relatively low risk of causing such complications. • Current research suggests it may have antiviral activity against influenza.
Benzocaine		• A local anesthetic used in many over-the-counter *topical* preparations (those applied to the skin surface). • Used for pain relief associated with cold sores, poison ivy, sore throats, and hemorrhoids. • Works by blocking the transmission of impulses by sensory nerves.
Lidocaine		• Structurally related to benzocaine. • More soluble than benzocaine, so it can be used in injections. • Local anesthetic most commonly administered by injection to prevent pain during dental work.

**The World Health Organization (WHO) Model List of Essential Medicines is a list of the most effective, safest, and cost-efficient medicines needed for a basic health-care system. From the April 2015 updated list.*

CIA Problem 17.1 *Salsalate*, which is an ester formed by the reaction of two molecules of salicylic acid, is another salicylate used as an aspirin alternative for those who are hypersensitive to aspirin. Draw the structures of salicylic acid and salsalate.

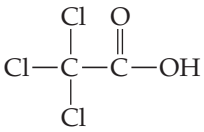
CIA Problem 17.2 What does NSAID stand for?

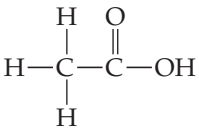
CIA Problem 17.3 Examine the structures of aspirin, acetaminophen, benzocaine, and lidocaine, and, for each compound, indicate whether it is acidic, basic, or neither.

Worked Example 17.4 Effect of Structure on Carboxylic Acid Strength

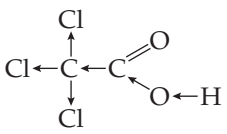
Write the structural formulas of trichloroacetic acid and acetic acid and explain why trichloroacetic acid is the much stronger acid of the two.

ANALYSIS


Trichloroacetic acid


Acetic acid

The structural difference is the replacement of three hydrogen atoms on the alpha carbon by three chlorine atoms. The chlorines are much more electronegative than the hydrogen and therefore draw electrons away from the rest of the molecule in trichloroacetic acid (indicated next by the arrows). The result is that the hydrogen atom of the —COOH group in trichloroacetic acid is held less strongly and is much more easily removed than the corresponding hydrogen atom in acetic acid.



SOLUTION

Since the —COOH hydrogen atom in trichloroacetic acid is held less strongly, it is the stronger acid.

PROBLEM 17.14

Write the products of the following reactions:

(a) $CH_3CH_2CH(CH_3)COOH + NaOH \longrightarrow ?$

(b) 2,2-Dimethylpentanoic acid + $KOH \longrightarrow ?$

PROBLEM 17.15

Write the formulas of potassium salicylate and disodium oxalate (refer to Table 17.1).

PROBLEM 17.16

Suppose that potassium acetate and disodium glutarate are dissolved in water. Write the formulas of each organic ion present in the solution (refer to Table 17.1).

17.3 Reactions of Carboxylic Acids: Ester and Amide Formation

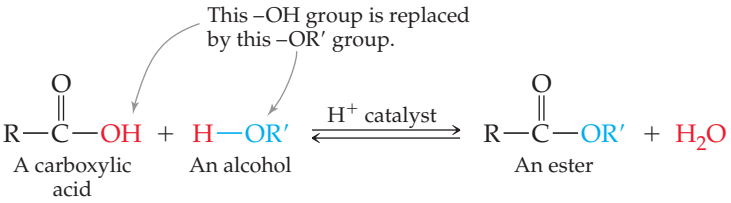
Learning Objective:

- Describe how esters and amides are formed from carboxylic acids

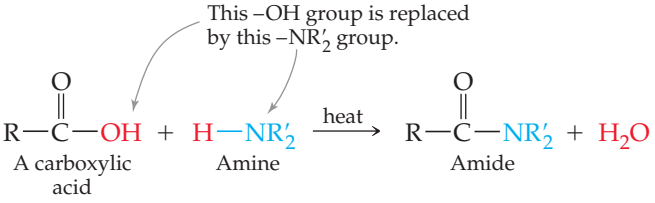
The reactions of alcohols and amines with carboxylic acids follow the same pattern—both result in substitution of other groups for the —OH of the acid and formation of water as a by-product. With alcohols, the —OH of the acid is replaced by the —OR′ of the alcohol. With amines, the —OH of the acid is replaced by the $—NH_2$, —NHR′, or $—NR'_2$ of the amine.

▲ The unique flavors and aromas of various beers are due in part to esters formed during fermentation.

Ester formation



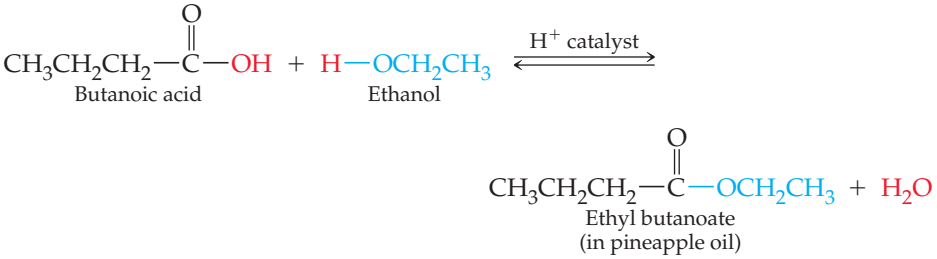
Amide formation



Esterification

Esterification The reaction between an alcohol and a carboxylic acid to yield an ester plus water.

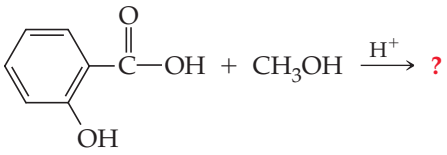
In the laboratory, ester formation, known as **esterification,** is carried out by warming a carboxylic acid with an alcohol in the presence of a strong acid catalyst such as sulfuric acid. For example,



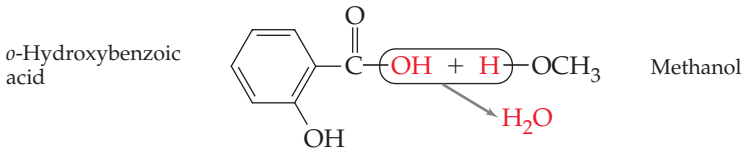
Esterification reactions are reversible and often reach equilibrium with approximately equal amounts of both reactants and products present. Ester formation is favored either by using a large excess of the alcohol or by continuously removing one of the products (e.g., by distilling off a low-boiling ester or removing water in a similar fashion). Both techniques are applications of Le Châtelier's principle (Section 7.9).

Worked Example 17.5 Writing the Products of an Esterification Reaction

The flavor ingredient in oil of wintergreen is an ester that is made by reaction of *o*-hydroxybenzoic acid (salicylic acid) with methanol. What is its structure?



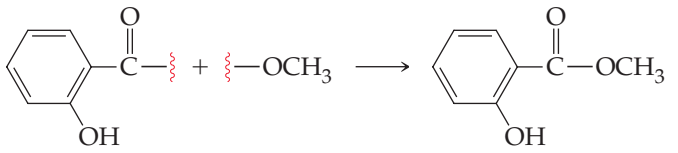
ANALYSIS First, write the two reaction partners so that the —COOH group of the acid and the —OH group of the alcohol face each other.



Next, remove —OH from the acid and —H from the alcohol to form water and then join the two resulting organic fragments with a single bond.

SOLUTION

The product is the ester.



PROBLEM 17.17

One of the compounds that gives orange oil its unique odor is an ester formed when acetic acid reacts with octan-1-ol. Draw the structure of this ester and name it.

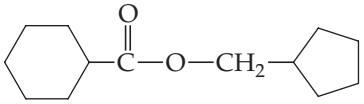
PROBLEM 17.18

Raspberry oil contains an ester that is made by reaction of formic acid with 2-methylpropan-1-ol. What is its structure?

$$HCOOH + (CH_3)_2CHCH_2OH \longrightarrow ?$$

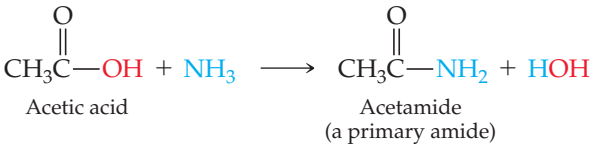
PROBLEM 17.19

Which carboxylic acid and alcohol are needed to make the following esters?

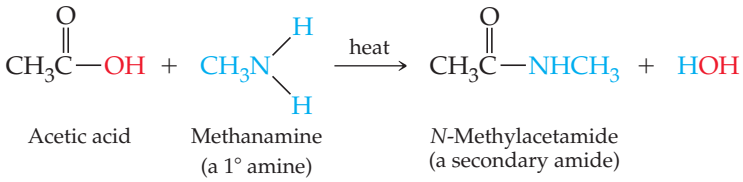
(a) Ph—CH_2—CH_2—C(=O)—O—$CH_2CH_2CH_3$ **(b)** 

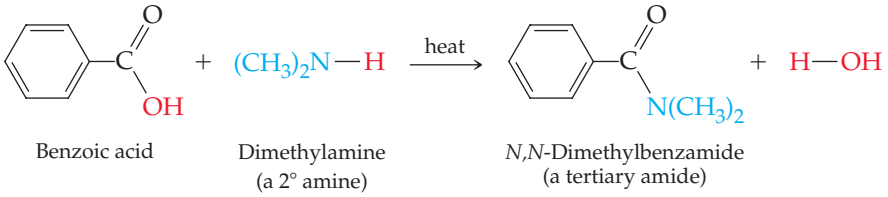
Amide Formation

Primary amides are formed by the reaction of carboxylic acids with ammonia (NH_3).



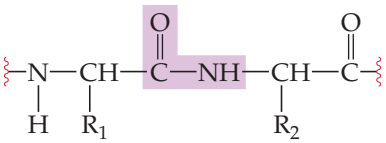
Secondary and tertiary amides are produced in reactions between primary or secondary amines and carboxylic acids, respectively.

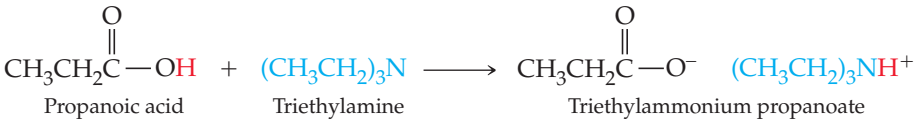




In all cases, the first step of the reaction is actually formation of the ammonium salt; the amide formation reactions must be heated to proceed as shown. In each case, the overall reaction is formation of an amide accompanied by formation of water by the —OH group of the acid and an —H atom from ammonia or an amine. Chemists have developed what are known as coupling reagents, making this reaction easier to do in the laboratory; biological systems use what are known as acyl transfer agents (Chapter 21). Tertiary amines (such as triethylamine) do not have a hydrogen on the amine nitrogen and therefore do not form amides, generating only the ammonium salt.

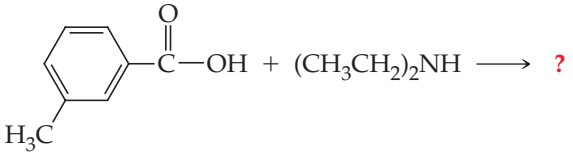
Proteins are constructed of long chains of amino acids held together by amide bonds. The biochemical synthesis of proteins, described in Section 26.10, is a strictly controlled process in which amino acids with different R groups must be assembled in an exact order that is determined by an organism's DNA sequence.



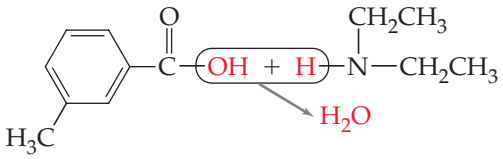


Worked Example 17.6 Writing the Products of Amide Formation

The mosquito and tick repellent DEET (diethyltoluamide) is prepared by reaction of diethylamine with *m*-methylbenzoic acid (*m*-toluic acid). What is the structure of DEET?



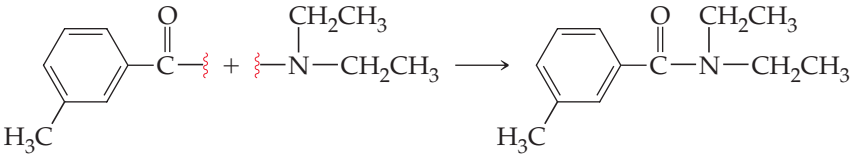
ANALYSIS First, rewrite the equation so that the —OH of the acid and the —H of the amine face each other.



Next, remove the —OH from the acid and the —H from the nitrogen atom of the amine to form water and then join the two resulting fragments together to form the amide product.

SOLUTION

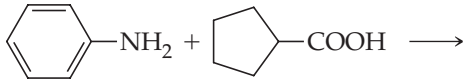
The structure of DEET is



N,N-Diethyltoluamide (DEET)

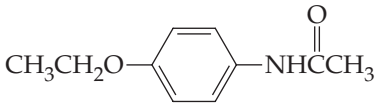
PROBLEM 17.20

Draw structures of the amides that can be made from the following reactants:

(a) $CH_3NH_2 + (CH_3)_2CHCOOH \longrightarrow$? **(b)**  ?

PROBLEM 17.21

Phenacetin (shown in the margin) was once used in headache remedies but is now banned because of its potential for causing kidney damage. (a) Identify all the functional groups present in phenacetin. (b) Draw the structures of the carboxylic acid and amine needed to prepare phenacetin.



Phenacetin

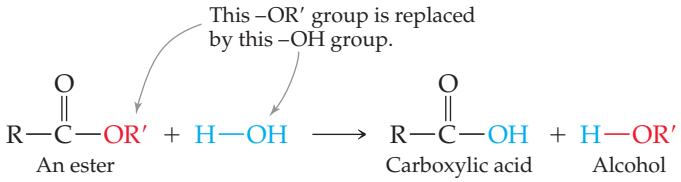
17.4 Hydrolysis of Esters and Amides

Learning Objective:

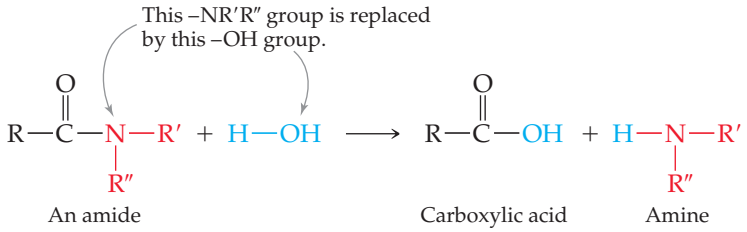
- Predict the hydrolysis products of esters and amides.

Recall that in hydrolysis a bond or bonds are broken and the —H and —OH of water add to the atoms that were part of the broken bond. Esters and amides undergo hydrolysis to give back carboxylic acids plus alcohols or amines in reactions that follow the carbonyl-group substitution pattern (see Section 17.4).

For esters, the net effect of hydrolysis is substitution of —OH for OR′.

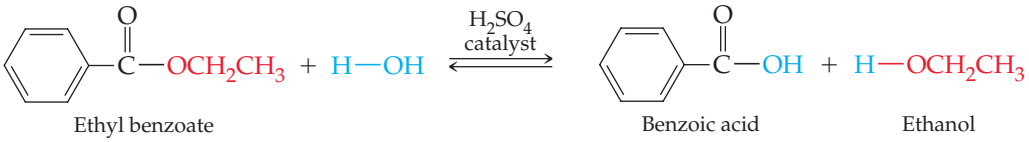


For amides, the net effect of hydrolysis is substitution of —OH for $—NH_2$, —NHR, or $—NR_2$.



Ester Hydrolysis

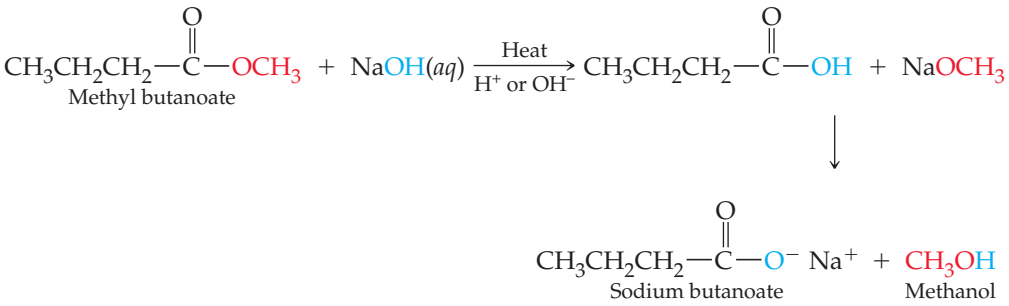
Both acids and bases can cause ester hydrolysis. Acid-catalyzed hydrolysis is simply the reverse of the esterification. An ester is treated with water in the presence of a strong acid catalyst such as sulfuric acid, and hydrolysis takes place.



An excess of water pushes the equilibrium to the right.

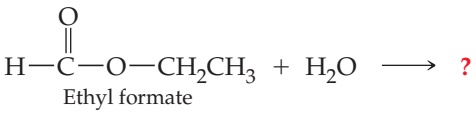
Saponification The reaction of an ester with aqueous hydroxide ion to yield an alcohol and the metal salt (usually sodium or potassium) of a carboxylic acid.

Ester hydrolysis using a base such as NaOH or KOH is known as **saponification** (after the Latin word *sapo,* soap). The product of saponification is a carboxylate anion rather than a free carboxylic acid; the initially formed carboxylic acid reacts with base to accomplish this. The use of saponification in making soap is discussed in Section 23.4.

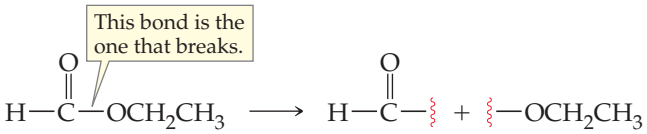


Worked Example 17.7 Writing the Products of an Ester Hydrolysis

What product would you obtain from acid-catalyzed hydrolysis of ethyl formate, a flavor constituent of rum?

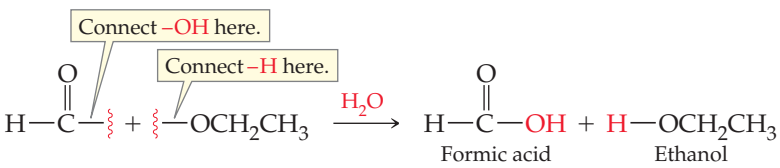


ANALYSIS The name of an ester gives a good indication of the names of the two products. Thus, ethyl formate yields ethanol and formic acid. To find the product structures in a more systematic way, write the structure of the ester and locate the bond between the carbonyl-group carbon and the —OR′ group.



SOLUTION

Carry out a hydrolysis reaction on paper. First form the carboxylic acid product by connecting an —OH to the carbonyl-group carbon. Then add an —H to the —OCH_2CH_3 group to form the alcohol product.



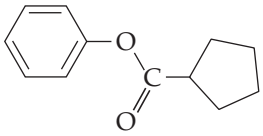
PROBLEM 17.22

If a bottle of aspirin tablets has the aroma of vinegar, it is time to discard those tablets. Explain why, and include a chemical equation in the explanation.

PROBLEM 17.23

Draw the products you would obtain from acid-catalyzed hydrolysis of the following esters.

(a) Isopropyl benzoate

(b) 

(c) $CH_3-CH_2-\overset{\overset{O}{\|}}{C}-O\,CH_2CH_3$

Amide Hydrolysis

Amides are extremely stable in water but do undergo hydrolysis with prolonged heating in the presence of acids or bases. The products are the carboxylic acid and amine from which the amide was synthesized.

$$RC(=O)-NHR + H-OH \longrightarrow RC(=O)-OH + HN(R)(H)$$

In practice, the products obtained depend on whether the hydrolysis is done using acid or base. Under acidic conditions, the carboxylic acid and amine salt are obtained. Doing this reaction using base produces the neutral amine and carboxylate anion. For example, in the hydrolysis of *N*-methylacetamide.

Hydrolysis products of* N-*Methylacetamide

$$CH_3C(=O)-NHCH_3 + H_3O^+ \longrightarrow CH_3C(=O)-OH + CH_3NH_3^+ \quad \text{Acid hydrolysis}$$

$$CH_3C(=O)-NHCH_3 + OH^- \longrightarrow CH_3C(=O)-O^- + CH_3NH_2 \quad \text{Base hydrolysis}$$

In Chapter 25, you will see that the cleavage of amide bonds by hydrolysis is the key process that occurs in the stomach during digestion of proteins.

Worked Example 17.8 Writing the Products of an Amide Hydrolysis

What carboxylic acid and amine are produced by the hydrolysis of *N*-ethylbutanamide?

$$CH_3CH_2CH_2C(=O)-NHCH_2CH_3 + H_2O \longrightarrow ?$$

N-Ethylbutanamide

ANALYSIS First, look at the name of the starting amide. Often, the amide's name incorporates the names of the two products. Thus, *N*-ethylbutanamide yields ethanamine and butanoic acid. To find the product structures systematically, write the amide and locate the bond between the carbonyl-group carbon and the nitrogen. Then break this amide bond and write the two fragments.

This amide bond is the one that breaks.

$$CH_3CH_2CH_2C(=O)-NHCH_2CH_3 \longrightarrow CH_3CH_2CH_2C(=O)-\sim + \sim-NHCH_2CH_3$$

—continued on next page

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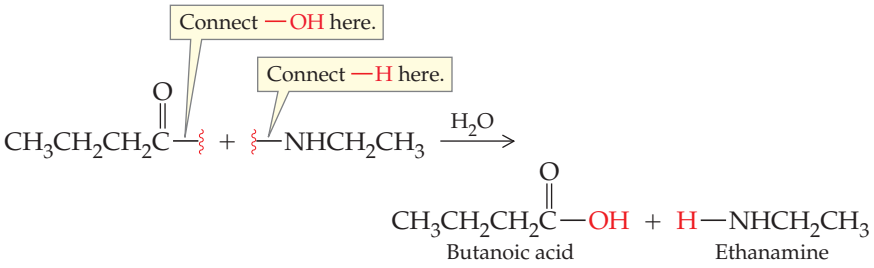
SOLUTION

Carry out a hydrolysis reaction on paper and form the products by connecting an —OH to the carbonyl-group carbon and an —H to the nitrogen.



PROBLEM 17.24

What carboxylic acids and amines result from hydrolysis of the following amides?

(a) $CH_3CH{=}CHC(=O){-}NHCH_3$ **(b)** *N,N*-Dimethyl-*p*-nitrobenzamide

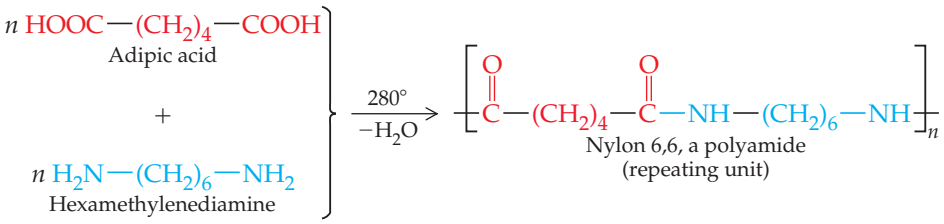
17.5 Polyamides and Polyesters

Learning Objective:

- Describe the formation and uses of polyesters and polyamides.

Imagine what would happen if a molecule with *two* carboxylic acid groups reacted with a molecule having *two* amino groups. Amide formation could join the two molecules together, but further reactions could then link more and more molecules together until a giant chain resulted. This is exactly what happens when certain kinds of synthetic polymers are made.

Nylons are *polyamides* produced by reaction of diamines with diacids. One such nylon, nylon 6,6 (pronounced "six-six"), is so named because of the structures of the two compounds that are used to produce it. Nylon 6,6 is made by heating adipic acid (hexanedioic acid, a 6-carbon dicarboxylic acid) with hexamethylenediamine (1,6-hexanediamine, a 6-carbon diamine) at 280 °C (553 K).

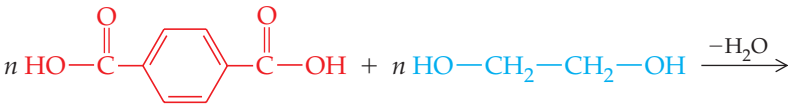


▲ Nylon being pulled from the interface between adipic acid and hexamethylenediamine.

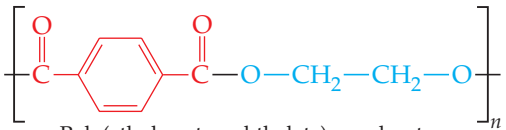
The polymer molecules are composed of thousands of the repeating units, shown here enclosed in square brackets. In the next chapter, you will see that proteins are also polyamides; unlike nylon, however, proteins do not normally have identical repeating units.

The properties of nylon make it suitable for a wide range of applications. High-impact strength, abrasion resistance, and a naturally slippery surface make nylon an excellent material for bearings and gears. It can be formed into very strong fibers, making it valuable for a range of applications from nylon stockings, to clothing, to mountaineering ropes and carpets. Sutures and replacement arteries are also fabricated from nylon, which is resistant to deterioration in body fluids.

Just as diacids and diamines react to yield polyamides, diacids and dialcohols react to yield *polyesters*. The most widely used polyester is made by the reaction of terephthalic acid (1,4-benzenedicarboxylic acid) with ethane-1,2-diol.



Terephthalic acid Ethane-1,2-diol

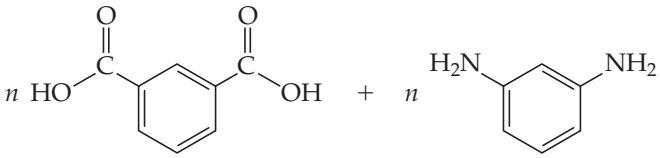


Poly(ethylene terephthalate), a polyester (repeating unit)

We know this polyester best in clothing fiber, where it has the trade name Dacron. Under the name Mylar it is used in plastic film and recording tape. Its chemical name, poly(ethylene terephthalate) or PET, is usually applied when it is used in clear, flexible soft-drink bottles.

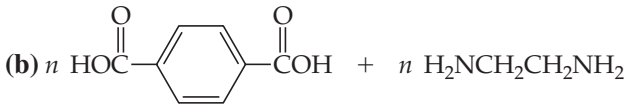
PROBLEM 17.25

One of the first polyaramides discovered was Nomex; it has excellent thermal, chemical, and radiation resistance. Provide the structure of the repeating unit in Nomex, given that it is made from the following compounds:



KEY CONCEPT PROBLEM 17.26

Give the structure of the repeating units in the polymers that are formed in the reactions of the following compounds.

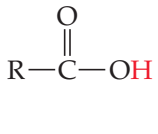


17.6 Phosphoric Acid Derivatives

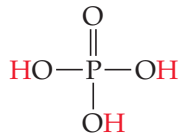
Learning Objective:

- Recognize and draw the structures of phosphate esters and their ionized forms.

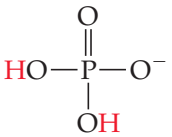
Phosphoric acid is an inorganic acid with a striking resemblance to a carboxylic acid; it has three acidic hydrogen atoms (red), allowing it to form three different anions.



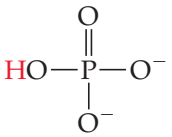
Carboxylic acid



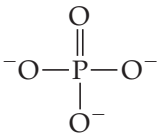
Phosphoric acid (H_3PO_4)



Dihydrogen phosphate ion ($H_2PO_4^-$)



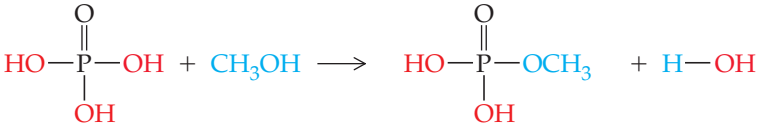
Hydrogen phosphate ion (HPO_4^{2-})



Phosphate ion (PO_4^{3-})

Phosphate ester A compound formed by reaction of an alcohol with phosphoric acid; may be a monoester, $ROPO_3H_2$; a diester, $(RO)_2PO_3H$; or a triester, $(RO)_3PO$; also may be a di- or triphosphate.

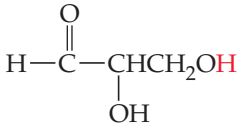
Just like a carboxylic acid, phosphoric acid reacts with alcohols to form **phosphate esters.** It may be esterified at one, two, or all three of its —OH groups by reaction with an alcohol. Reaction with one molecule of methanol gives the monoester.



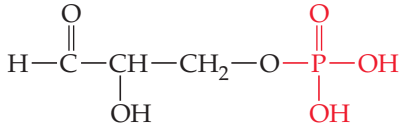
Methyl phosphate
(a phosphate monoester)

The corresponding diester and triester are also possible.

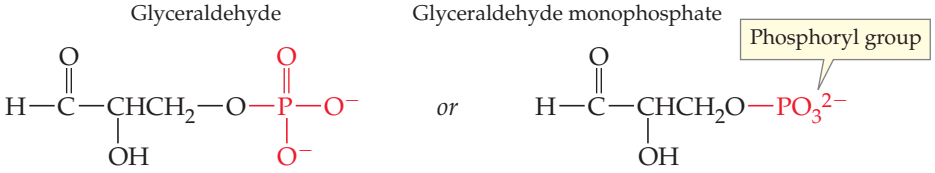
Phosphate monoesters and diesters are acidic because they still contain acidic hydrogen atoms and in most body fluids they are present as ions. Because of this, chemists usually write the phosphate groups in their ionized forms. For example, you will most often see the formula for glyceraldehyde monophosphate, a key intermediate in the metabolism of glucose (Section 22.2), written as an ion in one of these following two ways:



Glyceraldehyde



Glyceraldehyde monophosphate

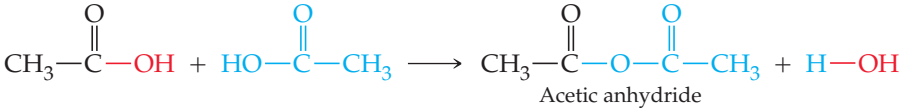


Ionized glyceraldehyde monophosphate

Phosphoryl group The $—PO_3^{2-}$ group in organic phosphates.

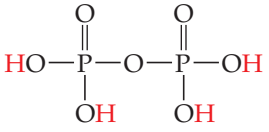
The $—PO_3^{2-}$ group as part of a larger molecule is referred to as a **phosphoryl group** (pronounced fos-for-*eel*).

One group of carboxylic acid derivatives we did not discuss are the acid anhydrides, formed when two carboxylic acids join together by eliminating a molecule of water.

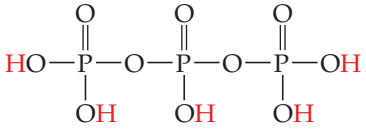


Acetic anhydride

Carboxylic acid anhydrides, although important in an organic chemistry lab, are of little importance in biochemistry, but the anhydrides of phosphoric acid *do* play a key role in biochemistry. If two molecules of phosphoric acid combine to lose water, they form a phosphoric acid anhydride. The resulting acid (*pyrophosphoric acid* or *diphosphoric acid*) reacts with yet another phosphoric acid molecule to give *triphosphoric acid.*

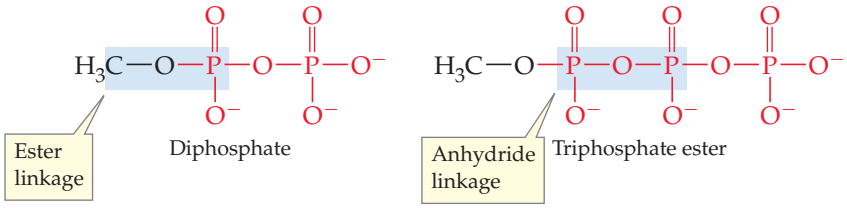


Pyrophosphoric acid



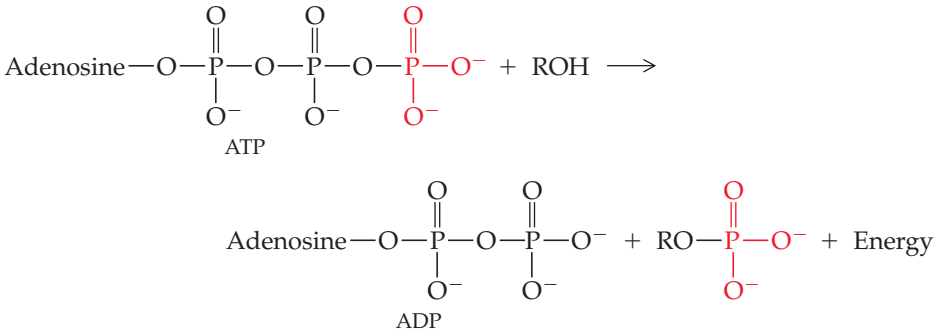
Triphosphoric acid

These anhydride-containing acids can also form esters, which are known as diphosphates and triphosphates.



Transfer of a phosphoryl group from one molecule to another is known as **phosphorylation.** In biochemical reactions, the phosphoryl groups are often provided by a triphosphate (adenosine triphosphate, ATP), which is converted to a diphosphate (adenosine diphosphate, ADP) in a reaction accompanied by the release of energy. The addition and removal of phosphoryl groups is a common mechanism for regulating the activity of biomolecules (Section 19.8).

Phosphorylation Transfer of a phosphoryl group, $-PO_3^{2-}$, between organic molecules.



Organic Phosphates:

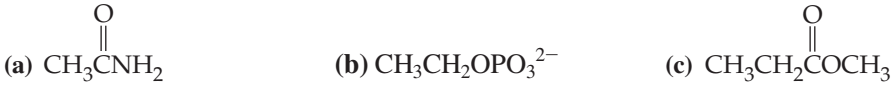
- Organic phosphates contain —C—O—P— linkages; those with one, two, or three R groups have the general formulas $ROPO_3H_2$, $(RO)_2PO_2H$, and $(RO)_3PO$.
- Organic phosphates with one or two R groups (monoesters, $ROPO_3^{2-}$, or diesters, $(RO)_2PO_2^-$) are acids and exist in ionized form in body fluids.
- The diphosphate and triphosphate groups, which are important in biomolecules, contain one or two P—O—P anhydride linkages, respectively.
- Phosphorylation is the transfer of a phosphoryl group ($-PO_3^{2-}$) from one molecule to another.

PROBLEM 17.27

Write the formula for the phosphate monoester formed from isopropanol and phosphoric acid.

PROBLEM 17.28

Identify the functional group in the following compounds and give the structures of the products of hydrolysis for these compounds.



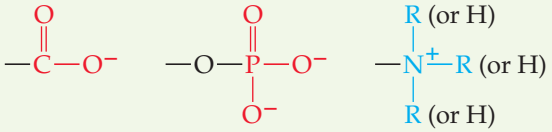
CHEMISTRY IN ACTION

Medications, Body Fluids, and the "Solubility Switch"

The chemical reactions that keep us alive occur in the aqueous solutions known as *body fluids*—blood, digestive juices, and the fluid inside cells, whereas waste products from these metabolic reactions are excreted in urine (Chapter 29). Additionally, the medicines we rely on to keep us well, which are often large, complex organic molecules, must also be able to function in this aqueous environment. For organic compounds of all classes, water solubility decreases as the hydrophobic portions of the molecules become larger and molecular mass increases, so how can a drug that is primarily hydrophobic work in an aqueous environment?

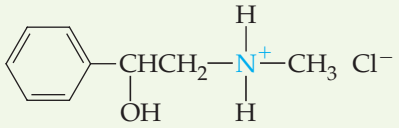
Luckily, many biologically active molecules contain acidic and basic functional groups. At the pH of body fluids (e.g., approximately 7.4 for blood), many of these groups are ionized and thus water-soluble, providing what is often called a *solubility switch.* The most frequently seen ionized functional groups present in biomolecules are carboxylate (pronounced car-*box*-*ill*-late) groups (from carboxylic acids, —COOH, discussed in Section 17.3), phosphate groups (as well as diphosphates and triphosphates, discussed in Section 17.6), and ammonium groups. These same groups are also present in many of the medicines we use.

Ionic solubility switches

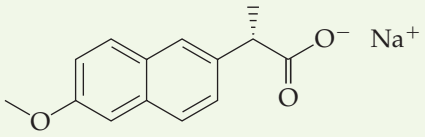


For a drug to be able to be absorbed in the stomach or intestine, or be injected, it must first be soluble in water. Medications must be soluble in body fluids in order to be transported from their entry point in the body to their site of action. Many drugs are weak acids or bases and therefore are present as their ions in body fluids. Examples include aspirin and naproxen (both carboxylic acids; see the Chemistry in Action "Medicinally Important Carboxylic Acids and Derivatives," p. 568) and morphine and codeine (both weak bases; see Table 16.2).

The extent of ionization of a drug helps determine how it is distributed in the body. Weak acids, such as aspirin and naproxen, are essentially un-ionized in the acidic environment in the stomach and are therefore readily absorbed there. On the other hand, weak bases, such as the decongestant phenylephrine and the anoxlytics discussed in the Chemistry in Action "Calming a Stormy Mind: Amines as Anti-Anxiety Medications" in Chapter 16, are completely ionized in the stomach, and therefore no significant absorption occurs there. It is not until they reach the more basic environment of the small intestine that these weak bases revert to their neutral form and are absorbed. For mostly formulation reasons, many oral pharmaceutical agents must be delivered to the body in their more water-soluble, salt forms. Amines are typically converted to their ammonium salts and carboxylic acids to their carboxylate salt form. For example, phenylephrine is converted to its ammonium hydrochloride, while naproxen is converted to its sodium salt.



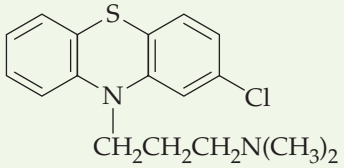
Phenylephrine hydrochloride
(a decongestant)



naproxen sodium
(an NSAID)

It is crucial that injectable medications, such as morphine, be delivered to the body in their more water-soluble form; thus converting morphine to its sulfate salt is a common strategy to increase its solubility to the point where delivery in solution is possible. Some drugs, however, such as Taxol (see the Chemistry in Action feature "When Is Toxicity Beneficial?", Chapter 15), a promising candidate in the war on cancer, suffers from poor solubility due to lack of these switches. Strategies such as those outlined earlier may one day soon allow modified versions of this important medicine to be synthesized so that it can be used as a chemotherapeutic agent.

CIA Problem 17.4 Promazine, a potent antipsychotic tranquilizer, is administered as the hydrochloride salt. Write the formula of the salt (there is only one HCl in the salt).

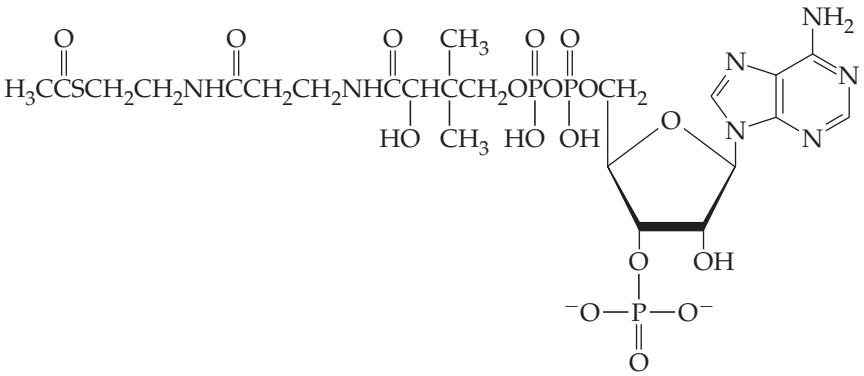


Promazine

CIA Problem 17.5 Why is naproxen converted to its sodium salt before being administered?

PROBLEM 17.29

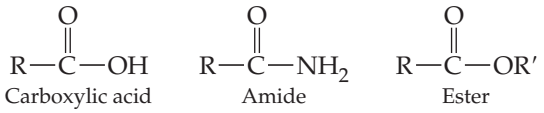
In the structure of acetyl coenzyme A drawn here, identify a phosphate monoester group, a phosphorus anhydride linkage, two amide groups, and the acetyl group.



Acetyl coenzyme A
(AcCoA)

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Compare and contrast the structures, reactions, hydrogen bonding, water solubility, boiling points, and acidity or basicity of carboxylic acids, esters, and amides.** *Carboxylic acids, amides,* and *esters* have the following general structures:



They undergo *carbonyl-group substitution reactions.* Most carboxylic acids are weak acids (a few are strong acids), but esters and amides are neither acids nor bases, being pH neutral. Acids and unsubstituted (primary) or monosubstituted (secondary) amides hydrogen bond with each other, but esters and disubstituted (tertiary) amide molecules do not. Simple acids and esters are liquids; all amides (except formamide) are solids. The simpler compounds of all three classes are water-soluble or partially water-soluble *(see Problems 30, 32, 35, 62, 63, 66, 67, 76, 78, and 79).*

- **Name simple carboxylic acids, esters, and amides given a structure and write a structure given a name.** Many carboxylic acids are best known by their common names (Table 17.1), and these names are the basis for the common names of esters and amides. Esters are named with two words: The first is the name of the alkyl group from the alcohol that has replaced the —H in —COOH, and the second is the name of the parent acid with *-ic acid* replaced by *-ate* (e.g., methyl acetate). For amides, the ending *-amide* is used, and when there are organic groups on the N, these are named first, preceded by *N* (as in *N*-methylacetamide) *(see Problems 33, 35, 37, 40–55, 58, 77, 81, and 83).*

- **Describe the acidity of different carboxylic acids and predict the products obtained when they react with strong bases.** Carboxylic acids are weak acids, with acid dissociation constants typically in the 10^{-4} to 10^{-5} range (or pK_a 4–5). They undergo neutralization reactions with sodium and potassium hydroxide to form the sodium or potassium carboxylate salts ($RCOO^-Na^+$ or $RCOO^-K^+$). These salts are far more soluble than the carboxylic acids themselves; this property can be used to create water-soluble derivatives of medicines *(see Problems 31, 33, 38, 39, 50, 51, and 79).*

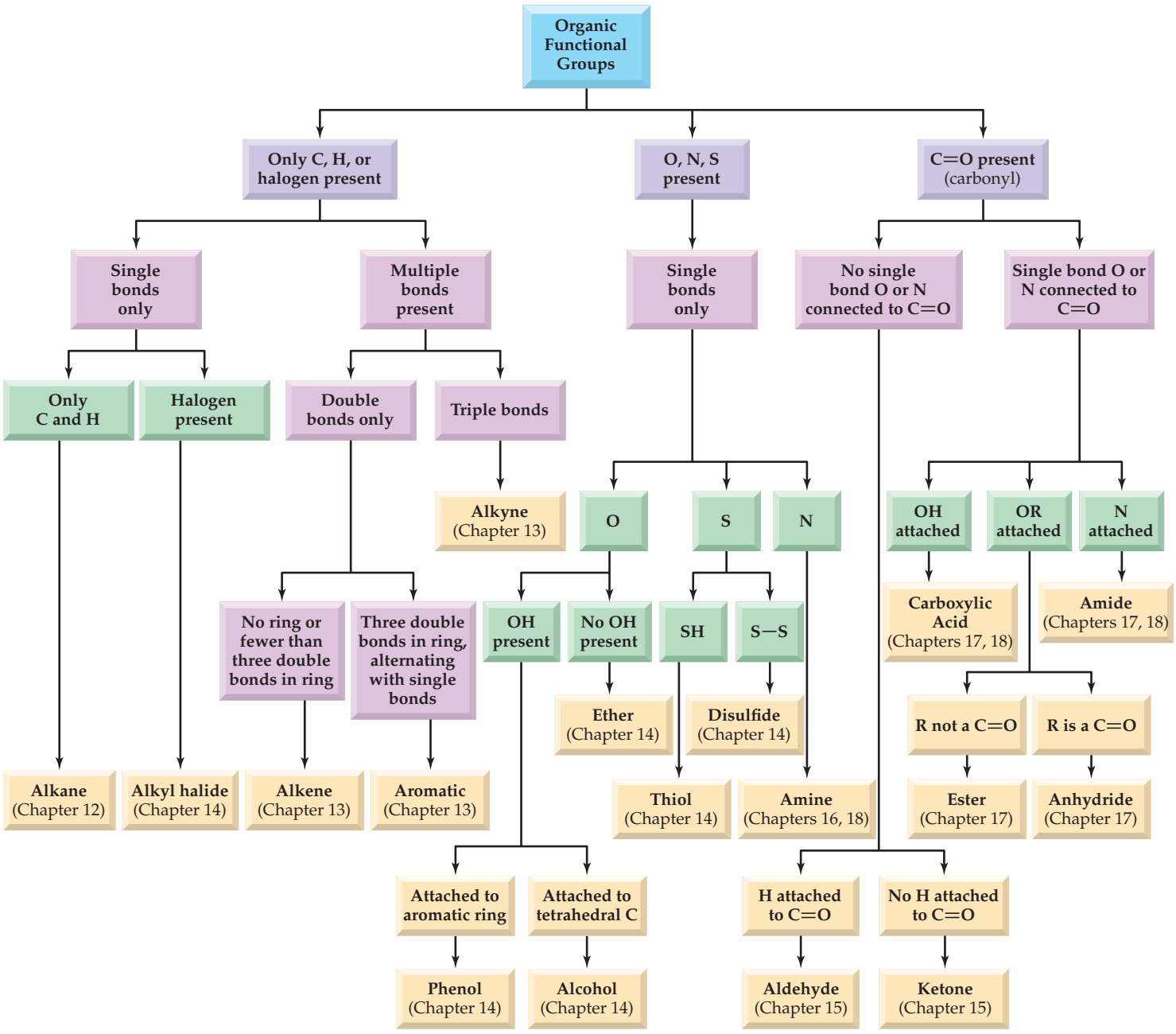
- **Describe how esters and amides are formed from carboxylic acids.** In ester formation, the —OH of a carboxylic acid group is replaced by the —OR' group of an alcohol. In amide formation, the —OH group of a carboxylic acid is replaced by NH_2 from ammonia to give primary amides or by —NHR' or $—NR'_2$ from an amine to give secondary and tertiary amides, respectively *(see Problems 32, 34, 56, 57, 60, 62, and 63).*

- **Predict the hydrolysis products of esters and amides.** Hydrolysis of esters with acids or bases breaks the C(=O)—OR' bond and adds an —H to the —OR' group and —OH to the C=O group to restore the carboxylic acid and the alcohol. Hydrolysis of amides with acids or bases adds an —H to the —N group and —OH to the C=O group to restore the carboxylic acid and ammonia or the amine used to form the amide *(see Problems 31, 36, and 61–67).*

- **Describe the formation and uses of polyesters and polyamides.** Polyesters and polyamides are formed when a dicarboxylic acid is allowed to react with either a dialcohol or a diamine, respectively. Dacron is an example of a polyester, while Nylon is an example of a polyamide. These polymers are used to make plastic bottles, recording tape, fabric, ropes, sutures, and even replacement arteries *(see Problems 34, 68, and 69).*

- **Recognize and draw the structures of phosphate esters and their ionized forms.** Phosphoric acid forms mono-, di-, and triesters: $ROPO_3H_2$, $(RO)_2PO_2H$, and $(RO)_3PO$. There are also esters that contain the diphosphate and triphosphate groups from pyrophosphoric acid and triphosphoric acid (p. 578). Esters that retain hydrogen atoms are ionized in body fluids—for example, $ROPO_3^{2-}$ and $(RO)_2PO^{2-}$. *Phosphorylation* is the transfer of a *phosphoryl group,* $—PO_3^{2-}$, from one molecule to another. In biochemical reactions, the phosphoryl group is often donated by a triphosphate (such as ATP) with release of energy *(see Problems 70–75).*

CONCEPT MAP: ORGANIC CHEMISTRY FAMILIES



▲ **Figure 17.1 Functional Group Concept Map.** This is the same concept map we saw at the end of Chapters 12 through 16, except the functional groups discussed in this chapter, carboxylic acids, esters, and amides have now been colorized.

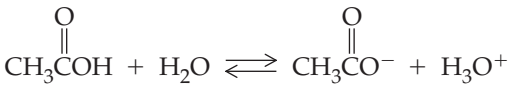
KEY WORDS

Acetyl group (Ac), *p. 560*
Acyl group, *p. 558*
Amide, *p. 557*
Carbonyl-group substitution reaction, *p. 558*
Carboxyl group, *p. 559*
Carboxylate anion, *p. 566*
Carboxylic acid, *p. 557*
Carboxylic acid salt, *p. 567*
Ester, *p. 557*
Esterification, *p. 570*
Phosphate ester, *p. 578*
Phosphoryl group, *p. 578*
Phosphorylation, *p. 579*
Saponification, *p. 574*

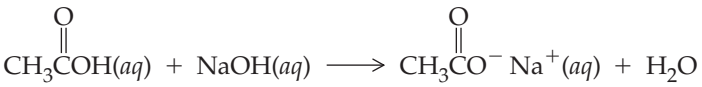
SUMMARY OF REACTIONS

1. Reactions of carboxylic acids

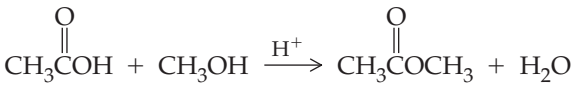
(a) Acid-base reaction with water (Section 17.2).



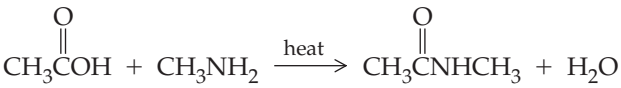
(b) Acid-base reaction with a strong base to yield a carboxylic acid salt (Section 17.3).



(c) Substitution with an alcohol to yield an ester (Section 17.4).

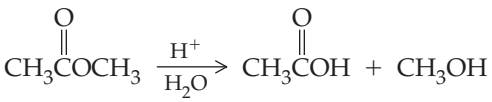


(d) Substitution with an amine to yield an amide (Section 17.4).

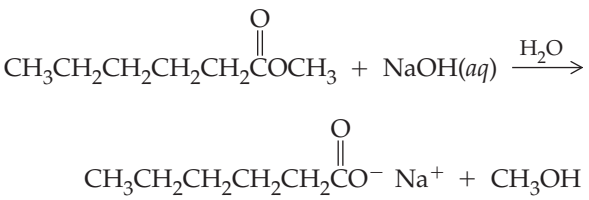


2. Reactions of esters (Section 17.4)

(a) Hydrolysis to yield an acid and an alcohol.

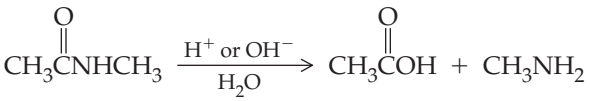


(b) Hydrolysis with a strong base to yield a carboxylate anion and an alcohol (saponification).



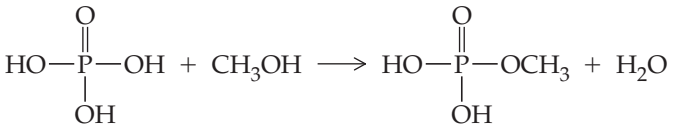
3. Reactions of amides (Section 17.4)

(a) Hydrolysis to yield an acid and an amine.

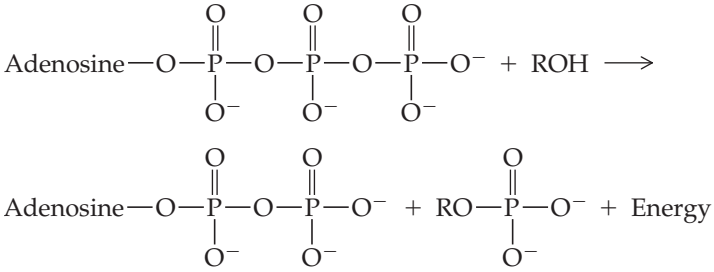


4. Phosphate reactions (Section 17.6)

(a) Phosphate ester formation

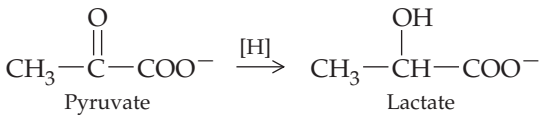


(b) Phosphorylation



UNDERSTANDING KEY CONCEPTS

17.30 Muscle cells deficient in oxygen reduce pyruvate (an intermediate in metabolism) to lactate at a cellular pH of approximately 7.4.



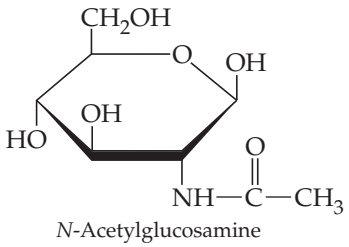
(a) Why do we say pyruvate and lactate, rather than pyruvic acid and lactic acid?

(b) Alter the above structures to create pyruvic acid and lactic acid.

(c) Show hydrogen bonding of water to both pyruvate and lactate. Would you expect a difference in water solubility of lactate and pyruvate? Explain.

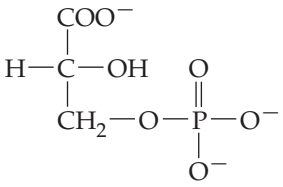
17.31 *N*-Acetylglucosamine (also known as NAG) is an important component on the surfaces of cells.

(a) Under what chemical conditions might the acetyl group be removed, changing the nature of the cell-surface components?



(b) Draw the structures of the products of acid hydrolysis.

17.32 One phosphorylated form of glycerate is 3-phosphoglycerate (a metabolic intermediate found in the glycolytic cycle, Section 22.3).

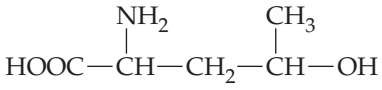


(a) Identify the type of linkage between glycerate and phosphate.

(b) 1,3-Bisphosphoglycerate (two phosphates on glycerate) has an anhydride linkage between the carbonyl at C1 of glycerate and phosphate. Draw the structure of 1,3-bisphosphoglycerate (another metabolic intermediate).

17.33 The names of the first nine dicarboxylic acids can be remembered by using the first letter of each word of the saying "*O*h *M*y, *S*uch *G*ood *A*pple *P*ie! *S*weet *A*s *S*ugar!" to remind us of *o*xalate, *m*alonate, *s*uccinate, *g*lutarate, *a*dipate, *p*imelate, *s*uberate, *a*zelate, and *s*ebacate (the dianionic form in which these acids occur at physiological pH). Write the structures of the first six dicarboxylate anions.

17.34 Consider the following unnatural amino acid:



(a) If two molecules react to form an ester, what is the structure of the ester product?

(b) If two molecules react to form an amide, what is the structure of the amide product?

(c) Draw the cyclic ester resulting from the intramolecular reaction of the hydroxyl group of this amino acid with its carboxyl group (cyclic esters are called *lactones*).

17.35 **(a)** Draw the structures of the following compounds and use dashed lines to indicate where they form hydrogen bonds to other molecules of the same kind: (i) formic acid, (ii) methyl formate, and (iii) formamide.

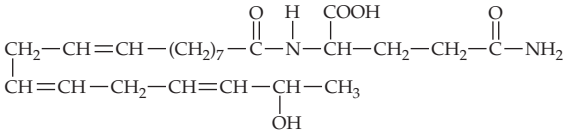
(b) Arrange these compounds in order of increasing boiling points and explain your rationale for the order.

17.36 Volicitin, in the "spit" from beet armyworms, causes corn plants to produce volatile compounds that act as signaling compounds for parasitoid wasps. Draw the three hydrolysis products that form from volicitin that match the common names given here.

(a) Glutamic acid (α-aminoglutaric acid)

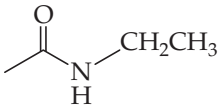
(b) Ammonia

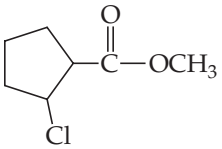
(c) 17-Hydroxylinolenic acid

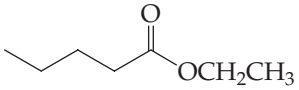


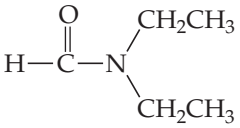
Volicitin

17.37 For the following compounds, give the systematic name.

(a) 

(b) 

(c) 

(d) 

ADDITIONAL PROBLEMS

CARBOXYLIC ACIDS (SECTIONS 17.1–17.2)

17.38 Write the equation for the ionization of hexanoic acid in water at pH 7.4. (Hint: See Section 17.2.)

17.39 Suppose you have a sample of benzoic acid dissolved in water.

(a) Draw the structure of benzoic acid.

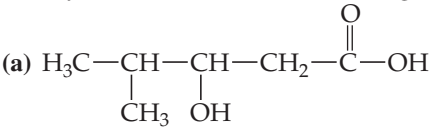
(b) Now assume that aqueous NaOH is added to the benzoic acid solution until pH 12 is reached. Draw the structure of the major organic species present.

(c) Finally, assume that aqueous HCl is added to the solution from (b) until pH 2 is reached. Draw the structure of the major organic species present.

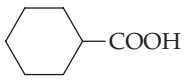
17.40 There are two different carboxylic acids with the formula $C_4H_8O_2$. Draw and name them.

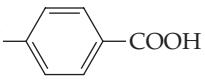
17.41 There are two different butanoic acids with the formula $C_5H_{10}O_2$. Draw and name them.

17.42 Give systematic names for the following carboxylic acids:

(a) 

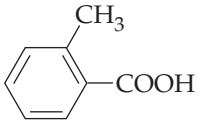
(b) $CH_3-(CH_2)_7-COOH$

(c) 

(d) 

17.43 Give systematic names for the following carboxylic acids:

(a) $BrCH_2CH_2CH(CH_3)COOH$

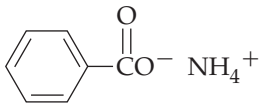
(b) 

(c) $(CH_3CH_2)_3CCOOH$

(d) $CH_3(CH_2)_5COOH$

17.44 Give systematic names for the following carboxylic acid salts:

(a) $CH_3CH_2CH(CH_2CH_3)CH_2CO^-\ K^+$

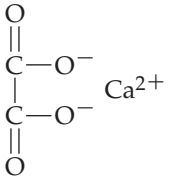
(b) 

(c) $[CH_3CH_2CO^-]_2\ Ca^{2+}$

17.45 Give systematic names and common names for the following carboxylic acid salts:

(a) $CH_3CO^-\ NH_4^+$

(b) $^-OOCCH(CH_2CH_3)(CH_2)_2COO^-\ 2Na^+$

(c) 

17.46 Draw structures corresponding to the following names:

(a) 3,4-Dimethylhexanoic acid

(b) Phenylacetic acid

(c) 3,4-Dinitrobenzoic acid

(d) Triethylammonium butanoate

17.47 Draw structures corresponding to the following names:

(a) 2,2,3-Trifluorobutanoic acid

(b) 3-Hydroxybutanoic acid

(c) 3,3-Dimethyl-4-phenylpentanoic acid

17.48 Malic acid, a dicarboxylic acid found in apples, has the systematic name hydroxybutanedioic acid. Draw its structure.

17.49 Fumaric acid is a metabolic intermediate that has the systematic name *trans*-2-butenedioic acid. Draw its structure.

17.50 What is the formula for the diammonium salt of fumaric acid? (See Problem 17.49)

17.51 Aluminum acetate is used as an antiseptic ingredient in some skin-rash ointments. Draw its structure.

ESTERS AND AMIDES (SECTIONS 17.3–17.4)

17.52 Draw and name compounds that meet these descriptions:

(a) Three different amides with the formula $C_5H_{11}NO$

(b) Three different esters with the formula $C_6H_{12}O_2$

17.53 Draw and name compounds that meet these descriptions:

(a) Three different amides with the formula $C_6H_{13}NO$

(b) Three different esters with the formula $C_5H_{10}O_2$

17.54 Give systematic names for the following structures and structures for the names:

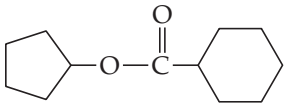
(a) $CH_3COCH_2CH_2CH(CH_3)CH_3$

(b) $CH_3CH(CH_3)CH_2CH_2COCH_3$

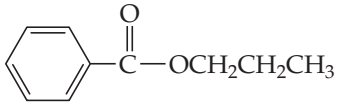
(c) Cyclohexyl acetate

(d) Phenyl-*o*-hydroxybenzoate

17.55 Give systematic names for the following structures and structures for the names:

(a) 

(b) Ethyl 2-hydroxypropanoate

(c) 

(d) Butyl 3,3-dimethylhexanoate

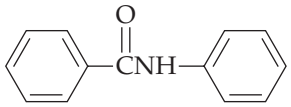
(e) $(CH_3)_2CHCOC(CH_3)_3$

17.56 Draw structures of the carboxylic acids and alcohols you would use to prepare each ester in Problem 17.54.

17.57 Draw structures of the carboxylic acids and alcohols you would use to prepare each ester in Problem 17.55.

17.58 Give systematic names for the following structures and structures for the names:

(a) $CH_3CH_2CH(CH_2CH_3)CONH_2$

(b) 

(c) *N*-Ethyl-*N*-methylbenzamide

(d) 2,3-Dibromohexanamide

17.59 Give systematic names for the following structures and structures for the names:

(a) 3-Methylpentanamide

(b) *N*-Phenylacetamide

(c) $HCON(CH_3)_2$

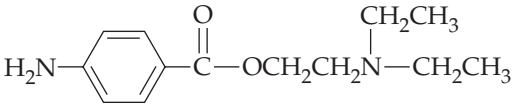
(d) $CH_3CH_2CONHCH(CH_3)CH_3$

17.60 Show how you would prepare each amide in Problem 17.58 from the appropriate carboxylic acid and amine.

17.61 What compounds are produced from hydrolysis of each amide in Problem 17.59?

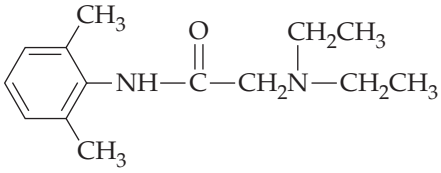
REACTIONS OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES (SECTIONS 17.3–17.4)

17.62 Procaine, a local anesthetic whose hydrochloride is Novocain, has the following structure. Identify the functional groups present, and show the structures of the alcohol and carboxylic acids you would use to prepare procaine.



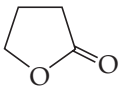
Procaine

17.63 Lidocaine (Xylocaine) is a local anesthetic closely related to procaine. Identify the functional groups present in lidocaine, and show how you might prepare it from a carboxylic acid and an amine.



Lidocaine

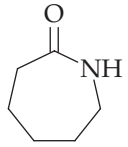
17.64 Lactones are cyclic esters in which the carboxylic acid part and the alcohol part are connected to form a ring. One of the most notorious lactones is gamma-butyrolactone (GBL), whose hydrolysis product is the "date-rape" drug GHB. Draw the structure of GHB.



GBL

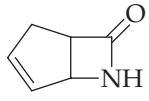
17.65 When both the carboxylic acid and the amine are in the same molecule, amide formation produces lactams. A *lactam* is a cyclic amide, where the amide group is part of the ring. Draw the structure of the product(s) obtained from acid hydrolysis of these lactams.

(a)



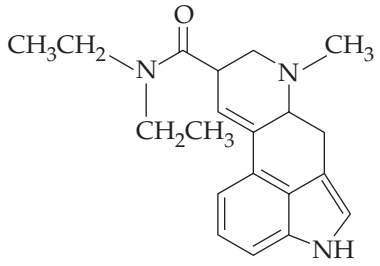
epsilon-lactam

(b)



beta-lactam

17.66 LSD (lysergic acid diethylamide), a semisynthetic psychedelic drug of the ergoline family, has the structure shown here. Identify the functional groups present, and give the structures of the products you would obtain from hydrolysis of LSD.

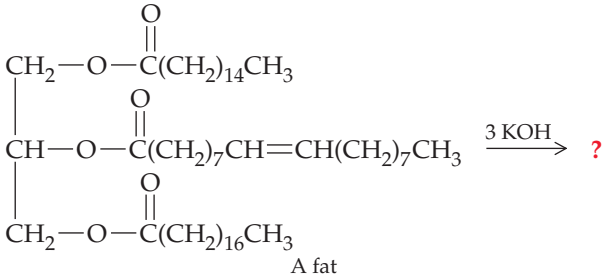


LSD

17.67 Household soap is a mixture of the sodium or potassium salts of long-chain carboxylic acids that arise from saponification of animal fat.

(a) Identify the functional groups present in the fat molecule shown in the following reaction.

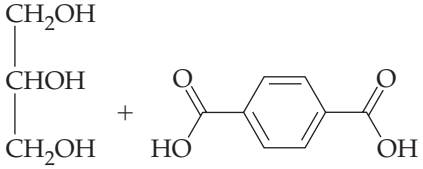
(b) Draw the structures of the soap molecules produced in the following reaction:



A fat

POLYESTERS AND POLYAMIDES (SECTION 17.5)

17.68 Baked-on paints used for automobiles and many appliances are often based on *alkyds,* such as can be made from terephthalic acid and glycerol. Sketch a section of the resultant polyester polymer that would be obtained if two glycerols reacted with two terephthalic acids, using the –OH on the first and third carbon of glycerol. Note that the glycerol can actually be esterified at any of the three alcohol groups, providing *cross-linking* to form a very strong surface.



Glycerol Terephthalic acid

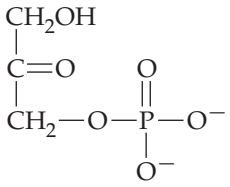
17.69 A simple polyamide can be made from ethylenediamine and oxalic acid (Table 17.1). Draw the polymer formed when three units of ethylenediamine reacts with three units of oxalic acid.

$H_2N—CH_2—CH_2—NH_2$

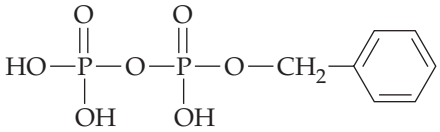
Ethylenediamine

PHOSPHATE ESTERS AND ANHYDRIDES (SECTION 17.6)

17.70 The following phosphate ester is an important intermediate in carbohydrate metabolism. What two products result from hydrolysis of this phosphate ester?



17.71 In the following compound



(a) Identify the phosphate ester linkage.

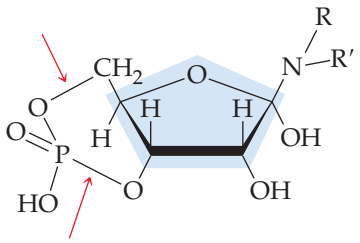
(b) Identify the phosphate anhydride linkage.

(c) When this molecule is treated with acid and water, three products are obtained. Draw them. (Hint: Two of the products formed are the same.)

17.72 The metabolic intermediate *acetyl phosphate* is an anhydride formed from acetic acid and phosphoric acid. What is the structure of acetyl phosphate?

17.73 Acetyl phosphate (see Problem 17.74) has what is called "high phosphoryl-group transfer potential." Write a reaction in which there is phosphoryl-group transfer from acetyl phosphate to ethanol to make a phosphate ester.

17.74 Cyclic ribose nucleotide phosphates, such as cyclic AMP (cAMP), are important signaling agents in living cells; all have the general structure shown here. What kind of linkage holds the phosphate to the ribose (see arrows; ribose is highlighted in blue)?



Cyclic Ribose Phosphate

17.75 What is the difference between a phosphate diester and an ester of a diphosphate? Give an example of each.

CONCEPTUAL PROBLEMS

17.76 Three amide isomers, *N,N*-dimethylformamide, *N*-methylacetamide, and propanamide, have respective boiling points of 153 °C (426 K), 202 °C (475 K), and 213 °C (486 K). Explain these boiling points in light of their structural formulas.

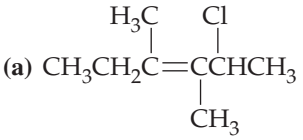
17.77 Salol, the phenyl ester of salicylic acid, is used as an intestinal antiseptic. Draw the structure of phenyl salicylate.

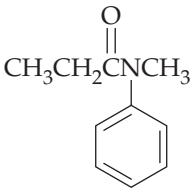
17.78 Propanamide and methyl acetate have about the same molar mass, both are quite soluble in water, and yet the boiling point of propanamide is 486 K, whereas that of methyl acetate is 330 K. Explain.

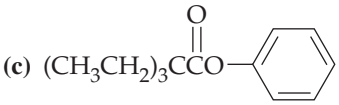
17.79 Mention at least two simple chemical tests by which you can distinguish between benzaldehyde and benzoic acid.

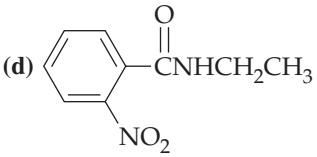
17.80 Write the formula of the triester formed from glycerol and stearic acid (Table 17.1).

17.81 Name the following compounds.

(a) 

(b) 

(c) 

(d) 

GROUP PROBLEMS

17.82 Each of the following materials has an ester that is responsible for its smell and/or flavor. Search the internet and determine what that ester is, draw its structure, and what carboxylic acid and alcohol are used to form it.

(a) Juicy Fruit gum flavoring

(b) Peach odor

(c) Apple odor

(d) Rum odor

17.83 Draw all possible carboxylic acids with the formula $C_5H_{10}O_2$.

17.84 Some of the most well-known antibiotics belong to a class of carboxylic acid derivatives known as beta-lactams. Search the internet and find at least four antibiotics that belong to this class. Draw their structures and identify the functional groups present. Other than the presence of the beta-lactam, what other common structural features and/or functional groups do they have in common?

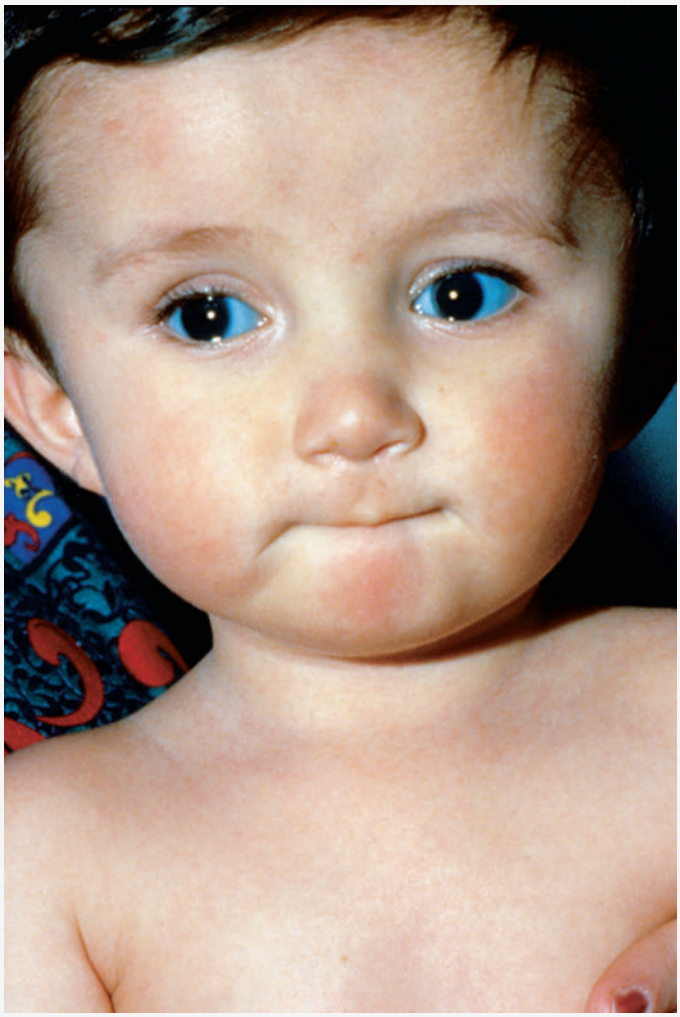
18

Amino Acids and Proteins

CONTENTS

CONCEPTS TO REVIEW

A. Acid-Base Properties (Sections 5.4, 10.2, and 17.2)
B. Hydrolysis Reactions (Section 17.4)
C. Intermolecular Forces (Section 8.2)
D. Polymers (Sections 13.7 and 17.5)



▲ Child with osteogenesis imperfecta, a genetic disease. One characteristic of osteogenesis imperfecta is the blue color of the sclera (whites) of the eyes.

Imagine being introduced to a newborn with startlingly blue eyes—not blue irises as we see typically but with the part of the eye known as the "white" or sclera completely blue instead, as in the picture above. This coloration of the sclera is an indication of a genetic disease called *osteogenesis imperfecta*, or brittle bone disease. Osteogenesis imperfecta is a result of the synthesis of imperfect collagen, the most abundant protein in the human body. Genetic mutations result in amino acid substitutions in collagen, creating imperfect collagen. Collagen is the scaffold for bone and is present in cartilage, connective tissue, and the sclera of the eye. You will learn more about collagen throughout this chapter, including how amino acids are bonded to form collagen as well as other proteins. Also, some functions of proteins will be discussed that help health professionals understand diseases such as osteogenesis imperfecta. The study of proteins and how they lead to diseases like osteogenesis imperfecta is just one example of a topic that falls under the discipline of biochemistry. Osteogenesis imperfecta is discussed further in the Chemistry in Action on page 617.

18.1 An Introduction to Biochemistry

Biochemistry, the study of molecules and their reactions in living organisms, is built upon the inorganic and organic chemical principles outlined in the first 17 chapters of this book. Now we are ready to investigate the chemical basis of life. Physicians are faced with biochemistry every day because all diseases are associated with abnormalities in biochemistry. Nutritionists evaluate our dietary needs based on our biochemistry. And the pharmaceutical industry designs molecules that mimic or alter the action of biomolecules. The ultimate goal of biochemistry is to understand the structures of biomolecules and the relationships between their structures and functions.

Biochemistry is the common ground for the life sciences. Microbiology, botany, zoology, immunology, pathology, physiology, toxicology, neuroscience, cell biology—in all these fields, answers to fundamental questions are found at the molecular level.

The principal classes of biomolecules are *proteins, carbohydrates, lipids,* and *nucleic acids.* Some biomolecules are small and have only a few functional groups. Others are huge and their biochemistry is governed by the interactions of large numbers of functional groups. Proteins, the subject of this chapter; nucleic acids (Chapter 26); and large carbohydrates (Section 20.7) are all polymers, some containing hundreds, thousands, or even millions of repeating units.

Biochemical reactions must continuously break down food molecules, generate and store energy, build up new biomolecules, and eliminate waste. Each biomolecule has its own role to play in these processes, but despite the huge size of some biomolecules and the complexity of their interactions, their functional groups and chemical reactions are no different from those of simpler organic molecules. *All the principles of chemistry introduced thus far apply to biochemistry.* Of the functional groups introduced in previous chapters, those listed in Table 18.1 are of greatest importance in biomolecules.

LOOKING AHEAD The focus in the rest of this book is on human biochemistry and the essential structure–function relationships of biomolecules. In this and the next chapter, we examine the structure of proteins and the roles of proteins and other molecules in controlling biochemical reactions. Next, we discuss the structure and function of carbohydrates (Chapter 20). Then, we present an overview of metabolism and the production of energy (Chapters 21 and 22). Then, we discuss the structure and function of lipids (Chapters 23 and 24), the role of nucleic acids in protein synthesis and heredity (Chapters 26 and 27), the metabolism of proteins (Chapter 25), the role of small molecules in neurochemistry (Chapter 28), and the chemistry of body fluids (Chapter 29).

18.2 Proteins and Their Functions: An Overview

Learning Objective:

- Describe the different functions of proteins and give an example for each function.

The word *protein* is a familiar one. Taken from the Greek *proteios,* meaning "primary," "protein" is an apt description for the biological molecules that are of primary importance to all living organisms. Approximately 50% of your body's dry mass is protein.

What roles do proteins play in living things? No doubt you are aware that a hamburger is produced from animal muscle protein and that we depend on our own muscle proteins for every move we make. But this is only one of many essential roles of proteins. They provide *structure* (keratin) and *support* (actin filaments) to tissues and organs throughout our bodies. As *hormones* (oxytocin) and *enzymes* (catalase), they control all aspects of metabolism. In body fluids, water-soluble proteins pick up other molecules for *storage* (casein) or *transport* (transferrin, Fe^{3+}). And the proteins of the immune system provide *protection* (Immunoglobulin G) against invaders such as bacteria and viruses. To accomplish their biological functions, which are summarized in Table 18.2, some proteins must be tough and fibrous, whereas others must be globular and soluble in body fluids. The overall shape of a protein molecule, as you will see often in the following chapters, is essential to the role of that protein in our metabolism.

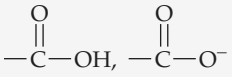
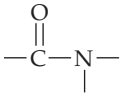
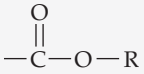
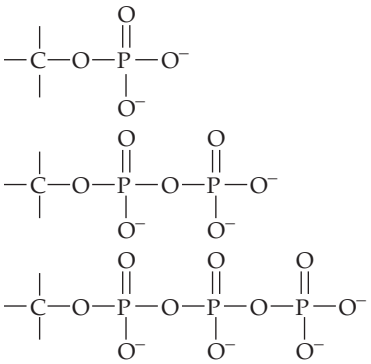
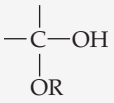
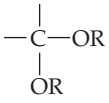
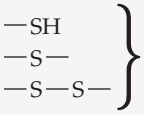
PROBLEM 18.1

Alcohol dehydrogenase, found in liver cells, converts ethanol into acetaldehyde. What type of protein is alcohol dehydrogenase?

PROBLEM 18.2

Cortisol levels rise under stressful conditions. Oxytocin can induce relaxation and romantic feelings. What type of protein are cortisol and oxytocin?

Table 18.1 Functional Groups of Importance in Biochemical Molecules

Functional Group	Structure	Type of Biomolecule
Ammonium ion, amino group	$-NH_3^+$, $-NH_2$	Amino acids and proteins (Sections 18.3 and 18.4)
Hydroxyl group	$-OH$	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 20.3 and 23.2)
Carbonyl group		Monosaccharides (carbohydrates); in acetyl group (CH_3CO) used to transfer carbon atoms during catabolism (Sections 21.4 and 21.8)
Carboxyl group, carboxylate anion		Amino acids, proteins, and fatty acids (lipids) (Sections 18.3, 18.4, and 23.2)
Amide group		Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Section 18.4)
Carboxylic acid ester		Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Section 23.2)
Phosphates, mono-, di-, tri-		Adenosine triphosphate (ATP) and many metabolism intermediates (Sections 17.6, 21.4, and throughout metabolism sections)
Hemiacetal group		Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 15.7 and 20.4)
Acetal group		Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 15.7, 20.6, and 20.7)
Thiols Sulfides Disulfides		Found in amino acids cysteine, methionine; structural components of proteins (Sections 14.8, 18.3, 18.8, and 18.10)

In Table 18.1, both the amino group and the carboxyl group are shown having two different structures. This is explained in Section 18.4.

Table 18.2 Classification of Proteins by Function

Type	Function	Example
Enzymes	Catalyze biochemical reactions	*Amylase*—begins digestion of carbohydrates by hydrolysis
Hormones	Regulate body functions by carrying messages to receptors	*Insulin*—facilitates use of glucose for energy generation
Storage proteins	Make essential substances available when needed	*Myoglobin*—stores oxygen in muscles
Transport proteins	Carry substances through body fluids	*Serum albumin*—carries fatty acids in blood
Structural proteins	Provide mechanical shape and support	*Collagen*—provides structure to tendons and cartilage
Protective proteins	Defend the body against foreign matter	*Immunoglobulin*—aids in destruction of invading bacteria
Contractile proteins	Do mechanical work	*Myosin* and *actin*—govern muscle movement

18.3 Amino Acids

Learning Objectives:

- Describe and recognize the 20 alpha amino acid structures and their side chains.
- Categorize amino acids by the polarity or neutrality of the side chain and predict which are hydrophilic and which are hydrophobic.
- Explain chirality and identify which amino acids are chiral.

Amino acids are the building blocks for the polymers called **proteins.** Every amino acid contains an amino functional group ($-NH_2$), a carboxyl functional group ($-COOH$), and an R group called a **side chain,** all bonded to the same carbon atom. This central carbon is known as the alpha (α)-carbon, named so because it is the carbon atom directly adjacent to a carboxyl functional group. Thus, the amino acids in proteins are **alpha-amino (α-amino) acids** because the amino group in each is connected to the alpha-carbon atom. Each α-amino acid has a different R group, and that is what distinguishes amino acids from one another. The R groups may be only hydrocarbons, or they may also contain a functional group.

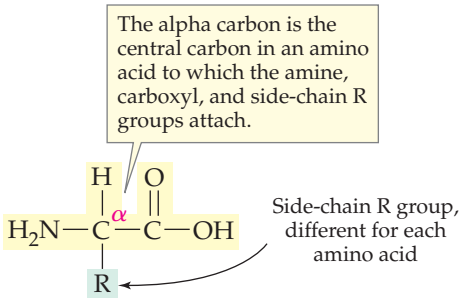
Amino acid A molecule that contains both an amino functional group and a carboxyl functional group.

Protein A large biological molecule made of many amino acids linked together through amide bonds.

Side chain (amino acid) The variable group bonded to the central carbon atom in an amino acid; different in each amino acid.

Alpha- (α-) amino acid An amino acid in which the amino group is bonded to the carbon atom next to the $-COOH$ group.

An α-amino acid



All of the diverse proteins in living organisms are built from just 20 common α-amino acids, listed in Table 18.3. Each amino acid has a three-letter shorthand code that is included in the table; for example, Ala for alanine, Gly for glycine, and Pro for proline. Biochemists use a one-letter code; for example, A for alanine, G for glycine, and P for proline. The one-letter codes are also in Table 18.3. All of these amino acids (with the exception of glycine and proline) have the same structure except for the side chain (R group) attached to the α-carbon. The different R groups of each amino acid give each its unique identity and determines its function. For example, alanine has a methyl (CH_3) group bonded to the alpha carbon, but cysteine has a thiol (SH) group. Glycine, the simplest amino acid, has an H atom instead of an alkyl side chain, whereas proline's amino nitrogen atom is bonded to the α-carbon atom forming a five-membered ring. Not included in this table are several rare amino acids found primarily in microbes. Table 18.3 identifies the different R groups of each amino acid in green.

PROBLEM 18.3

Consult Table 18.3 and draw alanine. Label the functional groups and give the three-letter abbreviation and the one-letter abbreviation. What group does the side chain fall into?

KEY CONCEPT PROBLEM 18.4

Examine the ball-and-stick model of valine in the margin. Identify the carboxyl group, the amino group, and the R group.

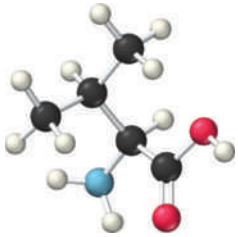
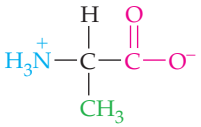
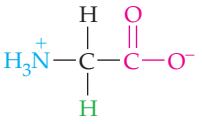
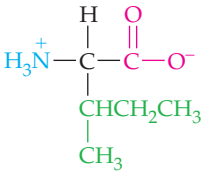


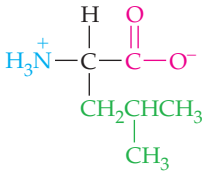
Table 18.3 The 20 α-Amino Acids Found in Proteins, with Their Abbreviations, One-Letter Codes, and Isoelectric Points. The structures are written here in their fully ionized forms. These ions and the isoelectric points given in parentheses are explained in Section 18.4.

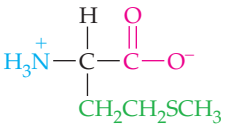
Nonpolar, Neutral Side Chains

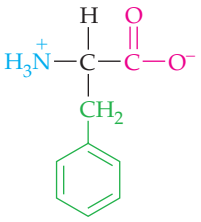

Alanine, Ala, A (6.0)

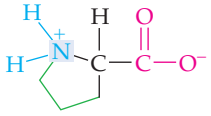

Glycine, Gly, G (6.0)

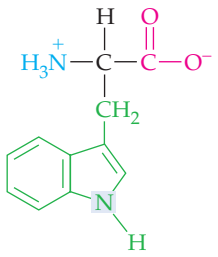

Isoleucine, Ile, I (6.0)

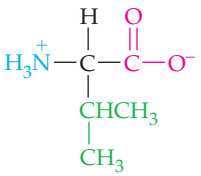

Leucine, Leu, L (6.0)


Methionine, Met, M (5.7)

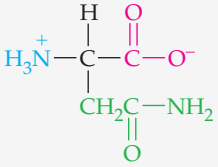

Phenylalanine, Phe, F (5.5)

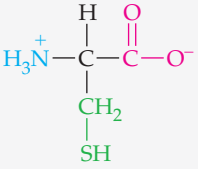

Proline, Pro, P (6.3)

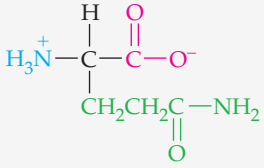

Tryptophan, Trp, W (5.9)

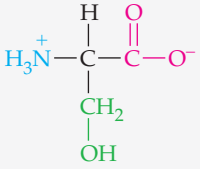

Valine, Val, V (6.0)

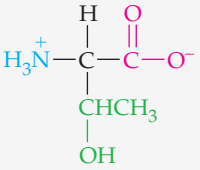
Polar, Neutral Side Chains

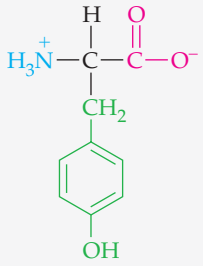

Asparagine, Asn, N (5.4)


Cysteine, Cys, C (5.0)

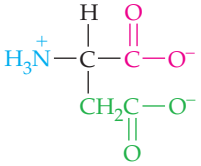

Glutamine, Gln, Q (5.7)

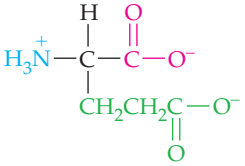

Serine, Ser, S (5.7)


Threonine, Thr, T (5.6)

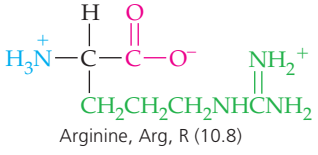

Tyrosine, Tyr, Y (5.7)

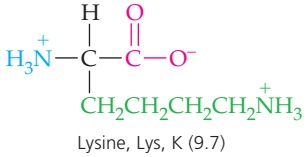
Acidic Side Chains

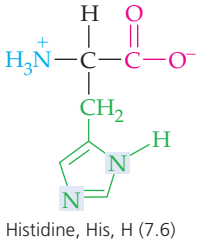

Aspartic acid, Asp, D (3.0)
(Aspartate)


Glutamic acid, Glu, E (3.2)
(Glutamate)

Basic Side Chains

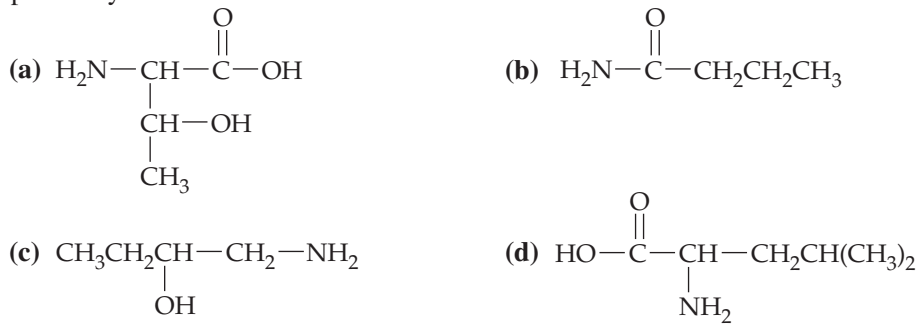

Arginine, Arg, R (10.8)


Lysine, Lys, K (9.7)


Histidine, His, H (7.6)

PROBLEM 18.5

Indicate whether each of the following molecules is an α-amino acid or not, and explain why.



PROBLEM 18.6

Using Table 18.3, name the α-amino acids that (a) contain an aromatic ring, (b) contain sulfur, (c) are alcohols, and (d) have alkyl-group side chains.

Side-Chain Polarity and Water Interactions

The 20 α-amino acids that make up proteins are classified as neutral, acidic, or basic, depending on the nature of their side chains. The 15 neutral amino acids are further divided into groups with nonpolar or polar side chains, which can be seen in Table 18.3. The neutral side chains contain alkyl groups that do not ionize to carry a positive or negative charge. Those with nonpolar side chains, such as leucine, contain only alkyl side chains. Several amino acids have polar side chains that do not ionize and are classed as neutral, polar. Serine is an example of this group; serine's side chain contains a hydroxyl group, which is polar. Two amino acids have side chains that contain the carboxylic acid functional group and can lose H^+, functioning as an acid; these are referred to as acidic amino acids. Three amino acids have an amine functional group in the side chain; the amine group can gain H^+ atoms, acting as a base. These are referred to as basic amino acids. As we explore the structure and function of proteins, you will see that it is the sequence of amino acids in a protein and the chemical nature of their side chains that enable proteins to perform their varied functions.

Intermolecular forces are of central importance in determining interactions between amino acids. In the context of biochemistry, it is more meaningful to refer to all interactions other than covalent bonding as **noncovalent forces.** The intermolecular forces present between amino acids or between protein chains are hydrogen bonding, Van der Waals forces, ionic bonding, and disulfide bonds.

The nonpolar side chains are **hydrophobic** ("water-fearing")—they are *not* attracted to water molecules and are not soluble in water. The polar, acidic, and basic side chains are **hydrophilic** ("water-loving"), polar side chains that *are* attracted to polar water molecules and are soluble in water.

CONCEPTS TO REVIEW The various types of intermolecular forces were introduced in Section 8.2. Review water interactions with other molecules in Section 9.2.

Noncovalent forces Forces of attraction other than covalent bonds that can act between molecules or within molecules.

Hydrophobic "Water-fearing;" a hydrophobic substance does not dissolve in water.

Hydrophilic "Water-loving;" a hydrophilic substance dissolves in water.

Worked Example 18.1 Determining Side-Chain Hydrophobicity/Hydrophilicity

Consider the structures of phenylalanine and serine in Table 18.3. Which of these two amino acids has a hydrophobic side chain and which has a hydrophilic side chain?

ANALYSIS Identify the side chains. The side chain in phenylalanine is an alkane. The side chain in serine contains a hydroxyl group.

SOLUTION

The hydrocarbon side chain in phenylalanine is an alkane, which is nonpolar and hydrophobic. Therefore phenylalanine is hydrophobic. The hydroxyl group in the side chain of serine is polar and is hydrophilic. Thus, serine is hydrophilic.

KEY CONCEPT PROBLEM 18.7

Valine is an amino acid with a nonpolar side chain and serine is one with a polar side chain. Draw the two amino acids.

(a) Why is the side chain for valine nonpolar, whereas the side chain for serine is polar?

(b) Which amino acid has a hydrophilic side chain and which has a hydrophobic side chain?

PROBLEM 18.8

Which amino acid is hydrophilic (dissolves in aqueous solutions)? Why?

(a) isoleucine **(b)** phenylalanine **(c)** aspartic acid

PROBLEM 18.9

Which amino acid is hydrophobic (does not dissolve in aqueous solutions)? Why?

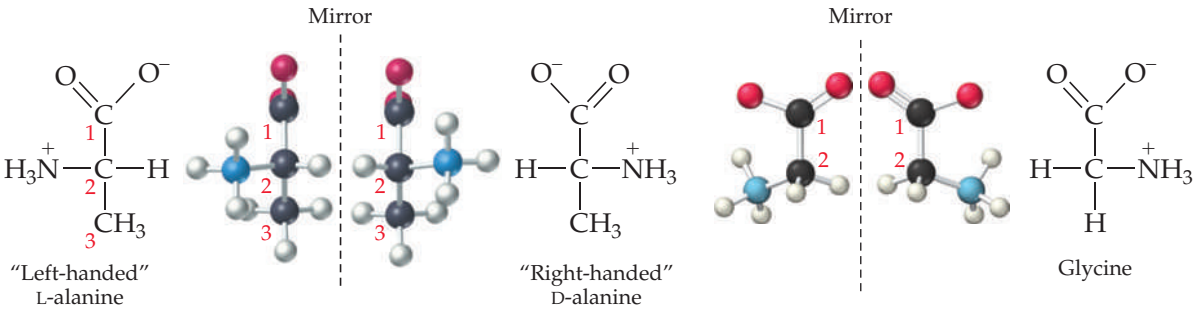
(a) glutamic acid **(b)** tryptophan **(c)** arginine

Chirality of Amino Acids

Review chirality in Section 14.10.

Of the 20 common amino acids, 19 are chiral. Only glycine is achiral. Even though the 19 chiral α-amino acids can exist either as D- or L-enantiomers, nature selectively uses only L-amino acids for making proteins. As shown next, alanine and glycine provide a visual comparison between chiral and achiral amino acids.

Alanine, a chiral molecule *Glycine, an achiral molecule*



Amino acids, as you have seen, are chiral. Chirality is an important property of another major class of biomolecules. The individual sugar units in all carbohydrates are chiral, a topic addressed in Section 20.2.

Because alanine is a chiral molecule, its mirror images cannot be superimposed. As a result, alanine exists in two forms that are mirror images of each other: a "right-handed" form known as D-alanine and a "left-handed" form known as L-alanine. Glycine, by contrast, is an achiral molecule. The molecule and its mirror image are identical, and it has no left- and right-handed isomers. A molecule needs only one chiral carbon atom to be chiral.

PROBLEM 18.10

Is serine chiral? Draw serine and identify the chiral atom. Explain why serine is chiral.

PROBLEM 18.11

Draw the mirror images of serine. Identify the D-form and the L-form.

PROBLEM 18.12

Two of the 20 common amino acids have two chiral carbon atoms in their structures. Identify these amino acids and their chiral carbon atoms.

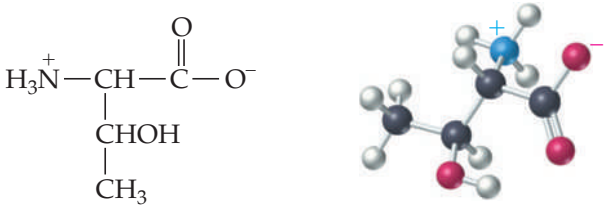
18.4 Acid-Base Properties of Amino Acids

Learning Objective:

- Draw all ionic structures for an amino acid under acidic and basic conditions, and identify the zwitterion.

Amino acids contain both an acidic group, —COOH (carboxyl group), and a basic group, $—NH_2$ (amino group). As you might expect, these two groups can undergo an intramolecular acid-base reaction, a reaction within the amino acid itself. The result is a loss of the hydrogen ion from the —COOH group (leaving the carboxylate anion, $—COO^-$) and a gain of a hydrogen ion to the $—NH_2$ group (forming $—NH_3^+$, the ammonium ion). This H^+ transfer within the amino acid forms a *dipolar* ion, an ion that has one positive charge and one negative charge and is thus electrically neutral because the sum of the charges on the molecule is zero. Dipolar ions are known as **zwitterions** (from the German *zwitter,* "hybrid"). The zwitterion form of threonine is shown here; however, the α-amino acids in Table 18.3 are shown in their fully ionized forms. If the R group contains either an acidic or basic group, that group is shown as ionized in Table 18.3 and that amino acid is not in the zwitterion form. Amino acids with neutral R groups are in the zwitterion form.

Zwitterion A neutral dipolar ion that has one positive charge and one negative charge.

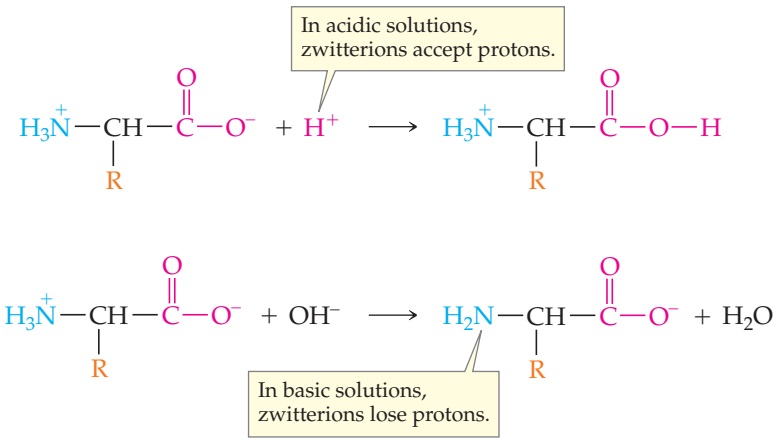


Threonine—zwitterion

Because they are zwitterions, amino acids have many of the physical properties we associate with salts. Pure amino acids can form crystals, have high melting points, and are soluble in water but not in hydrocarbon solvents.

In an acidic solution (low pH), amino acids accept protons on their basic $—COO^-$ groups, to leave only the positively charged $—NH_3^+$ groups. In basic solution (high pH), amino acids *lose* protons from their acidic $—NH_3^+$ groups, to leave only the negatively charged $—COO^-$ groups.

Review the properties of ionic compounds introduced in Section 3.10. Review properties of acids and bases introduced in Chapter 10.



Amino acids are present in the ionized form in both the solid state and in aqueous solution. The charge of an amino acid molecule at any given moment depends on the particular amino acid and the pH of the solution. The pH at which the net positive and negative charges are evenly balanced to form an electrically neutral molecule is the **isoelectric point (pI)** for that particular amino acid. At this point, the net charge of all the molecules of that amino acid in a pure sample is zero. The pI for each amino acid is different, due to the influence of the side-chain functional groups and can be found in parentheses next to the amino acid in Table 18.3. This electrically neutral molecule is the zwitterion form.

Isoelectric point (pI) The pH at which a sample of an amino acid has equal numbers of positive and negative charges.

A few amino acids have isoelectric points that are not near neutrality (pH 7). For example, the two amino acids with acidic side chains, aspartic acid and glutamic acid, have isoelectric points at more acidic (lower) pH values than those with neutral side

chains. Since the side-chain —COOH groups of these compounds are substantially ionized at physiological pH of 7.4, these amino acids are usually referred to as *aspartate* and *glutamate,* the names of the anions formed when the —COOH groups in the side chains are ionized. (Recall that the same convention is used, for example, for sulfate ion from sulfuric acid or nitrate ion from nitric acid; see Table 3.3.)

Side-chain interactions are important in stabilizing protein structure; thus, it is important to be aware of their charges at physiological pH (pH 7.4). Furthermore, pI influences protein solubility and determines which amino acids in an enzyme participate directly in enzymatic reactions. The acidic and basic side chains are particularly important because at physiological pH these groups are fully charged and can participate not only in ionic bonds within a protein chain but can also transfer H^+ from one molecule to another during reactions, as we will see in Chapter 19.

CHEMISTRY IN ACTION

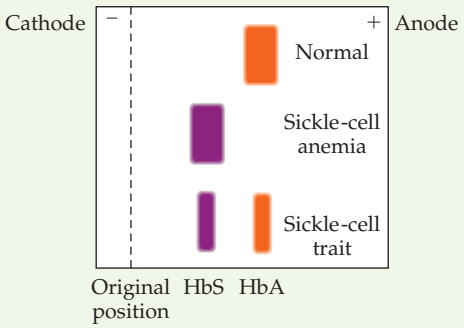
Protein Analysis by Electrophoresis

Protein molecules in solution can be separated from each other by taking advantage of their net charges. In the electric field between two electrodes, a positively charged particle moves toward the negative electrode and a negatively charged particle moves toward the positive electrode. This movement, known as *electrophoresis,* varies with the strength of the electric field, the charge of the particle, the size and shape of the particle, and the buffer/polymer gel combination through which the protein is moving.

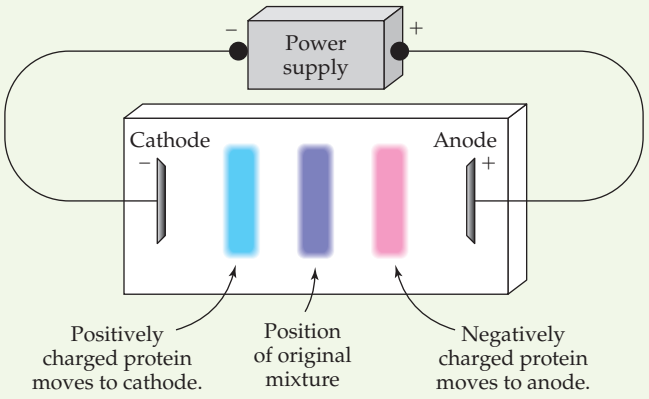
The net charge on a protein is determined by how many of the acidic or basic side-chain functional groups in the protein are ionized, and this, like the charge of an amino acid, depends on the pH. Thus, the mobility of a protein during electrophoresis depends on the pH of the buffer. If the buffer is at a pH equal to the isoelectric point of the protein, the protein does not move.

By varying the pH of the buffer between the electrodes and other conditions, proteins can be separated in a variety of ways, including by their molecular mass. Once the separation is complete, the various proteins are made visible by the addition of a dye.

Electrophoresis is routinely used in the clinical laboratory for determining which proteins are present, and in what amounts, in a blood sample. One commonly used test is for the diagnosis of sickle-cell anemia (p. 602). Normal adult hemoglobin (HbA) and hemoglobin showing the inherited sickle-cell trait (HbS) differ in their net charges. Therefore, HbA and HbS move different distances during electrophoresis. The accompanying diagram compares the results of electrophoresis of the hemoglobin extracted from red blood cells for a normal individual, one with sickle-cell anemia (two inherited sickle-cell genes) and one with sickle-cell trait (one normal and one inherited sickle-cell gene). With sickle-cell trait, an individual is likely to suffer symptoms of the disease only under conditions of severe oxygen deprivation.



▲ **Gel electrophoresis of hemoglobin.** Hemoglobin in samples placed at the original position in a porous polymer gel immersed in a constant pH buffer has moved left to right during electrophoresis. The normal individual has only HbA. The individual with sickle-cell anemia has no HbA, and the individual with sickle-cell trait has roughly equal amounts of HbA and HbS. HbA and HbS have negative charges of different magnitudes because HbS has two fewer Glu residues than HbA.



▲ Movement of charged molecules in electrophoresis.

CIA Problem 18.1 The proteins collagen, bovine insulin, and human hemoglobin have isoelectric points of 6.6, 5.4, and 7.1, respectively. Suppose a sample containing these proteins is subjected to electrophoresis in a buffer at pH 6.6. Describe the motion of each with respect to the positive and negative electrodes in the electrophoresis apparatus.

CIA Problem 18.2 Three dipeptides are separated by electrophoresis at pH 5.8. If the dipeptides are Arg-Trp, Asp-Thr, and Val-Met, describe the motion of each with respect to the positive and negative electrodes in the electrophoresis apparatus.

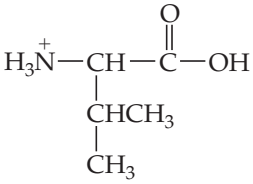
Worked Example 18.2 Drawing Zwitterion Forms

Look up the zwitterion form of valine in Table 18.3. Draw valine as it would be found (a) at low pH (acidic conditions) and (b) at high pH (basic conditions).

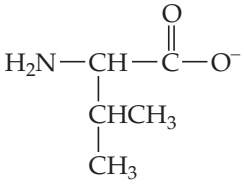
ANALYSIS At low pH, which is acidic, basic groups may gain H^+. At high pH, which is basic, acidic groups may lose H^+. In the zwitterion form of an amino acid, the $-COO^-$ group is basic and the $-NH_3^+$ is acidic.

SOLUTION

Valine has an alkyl-group side chain that is unaffected by pH. At low pH, valine adds a hydrogen ion to its carboxyl group to give the structure on the left. At high pH, valine loses a hydrogen ion from its acidic $-NH_3^+$ group to give the structure on the right.



Low (acidic) pH



High (basic) pH

PROBLEM 18.13

Draw the structure of glutamic acid at low pH, at high pH, and at the two forms that exist between low pH and high pH. Which of these structures represents the zwitterion?

PROBLEM 18.14

Use the definitions of acids and bases as proton donors and proton acceptors to explain which functional group in the zwitterion form of an amino acid is an acid and which is a base (see Section 10.3).

18.5 Peptides

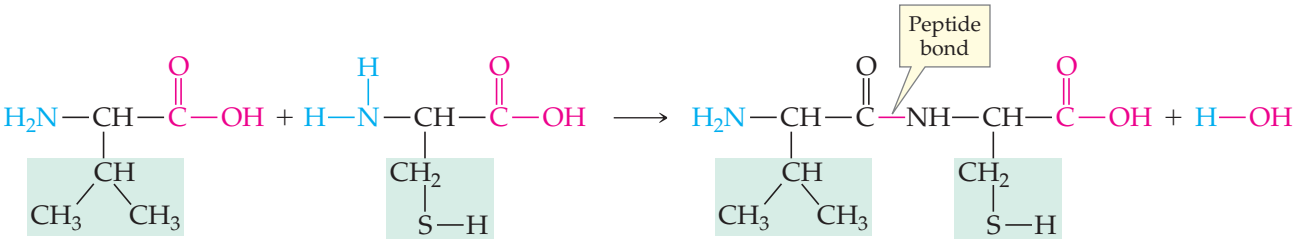
Learning Objectives:

- Identify a peptide bond, and explain how it is formed.
- Draw and name a simple protein structure given its amino acid sequence.
- Identify the amino-terminal end and the carboxyl-terminal end of a simple protein (peptide) structure given its amino acid sequence.

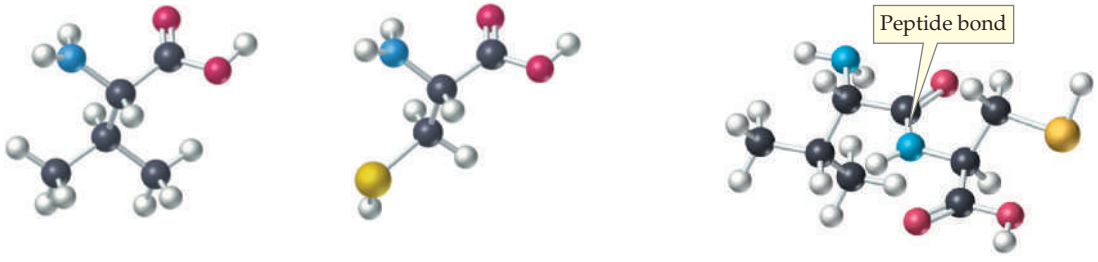
Two or more amino acids can link together by forming amide bonds, which are known as **peptide bonds** when they occur in proteins. A *dipeptide* results from the formation of a peptide bond between the $-NH_2$ group of one amino acid and the $-COOH$ group of a second amino acid. When this link is formed, an H^+ is released from the amino group of one amino acid and an $-OH^-$ group is released from the other amino acid. The H^+ and $-OH^-$ combine to form HOH, water. For example, valine and cysteine are connected in a dipeptide as follows:

Peptide bond An amide bond that links two amino acids together.

Review amide bonds in Section 17.3.

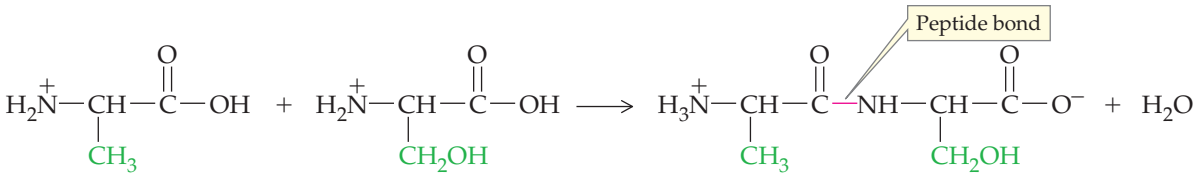


Valine Cysteine A dipeptide



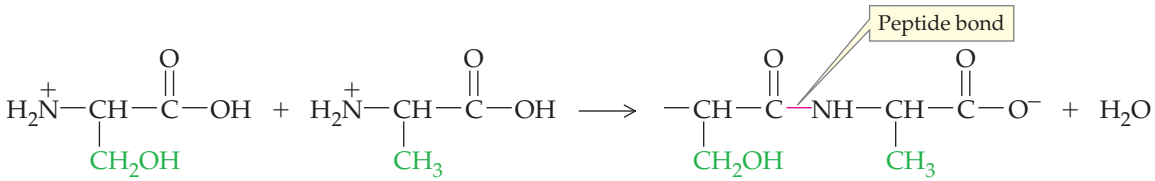
A *tripeptide* results from the linkage of three amino acids via two peptide bonds. Any number of amino acids can link together to form a linear chainlike polymer—a *polypeptide*. Very large peptides (oligopeptides) contain hundreds of amino acids and are referred to as proteins. Proteins have four levels of structure, each of which is explored later in this chapter.

The exact sequence of amino acids in a peptide or protein chain is important; variation in the sequence indicates a different molecule. A pair of amino acids—for example, alanine and serine—can be combined to form two different dipeptides. The —COOH in alanine can react with the $—NH_2$ in serine as follows:



Alanine (Ala, A) Serine (Ser, S) Alanylserine (Ala-Ser, AS)

Or the —COOH in serine can react with $—NH_2$ in alanine as follows:



Serine (Ser, S) Alanine (Ala, A) Serylalanine (Ser-Ala, SA)

Amino-terminal (N-terminal) amino acid The amino acid with the free $—NH_3^+$ group at the end of a protein.

Carboxyl-terminal (C-terminal) amino acid The amino acid with the free $—COO^-$ group at the end of a protein.

Residue An amino acid unit in a polypeptide.

After the formation of the peptide bond, an intramolecular proton exchange is considered. By convention, peptides and proteins are always written with the **amino-terminal amino acid** (also called N-terminal amino acid, the one with the free $—NH_3^+$) on the left and the **carboxyl-terminal amino acid** (also called the C-terminal amino acid, the one with the free $—COO^-$ group) on the right. The individual amino acids joined in the chain are referred to as **residues.**

A peptide is named by citing the amino acid residues in order, starting at the N-terminal amino acid and ending with the C-terminal amino acid. All residue names except the C-terminal one have the *-yl* ending instead of *-ine,* as in alanylserine (abbreviated Ala-Ser) or serylalanine (Ser-Ala). The one-letter name would be AS.

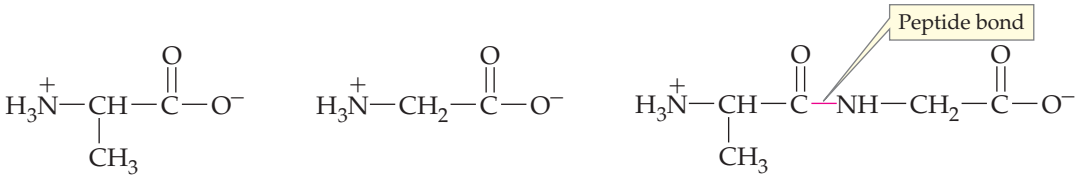
Worked Example 18.3 Drawing Dipeptides

Draw the structure of the dipeptide Ala-Gly.

ANALYSIS You need the names and structures of the two amino acids. Since alanine is named first, it is the N-terminal amino acid and glycine is the C-terminal amino acid. Ala-Gly must have a peptide bond between the $—COO^-$ on alanine and the $—NH_3^-$ on glycine.

SOLUTION

The structures of alanine and glycine in their zwitterionic form, and the structure of the Ala-Gly dipeptide are as follows:



Alanine (Ala, A) Glycine (Gly, G) Ala-Gly (AG)

HANDS-ON CHEMISTRY 18.1

Models of Amino Acids

Use either a molecular model kit or buy a package of small marshmallows and some toothpicks. Build alanine, glycine, and alanylglycine. Identify the chiral carbon atoms, the carboxyl groups, the amino groups, and the peptide bonds. What atoms were eliminated to form the peptide bond? What molecule do these atoms form?

PROBLEM 18.15

Valine is an amino acid with a nonpolar side chain, and serine is an amino acid with a polar side chain. Draw the two dipeptides that can be formed by these two amino acids. Identify the peptide bond.

PROBLEM 18.16

Tripeptides are composed of three amino acids linked by peptide bonds. Given a set of amino acids, you can make several different tripeptides.

(a) Use the three-letter shorthand notations to name all the tripeptides that can be made from serine, tyrosine, and glycine. Each amino acid will be used once in each tripeptide.

(b) Draw the complete structure of the tripeptides that have glycine as the N-terminal amino acid.

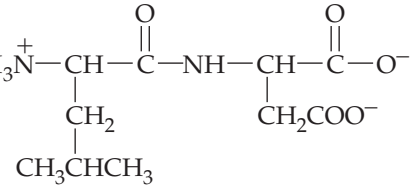
PROBLEM 18.17

Using three-letter abbreviations, show the six tripeptides that contain isoleucine, arginine, and valine.

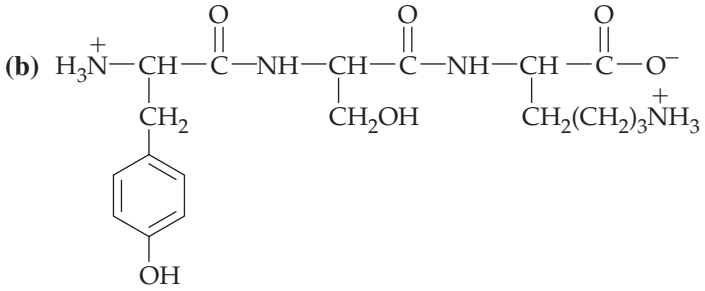
KEY CONCEPT PROBLEM 18.18

Identify the amino acids in the following dipeptide and tripeptide, and write the abbreviated forms of the peptide names. Copy the dipeptides, draw a box around the peptide bonds, and use an arrow to identify the α-carbon atoms. Draw a circle around the R groups, and indicate if the R groups are neutral, polar, acidic, or basic.

(a)



(b)



PROBLEM 18.19

There are eight amino acids in vasopressin. How many peptide bonds are in this small protein? You may find it helpful to look up the structure of this molecule.

CHEMISTRY IN ACTION

Proteins in the Diet

Proteins are a necessary part of the daily diet because our bodies do not store proteins like they do carbohydrates and fats. Children need large amounts of protein for proper growth, and adults need protein to replace what is lost each day by normal biochemical reactions. Furthermore, 9 of the 20 amino acids cannot be synthesized by adult humans and must be obtained in the diet. These are known as the *essential amino acids* (histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine).

▲ This traditional Mexican meal contains a complementary protein food combination: beans and rice.

The total recommended daily amount of protein for an adult, which is the *minimum* required for good health, is 0.8 g per kilogram of body mass. The average protein intake in the United States is about 110 g/day, well above what most of us need.

Not all foods are equally good sources of protein. A *complete* protein source provides each of the nine essential amino acids in sufficient amounts to meet our minimum daily needs. Most meat and dairy products meet this requirement, but many vegetable sources such as wheat and corn do not.

Vegetarians must be careful to adopt a diet that includes all of the essential amino acids, which means consuming a variety of foods. In some regions of the world, food combinations that automatically provide *complementary* proteins (proteins that together supply all of the essential amino acids) are traditional, such as rice and lentils in India, corn tortillas and beans in Mexico, and rice and black-eyed peas in the southern United States. Grains are low in lysine and threonine but contain methionine and tryptophan. In contrast, legumes (lentils, beans, and peas) supply lysine and threonine but are low in methionine and tryptophan. Thus, the two sources of protein complement each other.

When protein intake is inadequate, during starvation, a number of pathologic conditions including malignancies, malabsorption syndromes (such as celiac disease, an autoimmune disease caused by the protein gluten), and kidney disease occur. Health and nutrition professionals group all disorders caused by inadequate protein intake as *protein-energy malnutrition* (PEM). Children, because of their higher protein needs, suffer most from this kind of malnutrition. The problem is rampant where meat and milk are in short supply and where the dietary staples are vegetables or grains. An individual is malnourished to some degree if *any* of the essential amino acids is deficient in their diet. Protein deficiency alone is rare, however, and its symptoms are usually accompanied by those of vitamin deficiencies, infectious diseases, and starvation.

As a guide to a healthy diet, the U.S. Department of Agriculture has released a guide to healthy eating called MyPlate. As shown in the figure, half of the plate is filled with vegetables and fruits, while the other half is allotted for protein and carbohydrates. Additionally, a small side portion is allowed for dairy. The goal is to aid the public in understanding the role of each nutrient in the diet. Additional online resources exist to augment the visual information in MyPlate and can be found at http://www.choosemyplate.gov.

CIA Problem 18.3 Why is it more important to have a daily source of protein than a daily source of fat or carbohydrates?

CIA Problem 18.4 What is an incomplete protein?

CIA Problem 18.5 Two of the most complete (balanced) proteins (i.e., proteins that have the best ratio of the amino acids for humans) are cow's milk protein (casein) and egg-white protein. Explain why (not surprisingly) these are very balanced proteins for human growth and development.

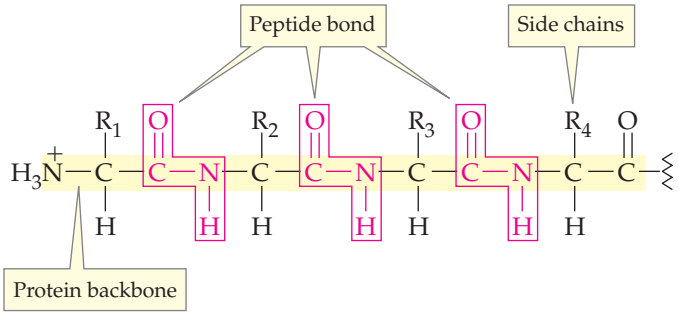
18.6 Protein Structure: An Overview and Primary Protein Structure (1°)

Learning Objectives:

- Define primary protein structure and explain how primary structures are represented.
- Describe the planar sections of the primary sequence, their influence on the shape of the protein backbone, and identify these sections given a drawing of the primary sequence.
- Give an example of how the change in primary sequence can change the function of a protein.

The **primary protein structure** (1°) of a protein is the sequence in which its amino acids are lined up and connected by peptide bonds. Along the *backbone* of the protein is a chain of alternating peptide bonds and α-carbon atoms. The amino acid side chains (R_1, R_2) are substituents along the backbone, where they are bonded to the α-carbon atoms. Note the positions of the hydrogen atoms bonded to the amino nitrogen atom, the R groups, and the carbonyl oxygen atom. These specific orientations contribute to secondary structure, which is discussed in the next section of this chapter.

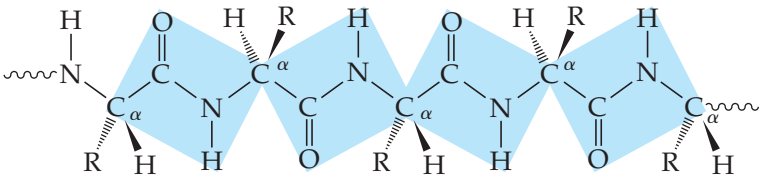
Primary protein structure The sequence in which amino acids are linked by peptide bonds in a protein.



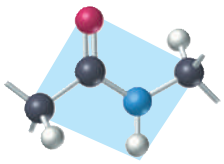
The carbon and nitrogen atoms along the backbone lie in a zigzag arrangement, with tetrahedral bonding around the α-carbon atoms. The free electron pair on each N-atom is shared with the adjacent C═O bond. This electron sharing is called delocalization, which you saw in the benzene molecule in Section 13.8. Sharing electrons from the N-atom makes the C—N bond similar to a double bond in that there is no rotation around it. The result is that the carbonyl group, the —NH group bonded to it, and the two adjacent α-carbons form a rigid, planar unit, as shown in the margin. The side-chain groups on the two α-carbons extend out to opposite sides of the plane. A long polymer chain forms a connected series of these planar peptide units, and the backbone NCC repeat is a zigzag form.

Review the properties of carbon—oxygen double bonds in Section 13.4.

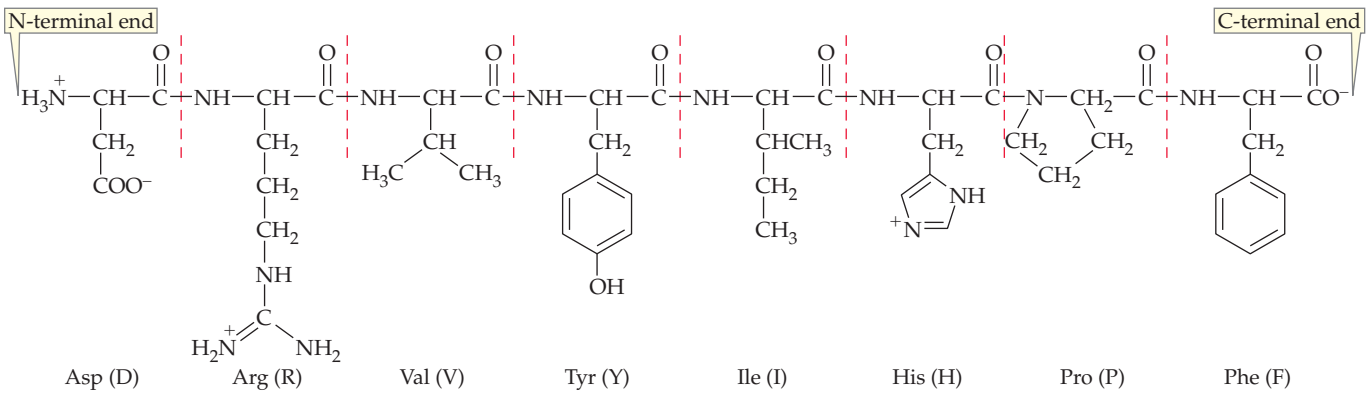
Planar units along a protein chain



One planar unit



The primary structure of a protein consists of the amino acids being lined up one by one to form peptide bonds in precisely the correct order for a specific protein. The number of arrangements for a set of amino acids can be calculated. If you have n amino acids, where n is an integer, then the number of arrangements are n factorial, represented as n! mathematically. For example, if $n = 3$, then $n! = 3!$ and $3! = 3 \times 2 \times 1 = 6$. Therefore, there are six ways in which three different amino acids can be joined, more than 40,000 ways in which eight amino acids can be joined, and more than 360,000 ways in which 10 amino acids can be joined. However, the equation predicts the total number of combinations only if each amino acid is represented once. Despite the rapid increase in possible combinations as the number of amino acid residues present increases, the function of a protein depends on the precise order of amino acids, and only the correct peptide can do the job. For example, human *angiotensin II* must have its eight amino acids arranged in exactly the correct order.



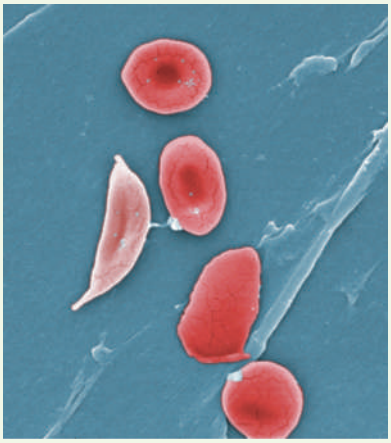
CHEMISTRY IN ACTION

What Is Sickle-Cell Anemia?

Sickle-cell anemia is a hereditary disease caused by a genetic difference that replaces one amino acid (glutamate, Glu) with another (valine, Val) in each of two polypeptide chains of the hemoglobin molecule resulting in a modified hemoglobin molecule. Affected red blood cells distort into a curved, sickle-like shape giving the disease its name. The change replaces a hydrophilic, carboxylic acid–containing side chain (Glu) in normal hemoglobin with a hydrophobic, neutral hydrocarbon side chain (Val) altering the shape of the hemoglobin molecule. (The effect of this change on the charge of hemoglobin is illustrated in the Chemistry in Action "Protein Analysis by Electrophoresis," p. 596.) Instead of hemoglobin retaining the normal soluble (globular) form both while carrying and after releasing oxygen, it forms fibrous chains after releasing oxygen due to the ability of modified hemoglobin molecules to associate in a "hooked" fashion as a result of the amino acid change in the primary structure. These associations of hemoglobin molecules in stiff, fibrous chains deform the red blood cells, causing the disease symptoms.

Sickled red blood cells are fragile and inflexible, blocking capillaries, causing inflammation and pain, and possibly restricting blood flow in a manner that damages major organs. Also, they have a shorter lifespan than normal red blood cells, causing afflicted individuals to become severely anemic.

Sickle-cell anemia arises by inheriting two defective copies of the hemoglobin gene, one from each parent. If a person has one functional gene and one defective gene, he or she is said to carry the sickle-cell trait but does not have sickle-cell anemia. The percentage of individuals carrying the genetic trait for sickle-cell anemia is highest among ethnic groups originating in tropical regions where malaria is prevalent. The ancestors of these individuals survived because malaria infections were not fatal. Malaria-causing parasites enter red blood cells and reproduce there. In a person with the sickle-cell trait, the cells respond by sickling and the parasites cannot multiply. As a result, the genetic trait for sickle-cell anemia is carried forward in the surviving population. Those who carry sickle-cell trait are generally healthy and lead normal lives; those who have sickle-cell anemia have multiple health problems.



▲ Four normal (convex) red blood cells and one sickled red blood cell. Because of their shape, sickled cells tend to clog blood vessels.

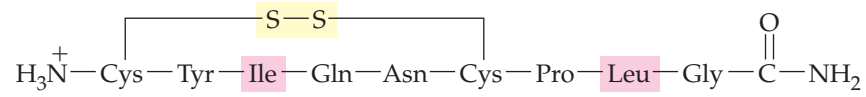
CIA Problem 18.6 Describe the symptoms of sickle-cell anemia.

CIA Problem 18.7 Explain the difference between sickle-cell anemia and sickle-cell trait.

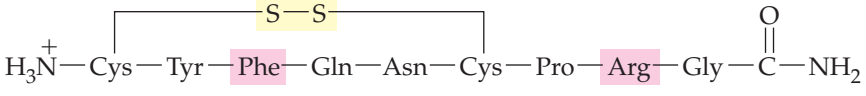
More than any other kind of biomolecule, proteins are in control of our biochemistry. Are you wondering how each of our thousands of proteins is produced with all their amino acids lined up in the correct order? The information necessary to do this is stored in deoxyribonucleic acid (DNA), and the remarkable machinery that does the job resides in the nuclei of our cells. Chapter 26 provides the details of how protein synthesis is accomplished. In order to synthesize proteins, our cells need a constant supply of amino acid building blocks from the diet because human cells can synthesize only some of the 20 amino acids used to make proteins. Read more about diet and protein requirements in the Chemistry in Action "Proteins in the Diet," page 600.

If its amino acids are not arranged properly, this hormone will not participate as it should in regulating blood pressure.

Sometimes one or two changes in the amino acids of a peptide change the function of the peptide. For example, two hormones secreted by the pituitary gland differ in only two amino acids, as seen in the following figure, and as a result have entirely different functions in the body. Oxytocin acts on uterine smooth muscle causing contractions during labor and on mammary gland tissue to encourage milk release. With two amino acid changes, the peptide becomes vasopressin and participates in blood pressure control by regulating both water reabsorption in the kidney and blood vessel constriction.



Oxytocin



Vasopressin

So crucial is the primary structure to function—no matter how big the protein—that the change of only one amino acid can sometimes drastically alter a protein's biological properties. Sickle-cell anemia is the result of a single amino acid substitution and is discussed further in the Chemistry in Action on page 602.

PROBLEM 18.20

(a) What atoms are present in a planar unit in a protein chain?
(b) How many amino acid units do these atoms come from? Why are these units planar?

PROBLEM 18.21

How many ways can four different amino acids be arranged in a peptide so that each peptide is unique?

PROBLEM 18.22

Why is the exact order of amino acids (primary structure) in a protein important?

18.7 Secondary Protein Structure (2°)

Learning Objectives:

- Identify the α-helix and β-sheet structures and give an example of a protein that contains primarily helix and one that contains primarily sheet secondary structure.
- Describe the specific hydrogen bonding responsible for secondary structures.
- Distinguish between fibrous and globular proteins.

Without interactions between atoms in amino acid side chains or along the backbone, protein chains would twist about randomly in body fluids like spaghetti strands in boiling water. The essential structure–function relationship for each protein depends on the polypeptide chain being held in its necessary shape by various interactions. As we look at the secondary, tertiary, and quaternary structures of proteins, it will be helpful to understand the kinds of interactions that determine the shapes of protein molecules for each level of structure.

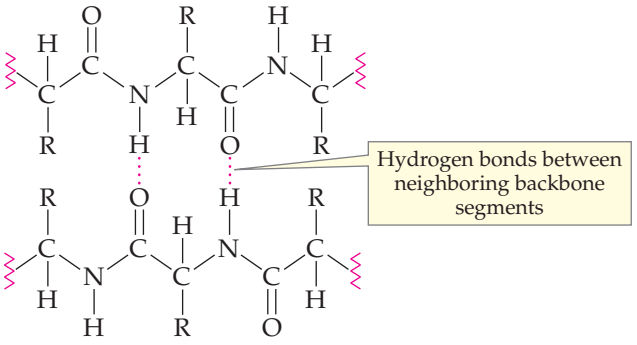
The spatial arrangement of the polypeptide backbones of proteins determines **secondary protein structure** (2°). The secondary structure includes two kinds of repeating patterns known as the *alpha-helix* (α-*helix*) and the *beta-sheet* (β-*sheet*). In both, hydrogen bonding between *backbone* atoms holds the polypeptide chain in place and connects the carbonyl oxygen atom of one peptide unit with the amide hydrogen atom of another peptide unit (—C═O · · · H—N—).

Secondary protein structure Regular and repeating structural patterns (e.g., α-helix and β-sheet) created by hydrogen bonding between backbone atoms in neighboring segments of protein chains.

Hydrogen Bonds along the Backbone

Hydrogen bonds form when a hydrogen atom bonded to a highly electronegative atom is attracted to another highly electronegative atom that has an unshared electron pair. The hydrogen atoms in the —NH— (amide) groups and the oxygen atoms in the —C═O (carbonyl) groups along protein backbones meet these conditions.

This type of hydrogen bonding creates both pleated sheet and helical secondary structures. Individual hydrogen bonds are weak forces, but the sum of many weak forces, as in the helical and sheet structures, is large enough to stabilize the structure.

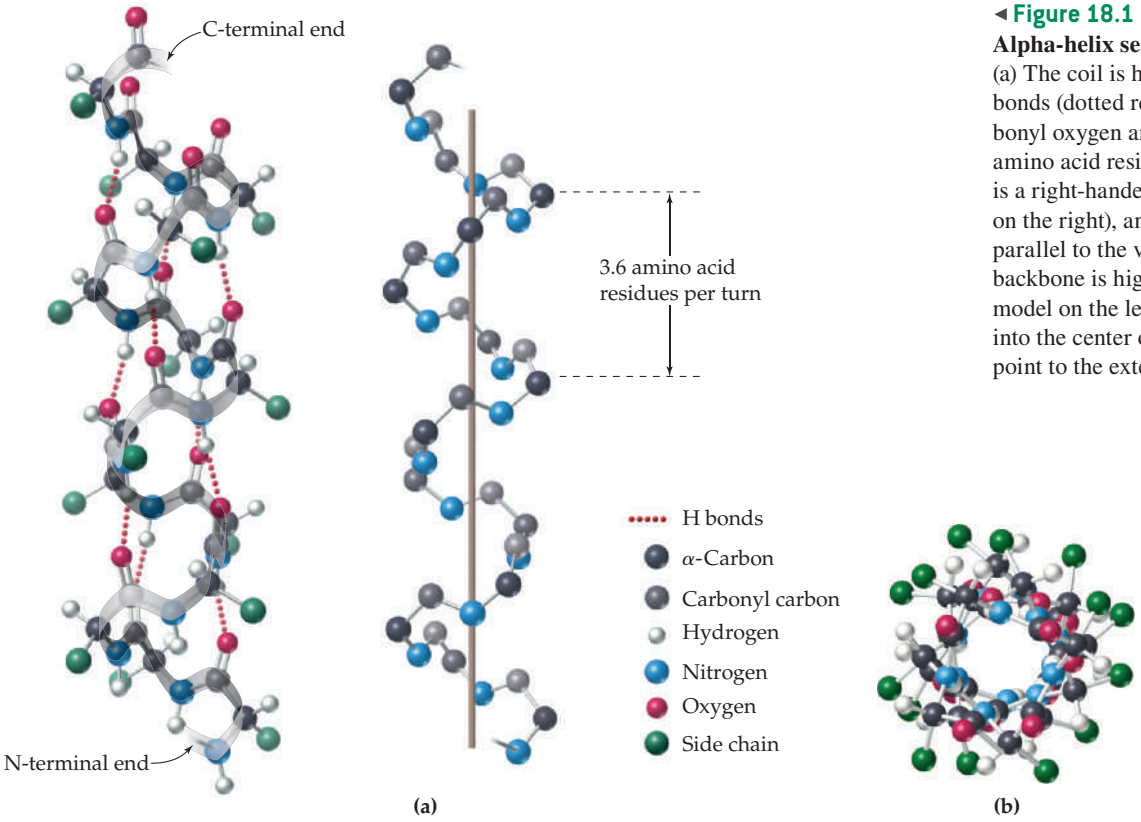


α-Helix

A single protein chain coiled in a spiral with a right-handed (clockwise) twist is known as an **alpha-helix (α-helix)** (Figure 18.1a). The helix, which resembles a coiled spring, is stabilized by hydrogen bonds between each backbone carbonyl oxygen atom and

Alpha-helix (α-helix) Secondary protein structure in which a protein chain forms a right-handed coil stabilized by hydrogen bonds between peptide groups along its backbone.

an amide hydrogen atom four amino acid residues farther along the backbone. The hydrogen bonds lie vertically along the helix, and the amino acid R groups extend to the outside of the coil. Although the strength of each individual hydrogen bond is small, the large number of bonds in the helix results in an extremely stable secondary structure. A view of the helix from the top (Figure 18.1b) clearly shows the side chains on the amino acids oriented to the exterior of the helix.



◂ Figure 18.1
Alpha-helix secondary structure. (a) The coil is held in place by hydrogen bonds (dotted red lines) between each carbonyl oxygen and the amide hydrogen four amino acid residues above it. The chain is a right-handed coil (shown separately on the right), and the hydrogen bonds lie parallel to the vertical axis. The protein backbone is highlighted by a ribbon in the model on the left. (b) Viewed from the top into the center of the helix, the side chains point to the exterior of the helix.

β-Sheet

Beta-sheet (β-sheet) Secondary protein structure in which adjacent protein chains either in the same molecule or in different molecules are held together by hydrogen bonds along the backbones, forming a flat sheet-like structure.

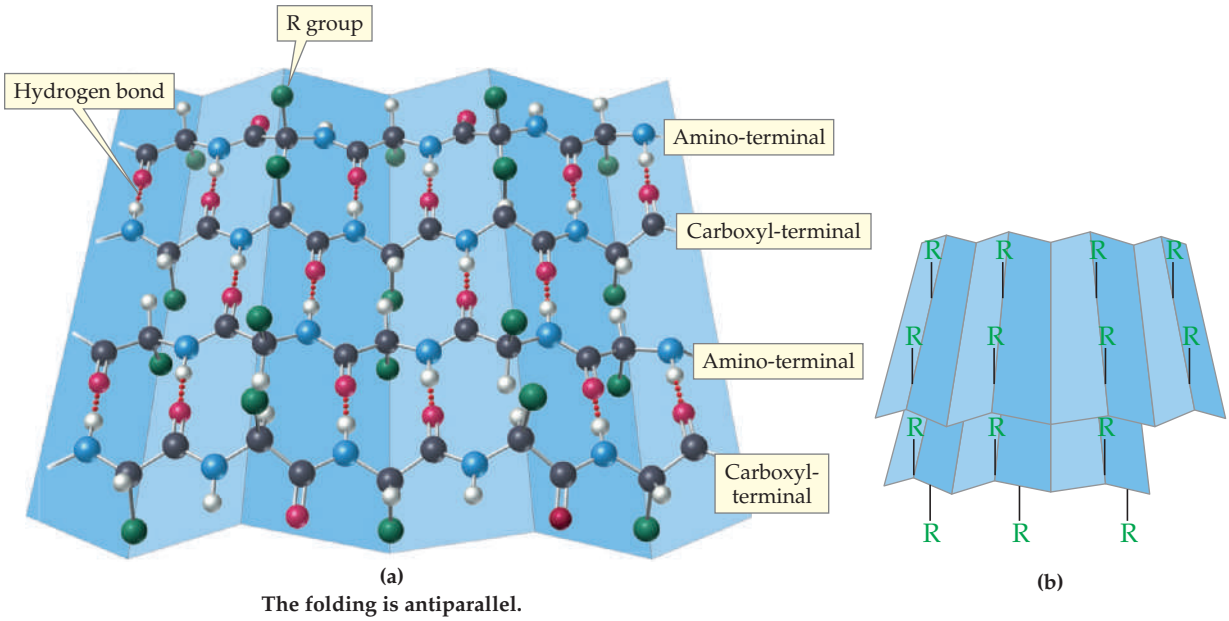
In the **beta-sheet (β-sheet)** structure, the polypeptide chains are held in place by hydrogen bonds between pairs of peptide units along neighboring backbone segments. The protein chains, which are extended to their full length, bend at each α-carbon so that the sheet has a pleated contour, with the R groups extending above and below the sheet (Figure 18.2).

PROBLEM 18.23

Examine the α-helix in Figure 18.1 and determine how many backbone C and N atoms are included in the loop between an amide hydrogen atom and the carbonyl oxygen to which it is hydrogen bonded.

PROBLEM 18.24

Consult the β-sheet in Figure 18.2 and (a) name the bonding responsible for the sheet formation and (b) identify the specific atoms responsible for this bonding.



▲ **Figure 18.2**
Beta-sheet secondary structure.
(a) The hydrogen bonds between neighboring protein chains. The protein chains usually lie side-by-side so that alternating chains run from the N-terminal end to the C-terminal end and from the C-terminal end to the N-terminal end (known as the *antiparallel* arrangement). (b) A pair of stacked pleated sheets illustrating how the R groups point above and below the sheets.

Secondary Structure in Fibrous and Globular Proteins

Proteins are classified in several ways, one of which is to identify them as either *fibrous proteins* or *globular proteins*. In an example of the integration of molecular structure and function that is central to biochemistry, fibrous and globular proteins each have functions made possible by their distinctive structures.

Secondary structure is primarily responsible for the function of **fibrous proteins**—tough, insoluble proteins in which the chains form long fibers. Wool, hair, and fingernails are made of fibrous proteins known as α-keratins, which are composed almost completely of α-helices. In α-keratins, pairs of α-helices are twisted together into small fibrils that are in turn twisted into larger and larger bundles. The hardness, flexibility, and stretchiness of the material vary with the number of disulfide bonds present. In fingernails, for example, large numbers of disulfide bonds hold the bundles in place.

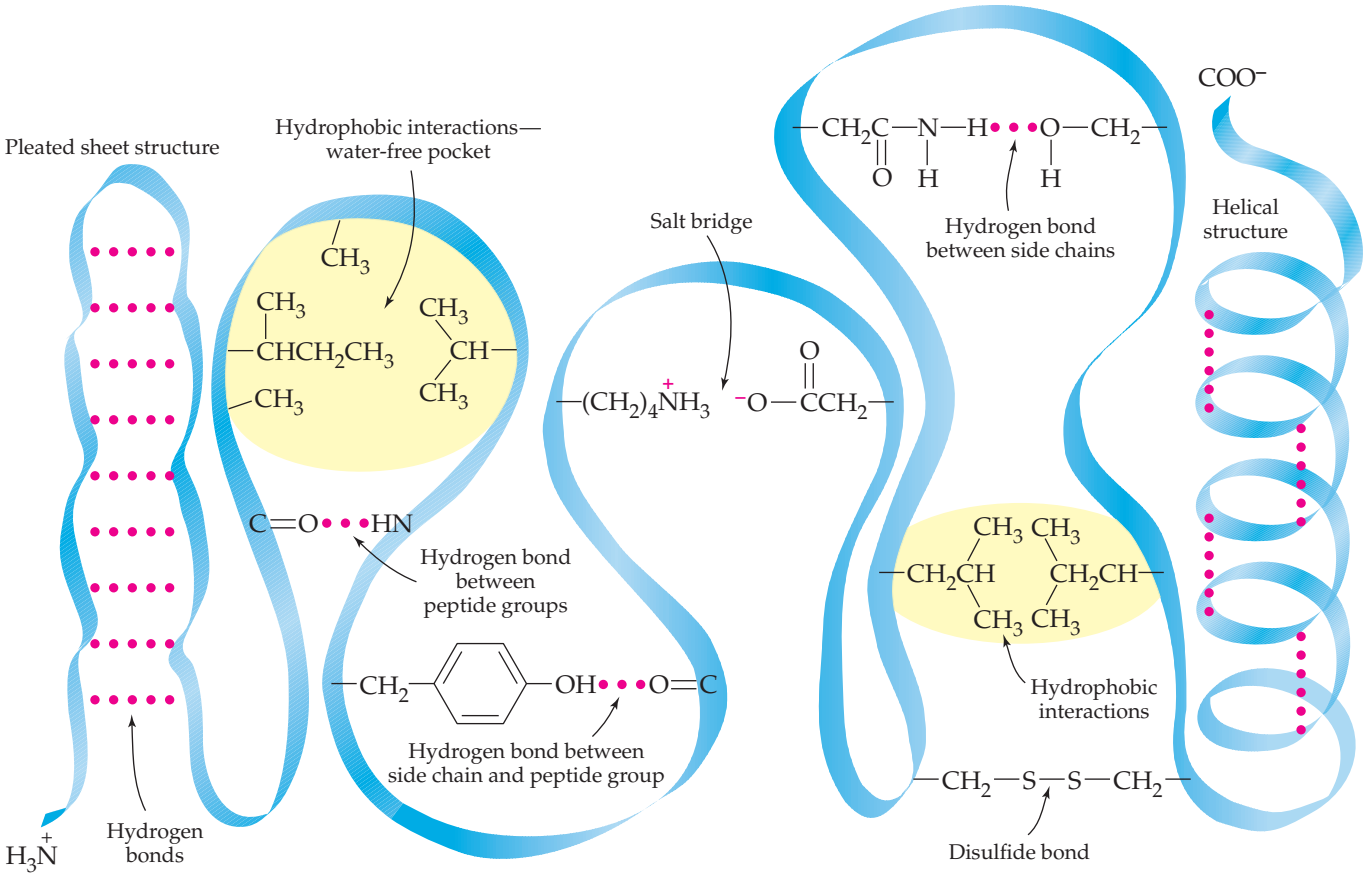
Natural silk and spider webs are made of *fibroin,* another fibrous protein almost entirely composed of stacks of β-sheet. For such close stacking, the R groups must be relatively small (see Figure 18.6b). Fibroin contains regions of alternating glycine (—H on the α carbon) and alanine (—CH_3 on the α carbon). The sheets stack so that sides with the smaller glycine hydrogen atoms face each other and sides with the larger alanine methyl groups face each other.

Unlike fibrous proteins, **globular proteins** are water-soluble proteins whose chains are folded into compact, globe-like shapes. Their structures, which vary widely with their functions, are not repeating structures like those of fibrous proteins. Where the protein chain folds back on itself, sections of α-helix and β-sheet are usually present, as illustrated in Figure 18.3. The presence of hydrophilic amino acid side chains on the outer surfaces of globular proteins accounts for their water solubility, allowing them to be soluble in both intercellular and extracellular body fluids in order to perform their disparate functions. Furthermore, many globular proteins are enzymes that are dissolved in the intercellular fluids inside cells. The overall shapes

Fibrous protein A tough, insoluble protein whose protein chains form fibers or sheets.

Globular protein A water-soluble protein whose chain is folded in a compact shape with hydrophilic groups on the outside.

▲ A spider web is made from fibrous protein. The proteins found in eggs, milk, and cheese are examples of globular proteins.



▲ **Figure 18.3**
Interactions that determine protein shape.
The regular pleated sheet *(left)* and helical structure *(right)* are created by hydrogen bonding between neighboring backbone atoms; the other interactions involve side-chain groups that can be nearby or quite far apart in the protein chain.

of globular proteins represent another level of structure, tertiary structure, discussed in the next section.

Table 18.4 compares the occurrences and functions of some fibrous and globular proteins.

Table 18.4 Some Common Fibrous and Globular Proteins

Name	Occurrence and Function
Fibrous proteins (insoluble)	
Keratins	Found in skin, wool, feathers, hooves, silk, and fingernails
Collagens	Found in animal hide (skin), tendons, bone, eye cornea, and other connective tissue
Elastins	Found in blood vessels and ligaments, where ability of the tissue to stretch is important
Myosins	Found in muscle tissue
Fibrin	Found in blood clots
Globular proteins (soluble)	
Insulin	Regulatory hormone for controlling glucose metabolism
Ribonuclease	Enzyme that catalyzes ribonucleic acid (RNA) hydrolysis
Immunoglobulins	Proteins involved in immune response
Hemoglobin	Protein involved in oxygen transport
Albumins	Proteins that perform many transport functions in blood; protein in egg white

PROBLEM 18.25

Complete the following two sentences with either globular or fibrous:

(a) Proteins with secondary structure composed primarily of alpha-helix are _____ proteins.

(b) Proteins with secondary structure composed primarily of beta-sheets are _____ proteins.

KEY CONCEPT PROBLEM 18.26

Why does your skin not dissolve when you go swimming or are caught in the rain?

18.8 Tertiary Protein Structure (3°)

Learning Objectives:

- Identify the four specific forces responsible for tertiary structure.
- Identify what forces or bonds exist between amino acid side chains.
- Distinguish between simple and conjugated protein.

The overall three-dimensional shape that results from the folding of a single protein chain is the protein's **tertiary protein structure** (3°). In contrast to secondary structure, which depends mainly on attraction between backbone amide peptide bonds (C═O to HN), resulting in hydrogen bonding, tertiary structure depends mainly on interactions of amino acid side chains (R groups) that are far apart along the entire backbone.

Tertiary protein structure The way in which an entire protein chain is coiled and folded into its specific three-dimensional shape.

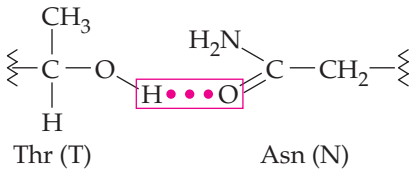
Although the bends and twists of the protein chain within a globular protein may appear irregular and the three-dimensional structure may appear random, this is not the case. Each protein molecule folds in a distinctive manner that is determined by its primary and secondary structure, with the forces described next holding the tertiary structure in place. The result is maximum stability for the native protein configuration. A **native protein** has the shape that allows it to function in living systems.

Native protein A protein with the shape (primary, secondary, tertiary, and quaternary structure) in which it exists naturally in living organisms.

Hydrogen Bonds of R Groups with Each Other or with Backbone Atoms

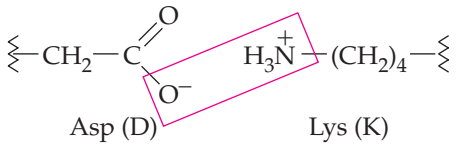
Some amino acid side chains contain atoms that can form hydrogen bonds. Side-chain hydrogen bonds can connect different parts of a protein molecule, whether they are in close proximity or far apart along the polypeptide chain. In the protein in Figure 18.3, hydrogen bonds between side chains have created folds in two places. Often, hydrogen-bonding side chains are present on the surface of a folded protein, where they can form hydrogen bonds with surrounding water molecules. Recall that hydrogen bonds are noncovalent bonds.

An example of R group hydrogen bonding between the hydrogen atom of a polar group such as hydroxyl and the oxygen or nitrogen atom of another polar group in a different amino acid is shown in the margin.



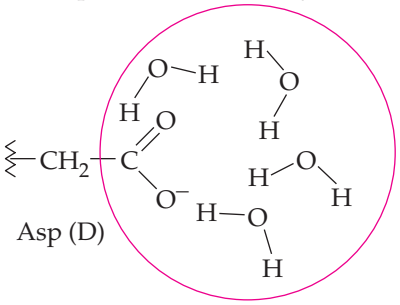
Ionic Attractions between R Groups (Salt Bridges)

Where there are ionized acidic and basic side chains, the attraction between their positive and negative charges creates *salt bridges*. A salt bridge is a noncovalent bond; it is an ionic bond (an attraction). For example, a basic lysine side chain and an acidic aspartate side chain have formed a salt bridge in the middle of the protein shown in Figure 18.3.



Hydrophilic Interactions between R Groups and Water

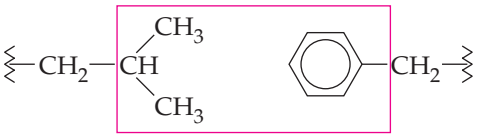
Amino acids with charged R groups will interact with water through hydrogen bonding. The figure in the margin shows the interaction between aspartic acid and water. These interactions are attractions not covalent bonds.



Review dispersion forces in Section 8.2 and Van der Waals forces in Section 9.2.

Hydrophobic Interactions between R Groups

Hydrocarbon side chains are attracted to each other by the dispersion forces (primarily Van der Waals forces) caused by a momentary uneven distribution of electrons. Although this attraction is noncovalent in nature, the result is that these groups cluster together in the same way that oil molecules cluster on the surface of water, so that these interactions are often referred to as *hydrophobic*. By clustering in this manner, the hydrophobic groups shown in Figure 18.3 and more explicitly in the margin create a water-free pocket in the protein chain. Although the individual attractions are weak, their large number in proteins plays a major role in stabilizing the folded structures.

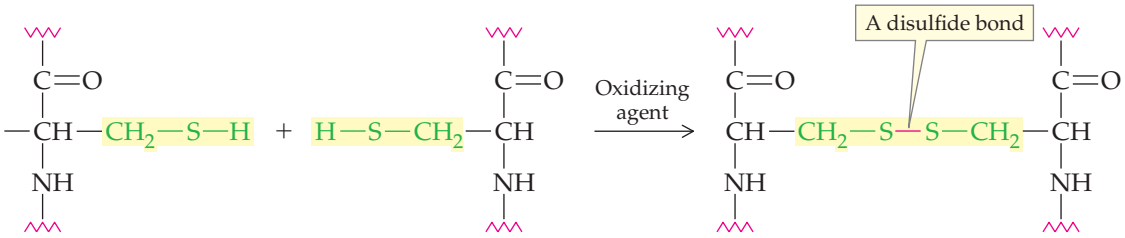


Phe (F) Leu (L)

Covalent Sulfur–Sulfur Bonds: The Disulfide Bridge

Disulfide bond formation was explored in Section 14.8.

In addition to the noncovalent interactions described above, one type of covalent bond plays a role in determining protein shape. Cysteine amino acid residues have side chains containing thiol functional groups (—SH) that can react to form sulfur–sulfur bonds (—S—S—).

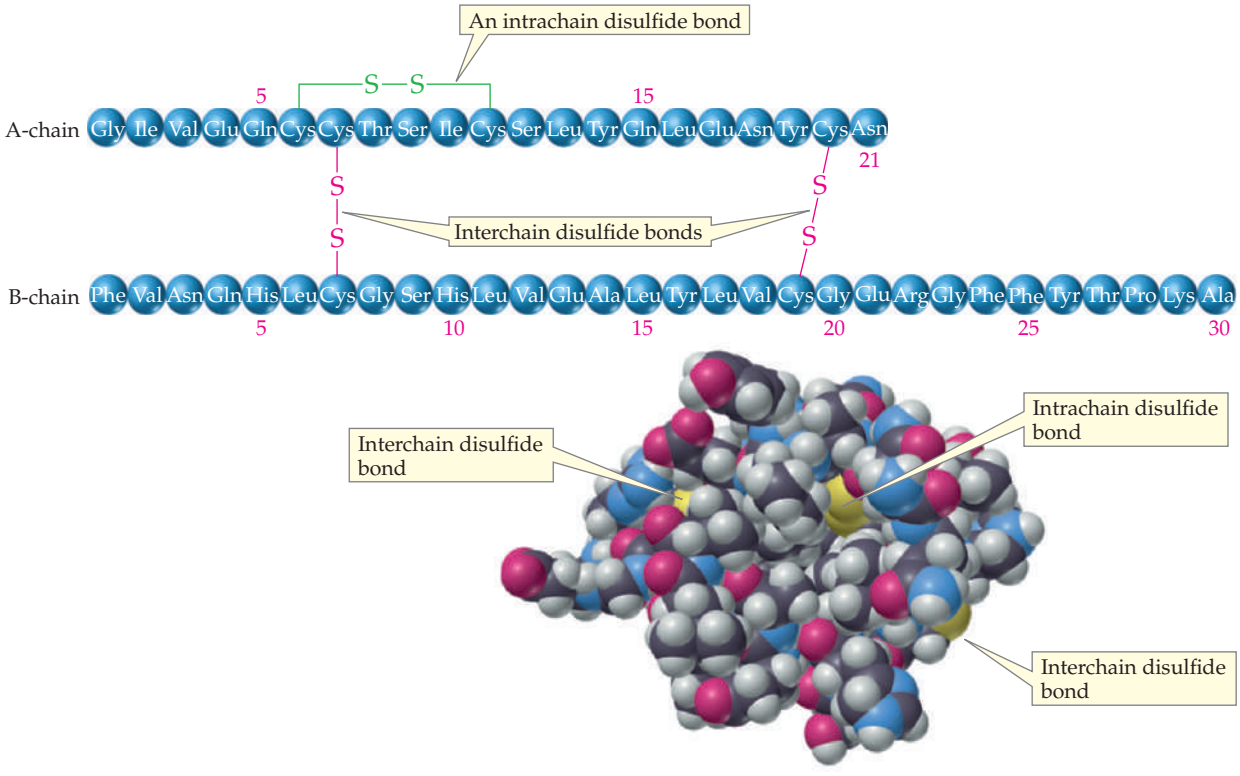


Cysteine (Cys, C) Cysteine (Cys, C)

Disulfide bond A S—S bond formed between two cysteine side chains; can join two separate peptide chains together or cause a loop in a single peptide chain.

If the two cysteine residues are in different protein chains, the two separate chains become covalently linked together by the disulfide bond. If the two cysteine residues are in the same chain, a loop is formed in the chain. Insulin provides a good example. It consists of two polypeptide chains connected by **disulfide bonds** in two different places connecting the A and B chains with two interchain bonds. Additionally, the A chain has an intrachain loop caused by a third disulfide bond.

Structure of insulin

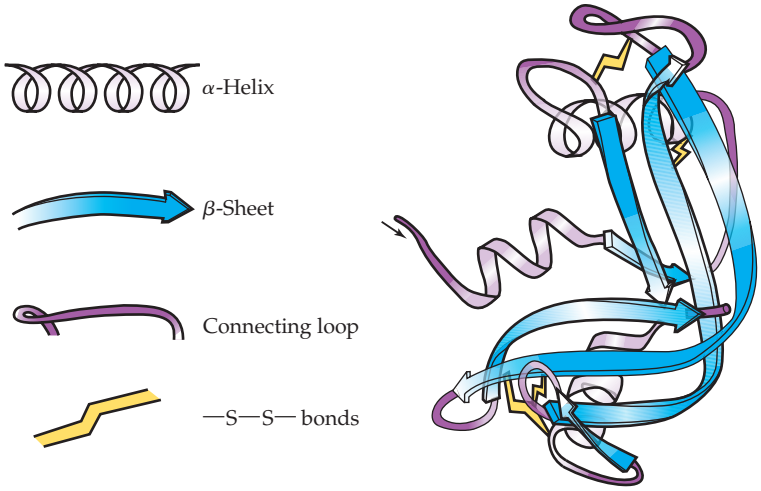


Insulin is representative of a class of small polypeptides (proteins) that function as hormones, which are released when a chemical message must be carried from one place to another (angiotensin II on p. 601 is another example of a polypeptide hormone). The structure and function of insulin are of intense interest because of its role in glucose metabolism and the need for supplementary insulin by individuals with diabetes. Insulin signals cells to take in glucose when blood glucose levels rise; many diabetics need supplemental insulin because their bodies either do not produce insulin or have lost the ability to respond to their own insulin. Diabetes and the role of insulin in glucose metabolism are discussed further in Section 22.7. Undoubtedly because of this need, studies of insulin have led the way in developing our ability to determine the structure of a biomolecule and prepare it synthetically.

We will learn more about polypeptide hormones in Chapter 28 and diabetes in Section 22.7.

In a historically important accomplishment, the amino acid sequence of insulin was determined in 1951—it was the *first* protein for which this was done. It took 15 years before the cross-linking and complete molecular structure were determined and a successful laboratory synthesis was carried out. With the advent of biotechnology in the 1980s, once again insulin was first. Until then, individuals with diabetes relied on insulin extracted from the pancreases of cows, and because of differences in three amino acids between bovine and human insulin, allergic reactions occasionally resulted. In 1982, human insulin became the first commercial product of genetic engineering to be licensed by the U.S. government for clinical use.

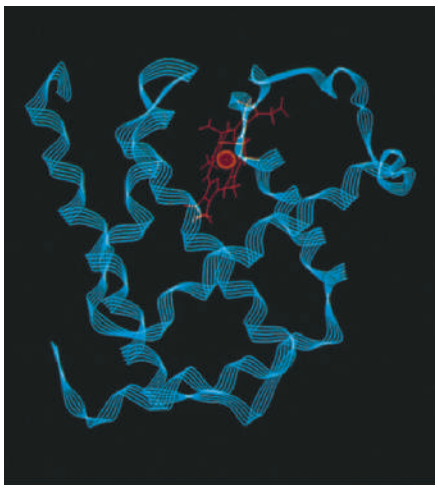
The four noncovalent interactions and disulfide covalent bonds described above govern tertiary structure. The enzyme *ribonuclease,* shown here as an example in its ribbon structure, is drawn in a style that shows the combination of α-helix and β-sheet regions, the loops connecting them, and four disulfide bonds.



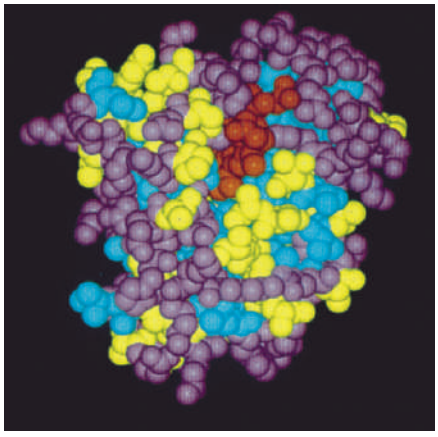
Ribonuclease

The structure of ribonuclease is representative of the tertiary structure of globular, water-soluble proteins. The hydrophobic, nonpolar side chains congregate in a hydrocarbon-like interior, and the hydrophilic side chains, which provide water solubility, congregate on the outside. Ribonuclease is classified as a **simple protein** because it is composed only of amino acid residues (124 of them). The drawing shows ribonuclease in a style that clearly represents the combination of primary and secondary structures in the overall tertiary structure of a globular protein. The symbols in the left side of the figure above are standard representations for these components of protein structure.

Simple protein A protein composed of only amino acid residues.



(a)



(b)

▲ **Figure 18.4**
Myoglobin, drawn in two styles.
In each panel, the red structure embedded in the protein is a molecule of heme, to which O_2 binds. (a) A protein *ribbon model* shows the helical portions as a ribbon. This type of representation clearly shows protein secondary structure. (b) A computer-generated space-filling model of myoglobin shows the hydrophobic residues in blue and the hydrophilic residues in purple. This type of representation better conveys the overall shape and dimensions of the protein.

Conjugated protein A protein that incorporates one or more non–amino acid units in its structure.

Myoglobin is an example of a small globular protein, consisting of a single amino acid chain. A relative of hemoglobin, myoglobin stores oxygen in skeletal muscles for use when there is an immediate need for energy. Structurally, the 153 amino acid residues of myoglobin are arranged in eight α-helical segments connected by short segments looped so that hydrophilic amino acid residues are on the exterior of the compact, spherical tertiary structure. Like many proteins, myoglobin is not a simple protein but is a **conjugated protein**—a protein that is aided in its function by an associated non–amino acid unit. The oxygen-carrying portion of myoglobin has a heme group embedded within the polypeptide chain. In Figure 18.4, the myoglobin molecule is shown in two different ways; both types of molecular representation are routinely used to illustrate the shapes of protein molecules. Some examples of other kinds of conjugated proteins are listed in Table 18.5.

Table 18.5 Some Examples of Conjugated Proteins

Class of Protein	Nonprotein Part	Examples
Glycoproteins	Carbohydrates	Glycoproteins in cell membranes (Section 20.7)
Lipoproteins	Lipids	High- and low-density lipoproteins that transport cholesterol and other lipids through the body (Section 24.2)
Metalloproteins	Metal ions	The enzyme cytochrome oxidase, necessary for biological energy production, and many other enzymes
Phosphoproteins	Phosphate groups	Milk casein, which provides essential nutrients to infants
Hemoproteins	Heme	Hemoglobin (transports oxygen) and myoglobin (stores oxygen)
Nucleoproteins	RNA	Found in cell ribosomes, where they take part in protein synthesis

How do proteins "know" the correct three-dimensional structure to fold up into? As a protein is synthesized, adding amino acids one at a time, from the N-terminal end to the C-terminal end of the protein, it is anchored to a structure called a ribosome (see Chapter 26). The lengthening protein chain folds in a manner that allows hydrophilic residues to interact with the aqueous cellular environment and sequesters the hydrophobic residues in the interior of the final structure. This folding is encouraged by amino acid side chains that interact either with each other or with the aqueous environment, resulting in the lowest energy state possible for the folded protein, stabilizing the structure. Many proteins spontaneously fold into the native structure during synthesis. However, some do not. Proteins referred to as "chaperones" guide their folding, especially if the final structure of the protein being synthesized is unstable. The folding step for each protein must result in a functional protein. Misfolded proteins typically are nonfunctional and often toxic.

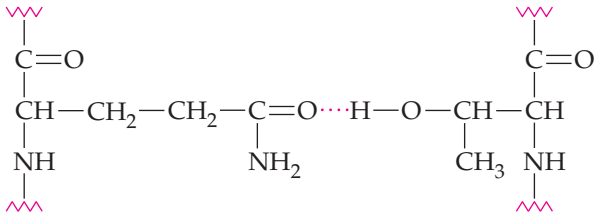
Worked Example 18.4 Drawing Side-Chain Interactions

What type of noncovalent interaction occurs between the glutamine and threonine side chains? Draw the structures of these amino acids to show the interaction.

ANALYSIS The side chains of glutamine and threonine contain an amide group and a hydroxyl group, respectively. Since the hydroxyl group does not ionize, this pair will not form salt bridges. They are polar and therefore not hydrophobic. This pair of amino acids can form a hydrogen bond between the oxygen of the amide carbonyl group and the hydrogen of the hydroxyl group.

SOLUTION

The noncovalent, hydrogen bond interaction between threonine and glutamine is as follows:



Worked Example 18.5 Identifying Groups Involved in Hydrogen Bonding

Hydrogen bonds are important in stabilizing both the secondary and tertiary structures of proteins. How do the groups that form hydrogen bonds in the secondary and tertiary structures differ?

ANALYSIS Examine the hydrogen bonding in secondary structure. See Figures 18.1 and 18.2. Note the regularity along the backbone of the hydrogen bonding. Only hydrogen atoms on backbone nitrogen atoms and oxygen atoms on nearby carbonyl carbon atoms are involved in this bonding. In tertiary structure hydrogen bonding occurs primarily between polar R groups and these groups are not necessarily nearby.

SOLUTION

Secondary structure is the product of regular, repetitive bonding between hydrogen atoms on backbone nitrogen atoms and oxygen atoms on nearby carbonyl carbon atoms. The regular, repetitive bonding leads to alpha-helix and beta-pleated sheet structures.

Tertiary structure depends on several different types of bonding and not totally on hydrogen bonding. The hydrogen bonding is primarily between R group atoms and is spread irregularly throughout the molecule.

PROBLEM 18.27

Which of the following pairs of amino acids can form hydrogen bonds between their side-chain groups? Draw the pairs that can hydrogen bond through their side chains and indicate the hydrogen bonds.

(a) Phe, Thr **(b)** Asn, Ser **(c)** Thr, Tyr **(d)** Gly, Trp

KEY CONCEPT PROBLEM 18.28

Look at Table 18.3 and identify the type of noncovalent interaction expected between the side chains of the following pairs of amino acids:

(a) Glutamine and serine
(b) Isoleucine and proline
(c) Aspartate and lysine
(d) Alanine and phenylalanine

PROBLEM 18.29

In Figure 18.3, identify the amino acids that have formed (a) hydrogen bonds from their side chains and (b) hydrophobic side-chain interactions.

PROBLEM 18.30

For each of the conjugated proteins described, identify to which class of conjugated protein it belongs.

(a) Cholesterol is attached to this protein in order to move through the blood system.
(b) Ionized zinc is attached to this protein so the protein can function.
(c) Phosphate groups are attached to this protein.
(d) Complex sugars are attached to this membrane protein.
(e) A large multi-ring, conjugated hydrocarbon containing a ferric ion enables this protein to function.
(f) RNA attached to this protein facilitates protein synthesis.

18.9 Quaternary Protein Structure (4°)

Learning Objectives:

- Define quaternary structure.
- Identify the forces responsible for quaternary structure.
- Give examples of proteins with quaternary structure.

Quaternary protein structure The way in which two or more protein chains aggregate to form large, ordered structures.

The fourth and final level of protein structure, and the most complex, is **quaternary protein structure** (4°)—the way in which two or more polypeptide subunits associate to form a single three-dimensional protein unit. The individual polypeptides are held together by the same noncovalent forces responsible for tertiary structure. In some cases, there are also covalent bonds (disulfide bonds) and the protein may incorporate a non–amino acid portion. *Hemoglobin* and *collagen* are both well-understood examples of proteins with quaternary structure essential to their function.

Cellular protein A protein found inside cells.

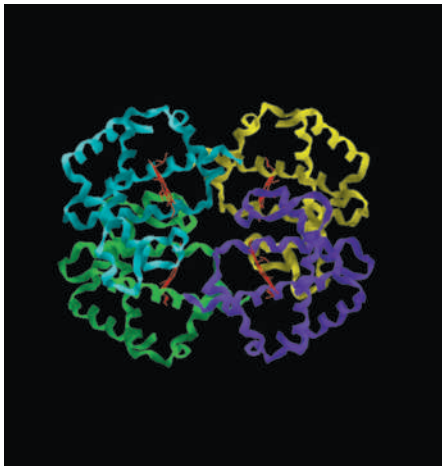
Mobile protein A protein found in body fluids such as blood.

We will learn more about oxygen transport in Chapter 29.

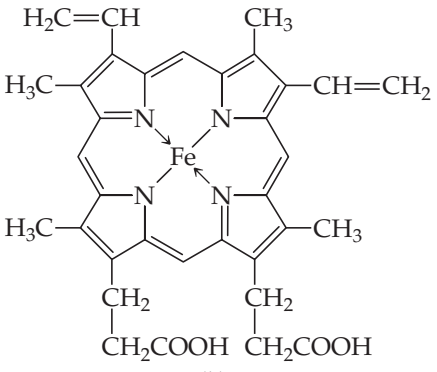
Hemoglobin

Hemoglobin (Figure 18.5a) is a conjugated quaternary protein composed of four polypeptide chains (two each of two different polypeptides called the α-chain and the β-chain) held together primarily by the interaction of hydrophobic groups and four heme groups, one per chain. Each polypeptide is similar in composition and tertiary structure to myoglobin (Figure 18.4). The α-chains have 141 amino acids, and the β-chains have 146 amino acids.

The heme unit (Figure 18.5) contains an iron atom that is essential to its function. One heme unit is found in each of the four polypeptides that make up a hemoglobin molecule. The association of the four polypeptide chains with their heme units is the quaternary structure of hemoglobin, the oxygen carrier in red blood cells. In the lungs, O_2 binds to Fe^{2+}, so that each hemoglobin molecule can carry a maximum of four O_2 molecules. In tissues in need of oxygen, O_2 is released, and CO_2 (the product of respiration) is picked up and carried back to the lungs. Although hemoglobin is a soluble protein, it is a **cellular protein** normally found only inside cells and carried throughout the body inside red blood cells. Serum albumin, also a soluble protein, is referred to as a **mobile protein** because it is dissolved in an extracellular (outside the cell) fluid and acts as a carrier for proteins and fatty acids.



(a)



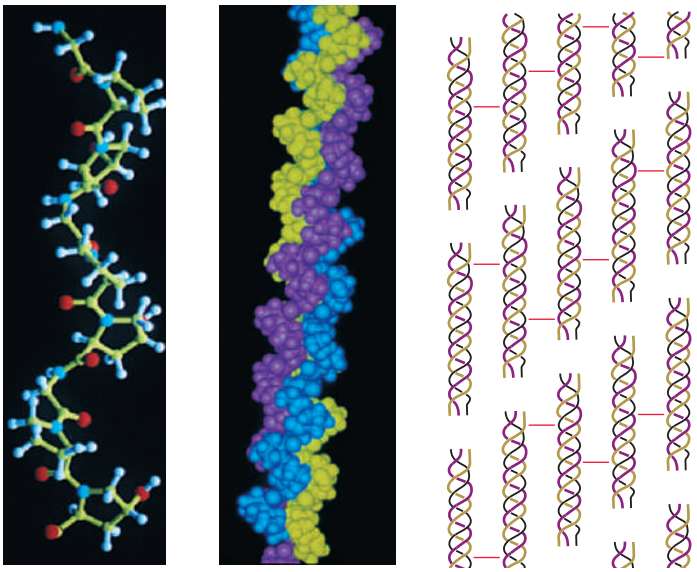
(b)

▲ **Figure 18.5**
Heme and hemoglobin, a protein with quaternary structure.
(a) The polypeptides are shown in purple, green, blue, and yellow, with their heme units in red. Each polypeptide resembles myoglobin in structure. (b) A heme unit is present in each of the four polypeptides in hemoglobin.

Collagen

Collagen is the most abundant of all proteins in mammals, making up 30% or more of the total. A fibrous protein, collagen is the major constituent of skin, tendons, bones, blood vessels, and other connective tissues. The basic structural unit of collagen *(tropocollagen)* consists of three intertwined chains of about 1000 amino acids each. Each chain is loosely coiled in a left-handed (counter-clockwise) direction (Figure 18.6a). Three of these coiled chains wrap around one another (in a clockwise direction) to form a stiff, rod-like tropocollagen triple helix (Figure 18.6b) in which the chains are held together by hydrogen bonds.

There are several different types of collagen found throughout the body that vary slightly in their primary sequence of amino acids. However, all the various kinds of collagen have in common a glycine residue at every third position. Only glycine residues (with —H as the side chain on the α-carbon) can fit in the center of the tightly coiled tropocollagen triple helix. The larger side chains face the exterior of the helix. After the collagen protein is synthesized, hydroxyl (—OH) groups are added to some of its proline residues in a reaction that requires vitamin C. This hydroxylation of proline residues is important for strong collagen fiber formation. Herein lies the explanation for the symptoms of scurvy, the disease that results from vitamin C deficiency. When vitamin C is in short supply, collagen is deficient in hydroxylated proline residues and, as a result, forms fibers poorly. This results in



◀ **Figure 18.6**
Collagen.
(a) A single collagen helix (carbon, green; hydrogen, light blue; nitrogen, dark blue; oxygen, red). (b) The triple helix of tropocollagen. (c) The quaternary structure of a cross-linked collagen, showing the assemblage of tropocollagen molecules.

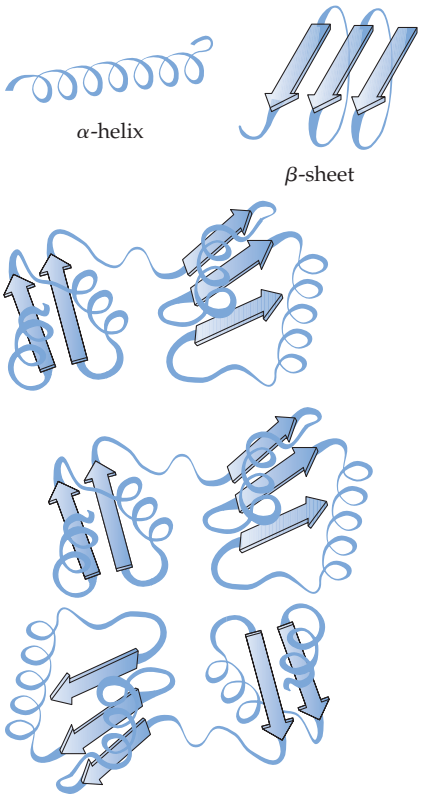
the skin lesions and fragile blood vessels that accompany scurvy, an uncommon disease in modern times.

The tropocollagen triple helices are assembled into collagen in a quaternary structure formed by a great many strands overlapping lengthwise (Figure 18.6). Depending on the exact purpose collagen serves in the body, further structural modifications occur. In connective tissue like tendons, covalent bonds between strands give collagen fibers a rigid, cross-linked structure. In teeth and bones, calcium hydroxyapatite $[Ca_5(PO_4)_3OH]$ deposits in the gaps between chains to further harden the overall assembly.

For more on the role of vitamin C in collagen synthesis, see Section 19.9.

Protein Structure Summary

- **Primary structure**—the sequence of amino acids connected by peptide bonds in the polypeptide chain; for example, Asp-Arg-Val-Tyr.
- **Secondary structure**—the arrangement in space of the polypeptide chain, which includes the regular patterns of the α-helix and the β-sheet formations (held together by hydrogen bonds between backbone carbonyl oxygen atoms and backbone amino hydrogen atoms in amino acid residues) plus the loops that connect these segments.
- **Tertiary structure**—the folding of a single protein chain into a specific three-dimensional shape held together by noncovalent interactions (salt bridges, hydrogen bonding, hydrophobic interactions) primarily between amino acid side chains, in some cases, by disulfide bonds between side-chain thiol groups.
- **Quaternary structure**—two or more protein chains assembled in a larger three-dimensional structure held together by noncovalent interactions.



Classes of Proteins Summary

- *Fibrous proteins* are tough, insoluble, and composed of fibers and sheets.
- *Globular proteins* are water-soluble and have chains folded into compact shapes.
- *Simple proteins* contain only amino acid residues.
- *Conjugated proteins* include one or more non–amino acid units.
- *Native proteins* are functional, nondenatured proteins.
- *Mobile proteins* are soluble and move through the body in extracellular fluid such as blood. An example is serum albumin.
- *Cellular proteins* are soluble and remain inside a cell. An example is hemoglobin.

Note that a protein may belong to more than one class listed above. For example, functioning hemoglobin is a native protein, which is globular, conjugated, and cellular.

Worked Example 18.6 Identifying Levels of Protein Structure

Identify the following statements as descriptive of the secondary, tertiary, or quaternary structure of a protein. What types of interactions stabilize each type of structure?

(a) The polypeptide chain has a number of bends and twists, resulting in a compact structure.

(b) The polypeptide backbone forms a right-handed coil.

(c) The four polypeptide chains are arranged in a spherical shape.

ANALYSIS Consider what you know about secondary, tertiary, and quaternary structure. Quaternary structure occurs when more than one polypeptide chain is present. A right-hand coil is characteristic of one type of secondary structure. Many bends and twists as well as a compact structure are characteristic of some kinds of tertiary structure.

SOLUTION

(a) Tertiary structure—stabilized by hydrophilic and hydrophobic interactions, salt bridges, hydrogen bonds, and disulfide bonds

(b) Secondary structure—stabilized by hydrogen bonds between backbone carbonyl oxygen atoms and backbone amino hydrogen atoms

(c) Quaternary structure—the same interactions that stabilize tertiary structure

PROBLEM 18.31

Both α-keratin and tropocollagen have helical secondary structure. How do these molecules differ in (a) amino acid composition and (b) three-dimensional structure?

18.10 Chemical Properties of Proteins

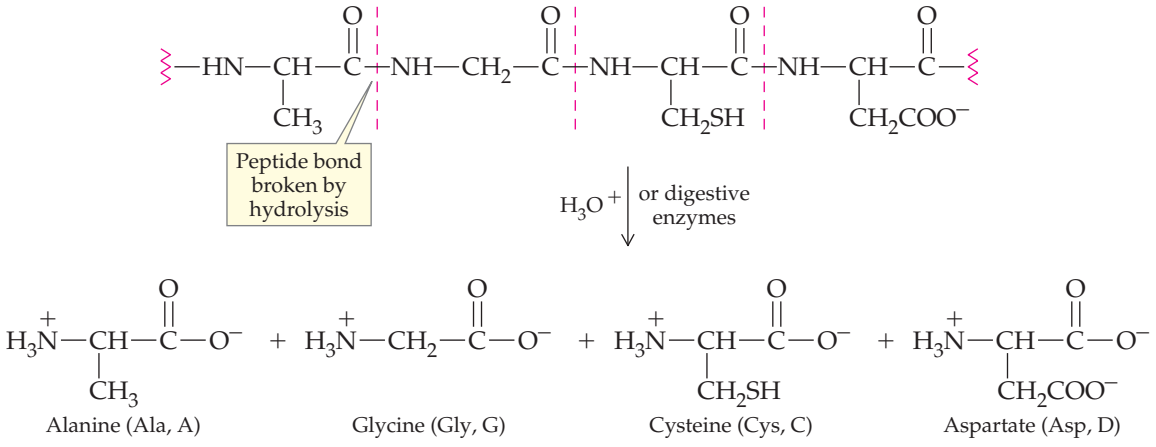
Learning Objectives:

- Describe both chemical and enzymatic protein hydrolysis.
- Define denaturation and give some examples of agents that cause denaturation.

Protein Hydrolysis

Review amide bond hydrolysis in Section 17.4.

Just as a simple amide can be hydrolyzed to yield an amine and a carboxylic acid, a protein can also be hydrolyzed. In protein hydrolysis, the reverse of protein formation, peptide bonds are hydrolyzed to yield amino acids. In fact, digestion of proteins in the diet involves nothing more than hydrolyzing peptide bonds. For example,



A chemist in the laboratory would preferentially choose to hydrolyze a protein by heating it in a solution of hydrochloric acid rather than in sodium hydroxide, because the basic solution destroys some of the amino acids. Digestion of proteins in the body takes place in the stomach and small intestine, where the process is catalyzed by enzymes. Endoproteases are enzymes that hydrolyze the peptide bonds in proteins at specific points within their sequences. Chymotrypsin is an endoprotease that hydrolyzes a peptide bond on the carboxyl-terminal side of aromatic amino acids. A second endoprotease is trypsin that hydrolyzes peptide bonds on the carboxyl side of lysine and arginine. Once individual amino acids are hydrolyzed from proteins, they are absorbed through the wall of the intestine and transported in the bloodstream to wherever they are needed.

Digestion is discussed further in Section 22.1.

Worked Example 18.7 Identifying Protein Hydrolysis Fragments

In Table 18.3, identify the amino acids that have aromatic side chains. Now determine the number of fragments that result when chymotrypsin reacts with vasopressin, which has the structure

Asp-Tyr-Phe-Glu-Asn-Cys-Pro-Lys-Gly,

and then write out the sequences of these fragments using the standard three-letter designator for each amino acid.

ANALYSIS Identify the three aromatic amino acids in vasopressin. Recall that hydrolysis is the addition of water to a bond resulting in breaking that bond, in this case the peptide bond between a pair of amino acids. The enzyme chymotrypsin will hydrolyze vasopressin on the C-terminal side of aromatic amino acids.

SOLUTION

The aromatic amino acids present are tyrosine and phenylalanine. The "cuts" in a chain will produce three fragments. These fragments are as follows:

Asp-Tyr Phe Glu-Asn-Cys-Pro-Lys-Gly

PROBLEM 18.32

Another endoprotease is trypsin. Trypsin hydrolyzes peptide bonds on the carboxyl side of lysine and arginine. If the following peptide sequence is hydrolyzed by trypsin, how many fragments will there be? Use the three-letter amino acid abbreviations to write the fragments out.

Ala-Phe-Lys-Cys-Gly-Asp-Arg-Leu-Leu-Phe-Gly-Ala

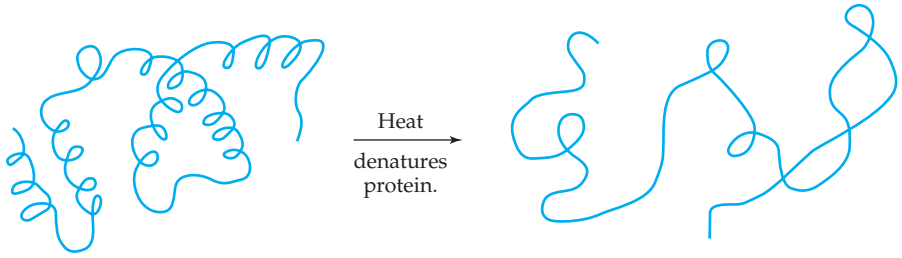
PROBLEM 18.33

If the same peptide found in Problem 18.32 is subjected to acid hydrolysis, how many fragments will result? Why?

Protein Denaturation

Since the overall shape of a protein is determined by a delicate balance of noncovalent forces as we saw in previous sections, it is not surprising that a change in protein shape often results when that balance is disturbed. A disruption in shape that does not affect the protein's primary structure (the order of the amino acids within the protein chain) is known as **denaturation.** When denaturation of a globular protein occurs, for example, the structure unfolds from a well-defined globular shape to a randomly looped chain, but the order of amino acids within the chain does not change.

Denaturation The loss of secondary, tertiary, or quaternary protein structure due to disruption of noncovalent interactions and/or disulfide bonds that leaves peptide bonds and primary structure intact.



▲ Protein denaturation in action: The egg white denatures as the egg fries.

Denaturation is accompanied by changes in physical, chemical, and biological properties. Solubility is often decreased by denaturation, as occurs when egg whites are cooked and the albumins coagulate into an insoluble white mass. Enzymes lose their catalytic activity, and other proteins are no longer able to carry out their biological functions when their shapes are altered by denaturation.

Agents that cause denaturation include heat, mechanical agitation, detergents, organic solvents, extremely acidic or basic pH, and inorganic salts.

- **Heat** The weak side-chain attractions in globular proteins are easily disrupted by heating, in many cases only to temperatures above 50 °C (323 K). Cooking meat converts some of the insoluble collagen into soluble gelatin, which can be used in glue and for thickening sauces.
- **Mechanical agitation** The most familiar example of denaturation by agitation is the foam produced by beating egg whites. Denaturation of proteins at the surface of the air bubbles stiffens the protein and causes the bubbles to be held in place.
- **Detergents** Even very low concentrations of detergents can cause denaturation by disrupting the association of hydrophobic side chains.
- **Organic compounds** Polar solvents such as acetone and ethanol interfere with hydrogen bonding by competing for bonding sites. The disinfectant action of ethanol, for example, results from its ability to denature bacterial protein.
- **pH change** Excess H^+ or OH^- ions react with the basic or acidic side chains in amino acid residues and disrupt salt bridges. One familiar example of denaturation by pH change is the protein coagulation that occurs when milk turns sour because it has become acidic as milk bacteria convert lactose to lactic acid.
- **Inorganic salts** Sufficiently high concentrations of ions can disturb salt bridges.

Most denaturation is irreversible: Hard-boiled eggs do not soften when their temperature is lowered. Many cases are known, however, in which unfolded proteins spontaneously undergo *renaturation*—a return to their native state when placed in a nondenaturing solution. Renaturation is accompanied by recovery of biological activity, indicating that the protein has completely refolded to its stable secondary and tertiary structure. By spontaneously refolding into their native shapes, proteins demonstrate that all the information needed to determine these shapes is present in the primary structure.

Misfolding of proteins, either during synthesis or later on, leads to abnormal secondary and tertiary structures that compromise the original function of the protein. Technically, misfolded proteins are denatured since they cannot function properly. These misfolded proteins often form aggregates in the cell that the cell may not be able to degrade. One disease where aggregates of protein (called plaques) are seen is Alzheimer's disease, a neurological disease resulting in degeneration of brain functions. Other, unrelated diseases that involve misfolded proteins are prion diseases such as Creutzfeldt–Jacob disease, scrapie in sheep, kuru in some New Guinea natives, and "mad cow disease" (bovine spongiform encephalopathy). These diseases are the result of prions duplicating themselves in brain tissue, causing either tangles of protein or open spaces in brain tissue.

HANDS-ON CHEMISTRY 18.2

Demonstrate for yourself that the denaturing methods listed above are effective.

1. Heat an egg in a frying pan and observe the changes in the egg white.
2. Gently mix an egg white in a household acid such as vinegar or pickle juice.
3. Gently mix an egg white in a solution of dish detergent and water.
4. Make a lemon meringue pie. What did you do to the egg whites to produce the meringue?

Note: The suggested protein to use is egg whites. All activities are done with a raw egg, minus the shell. If the egg whites stiffen into any shape, including "strings," the albumins within have denatured.

CHEMISTRY IN ACTION

Imperfect Collagen—An Unfortunate Event

Remember the infant in the chapter-opening photo with the strikingly blue eyes? This same six-month-old girl also suffered a broken arm, but what could have happened to the infant to cause her broken arm? The two most obvious assumptions are accident or child abuse; however, there is a third possibility. This child's osteogenesis imperfecta, known as brittle bone disease, an incurable, inherited genetic disease also caused the broken bone.

Osteogenesis imperfecta is a collagen disease. The genetic defect is dominant, meaning that it will occur even when inherited from only one parent. The primary symptoms of the most common form of this disease are spontaneous broken bones, thin skin, abnormal teeth, weak tendons, and a blue tint to the sclera of the eyes. In severe forms of osteogenesis imperfecta, children may have numerous, frequent fractures, even before birth, small stature, and respiratory problems. Treatment is supportive, aimed at preventing fractures and strengthening muscles. There is no cure for osteogenesis imperfecta, although current research is directed at understanding the underlying biochemical defect in hopes of designing better treatment.

So how is collagen responsible? Collagen forms the scaffold for bone. Collagen fibers are the bone matrix, which is filled in with calcium-containing crystals of hydroxyapatite ($Ca_5[PO_4]_3OH$). The combination of collagen and hydroxyapatite makes strong bone tissue. In osteogenesis imperfecta, incorrectly synthesized collagen leads to weaker bone structures. Mutations in collagen genes lead to substitution of amino acids with bulky side chains for glycine in collagen. Normal collagen has a repeating sequence of glycine—proline—hydroxyproline. Glycine allows for the tight triple helix and strong fibrils of collagen. Bulky side chains on substituted amino acids prevent the tight triple helix from forming, weakening the fibrils and dependent structures such as skin, bone, and ligaments.

It can be difficult to distinguish osteogenesis imperfecta from child abuse. However, the types of spontaneous bone fractures seen in osteogenesis imperfecta are not the typical fractures seen in child abuse cases. A definitive diagnosis of osteogenesis imperfecta requires genetic testing of tissue from the child. Only a small amount of skin tissue is needed. (See Chapter 27, "Genomics," for DNA testing.) The child in the chapter opener tested positive for osteogenesis imperfecta.

CIA Problem 18.8 Describe the biochemical defect that results in osteogenesis imperfecta.

CIA Problem 18.9 Why is it important for collagen to be strong?

SUMMARY REVISITING THE LEARNING OBJECTIVES

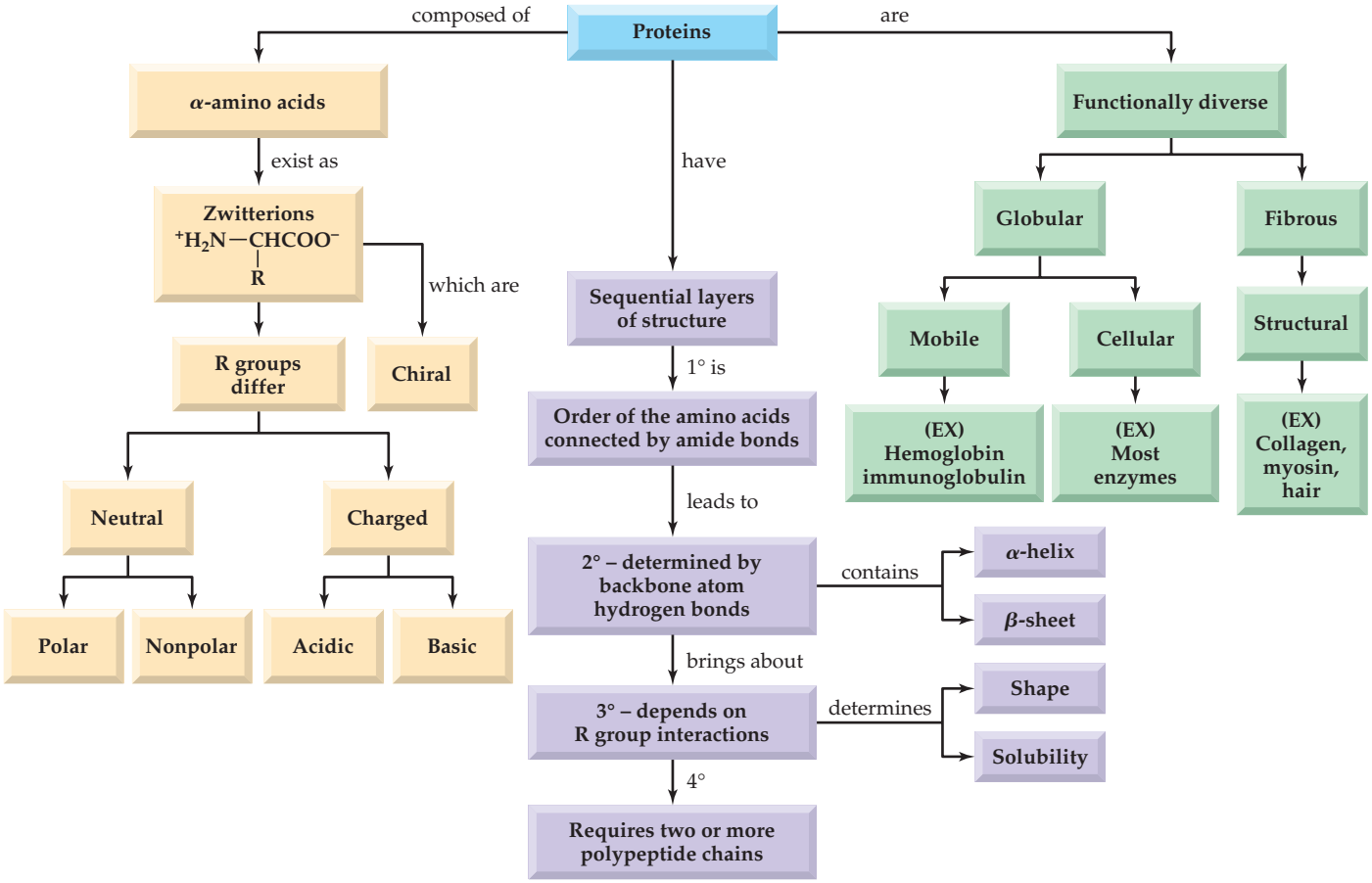
- **Describe the different functions of proteins and give an example for each function.** Proteins can be grouped by function such as structural, transport, etc. See Table 18.2 *(see Problems 40 and 41).*
- **Describe and recognize the 20 alpha amino acid structures and their side chains.** Amino acids in body fluids have an ionized carboxylic acid group ($-COO^-$), an ionized amino group ($-NH_3^+$), and a side-chain R group bonded to a central carbon atom (the α-carbon). Twenty different amino acids occur in *proteins* (Table 18.3) *(see Problems 38 and 42–45).*
- **Categorize amino acids by the polarity or neutrality of the side chain and predict which are hydrophilic and which are hydrophobic.** Amino acid side chains have acidic or basic functional groups or neutral groups that are either polar or nonpolar. Side chains that form hydrogen bonds with water are hydrophilic; nonpolar side chains that do not form hydrogen bonds with water are hydrophobic *(see Problems 50–51, 110, and 111).*
- **Explain chirality and identify which amino acids are chiral.** All α-amino acids except glycine are chiral *(see Problems 39 and 42–51).*
- **Draw all ionic structures for an amino acid under acidic and basic conditions, and identify the zwitterion.** The dipolar ion in which an amino group and a carboxylic acid group are both ionized is known as a *zwitterion* and the electrical charge on the molecule is zero. For each amino acid, there is a distinctive *isoelectric point*—the pH at which the numbers of positive and negative charges in a solution are equal. At a more acidic pH, all carboxylic acid groups are protonated; at a more basic pH, all NH_3^+ groups are deprotonated *(see Problems 34 and 52–59).*
- **Identify a peptide bond, and explain how it is formed.** The amide bond formed between the carboxyl group of one amino acid with the amino group of a second amino acid is called a peptide bond *(see Problems 36 and 60–65).*
- **Draw and name a simple protein structure given its amino acid sequence.** Peptides are named by combining the names of the amino acids. Amino acid sequences are often represented by using the three-letter or one-letter abbreviations for the amino acids in a left to right order *(see Problems 36 and 60–65).*
- **Identify the amino-terminal end and the carboxyl-terminal end of a simple protein (peptide) structure given its amino acid sequence.** Amino acid sequences are written with the amino group of the end amino acid on the left and the carboxyl group of the amino acid on the other end of the chain on the right *(see Problems 36 and 60–65).*
- **Define primary protein structure and explain how primary structures are represented.** Protein *primary structure* is the sequence in which the amino acids are connected by peptide bonds. Using formulas or amino acid abbreviations, the primary structures are written with the amino-terminal end on the left and the carboxyl-terminal end on the right *(see Problems 66–69).*

- **Describe the planar sections of the primary sequence, their influence on the shape of the protein backbone, and identify these sections given a drawing of the primary sequence.** Due to electron delocalization between the nitrogen atom and the carbonyl pi bond atom in the peptide bond, a planar structure develops between those atoms and the two alpha carbon atoms involved. Thus, there exists a series of planes along the backbone resulting in a zigzag formation for the backbone *(see Problems 66–69).*
- **Give an example of how the change in primary sequence can change the function of a protein.** Sickle-cell anemia results from a single amino acid change in the primary sequence of hemoglobin *(see Problems 66–69).*
- **Describe the α-helix and β-sheet structures and give an example of a protein that contains primarily helix and one that contains primarily sheet secondary structure.** Secondary structures include regular, repeating three-dimensional structures held in place by hydrogen bonding between backbone atoms within a chain or in adjacent chains *(see Problems 37, 70–75, and 103).*
- **Describe the specific hydrogen bonding responsible for secondary structures.** The α-helix is a coil with hydrogen bonding between carbonyl oxygen atoms and amide hydrogen atoms four amino acid residues farther along the same chain. The β-sheet is a pleated sheet with adjacent protein-chain segments connected by hydrogen bonding between peptide groups by the same atoms as in the alpha helix *(see Problems 37, 70–73, and 103).*
- **Distinguish between fibrous and globular proteins.** Secondary structure determines the properties of *fibrous proteins,* which are tough and insoluble. Fibrous proteins are insoluble and globular proteins are soluble in aqueous solutions *(see Problems 37, 74, and 75).*
- **Identify the four specific forces responsible for tertiary structure.** Tertiary structure is the overall three-dimensional shape of a folded protein chain. Protein chains are drawn into their native shapes by attractions between atoms along their backbones and between atoms in side-chain groups *(see Problems 76, 77, 82–87, 98, and 99).*
- **Identify what forces or bonds exist between amino acid side chains.** Note that *hydrogen bonding* can also occur between R group atoms or R groups and backbone atoms. *Noncovalent interactions* between side chains include ionic bonding and *hydrophobic interactions* among nonpolar groups. Covalent *disulfide bonds* form bridges between side chains containing cysteine *(see Problems 76–83).*
- **Distinguish between simple and conjugated proteins.** Simple proteins are composed only of amino acids while conjugated proteins, such as hemoglobin, contain a nonprotein group *(see Problems 76–83, 90, and 91).*
- **Define quaternary structure.** Proteins that incorporate more than one peptide chain have *quaternary structure (see Problems 84, 85, and 88).*
- **Identify the forces responsible for quaternary structure.** In a quaternary structure, two or more folded protein subunits are united in a single structure by noncovalent interactions *(see Problems 86 and 87).*
- **Give examples of proteins with quaternary structure.** Hemoglobin, for example, consists of two pairs of subunits, with a nonprotein heme molecule in each of the four subunits. Collagen is a fibrous protein composed of protein chains twisted together in triple helixes *(see Problem 89).*
- **Describe both chemical and enzymatic protein hydrolysis.** Peptide bonds are broken by *hydrolysis,* which may occur in acidic solution or during enzyme-catalyzed digestion of proteins in food. Hydrolysis yields the individual amino acids comprising the protein *(see Problems 92–97 and 106).*
- **Define denaturation and give some examples of agents that cause denaturation.** *Denaturation* is the loss of overall structure by a protein while retaining its primary structure. Among the agents that cause denaturation are heat, mechanical agitation, pH change, and exposure to a variety of chemical agents, including detergents *(see Problems 92–97 and 106).*

KEY WORDS

Alpha- (α-) amino acid, *p. 591*
Alpha-helix (α-helix), *p. 603*
Amino acid, *p. 591*
Amino-terminal (N-terminal) amino acid, *p. 598*
Beta-sheet (β-sheet), *p. 604*
Carboxyl-terminal (C-terminal) amino acid, *p. 598*
Cellular protein, *p. 612*
Conjugated protein, *p. 610*
Denaturation, *p. 615*
Disulfide bond (in protein), *p. 608*
Fibrous protein, *p. 605*
Globular protein, *p. 605*
Hydrophilic, *p. 593*
Hydrophobic, *p. 593*
Isoelectric point (pI), *p. 595*
Mobile protein, *p. 612*
Native protein, *p. 607*
Noncovalent forces, *p. 593*
Peptide bond, *p. 597*
Primary protein structure, *p. 601*
Protein, *p. 591*
Quaternary protein structure, *p. 612*
Residue (amino acid), *p. 598*
Secondary protein structure, *p. 603*
Side chain (amino acid), *p. 591*
Simple protein, *p. 609*
Tertiary protein structure, *p. 607*
Zwitterion, *p. 595*

CONCEPT MAP: AMINO ACIDS AND PROTEINS



▲ **Figure 18.7 Concept Map.** Although the wide variety of structures that various proteins assume can seem complex, examination of this concept map illustrates the connection between proteins, their building blocks (amino acids), and the fundamental principles underlying protein structure. The levels of structure are organized from simplest to most complex, and interrelated concepts are shown. The functional groups can be found in the Functional Group Concept Map (Figure 12.5) if you need to review those. Earlier concept maps (Figures 4.8 and 8.25) will aid in review of molecular interactions and bonding. All of these concepts are integrated in biological molecules.

UNDERSTANDING KEY CONCEPTS

18.34 Draw the structure of the following amino acids, dipeptides, and tripeptides at low pH (pH 1) and high pH (pH 14). At each pH, assume that all functional groups that might do so are ionized. (Hint: See Worked Example 18.2.)

(a) Val **(b)** Arg

(c) Tyr-Ser **(d)** Glu-Asp

(e) Gln-Ala-Asn **(f)** Met-Trp-Cys

18.35 Interactions of amino acids on the interior of proteins are key to the shapes of proteins. In group (a), which pairs of amino acids form hydrophobic interactions? In group (b), which pairs form ionic interactions? Which pairs in group (c) form hydrogen bonds?

(a) **1** Pro . . . Phe
2 Lys . . . Ser
3 Thr . . . Leu
4 Ala . . . Gly

(b) **1** Val . . . Leu
2 Glu . . . Lys
3 Met . . . Cys
4 Asp . . . His

(c) **1** Cys . . . Cys
2 Asp . . . Ser
3 Val . . . Gly
4 Met . . . Cys

18.36 Draw the hexapeptide Asp-Gly-Phe-Leu-Glu-Ala in linear form showing all of the atoms, and show (using dotted lines) the hydrogen bonding that stabilizes this structure if it is part of an α-helix.

18.37 Compare and contrast the characteristics of fibrous and globular proteins. Consider biological function, water solubility, amino acid composition, secondary structure, and tertiary structure. Give examples of three fibrous and three globular proteins. (Hint: Make a table.)

18.38 Cell membranes are studded with proteins. Some of these proteins, involved in the transport of molecules across the membrane into the cell, span the entire membrane and are called transmembrane proteins. The interior of the cell membrane is hydrophobic and nonpolar, whereas both the extracellular and intracellular fluids are water-based.

(a) List three amino acids you would expect to find in the part of a transmembrane protein that lies within the cell membrane.

(b) List three amino acids you would expect to find in the part of a transmembrane protein that lies outside the cell.

(c) List three amino acids you would expect to find in the part of a transmembrane protein that lies inside the cell.

18.39 Threonine has two chiral centers. Draw L-threonine and indicate which carbon atoms are chiral. Which carbon atom is responsible for D and L configuration?

ADDITIONAL PROBLEMS

PROTEINS AND THEIR FUNCTIONS: AN OVERVIEW (SECTION 18.2)

18.40 Name four biological functions of proteins in the human body, and give an example of a protein for each function.

18.41 What kind of biological function would each of the following proteins perform?

(a) Human growth hormone **(b)** Myosin

(c) Protease **(d)** Myoglobin

AMINO ACIDS (SECTION 18.3)

18.42 What amino acids do the following abbreviations stand for? Draw the structure of each.

(a) Val **(b)** Ser **(c)** Glu

18.43 What amino acids do the following abbreviations stand for? Draw the structure of each.

(a) Ile **(b)** Thr **(c)** Gln

18.44 Name and draw the structures of the amino acids that fit the following descriptions:

(a) Contains a thiol group **(b)** Contains a phenol group

18.45 Name and draw the structures of the amino acids that fit the following descriptions:

(a) Contains an isopropyl group

(b) Contains a secondary alcohol group

18.46 What does the term *chiral* mean? Give two examples.

18.47 What does the term *achiral* mean? Give two examples.

18.48 Draw leucine and identify any chiral carbon atoms with arrows.

18.49 Draw isoleucine and identify any chiral carbon atoms with arrows.

18.50 Is phenylalanine hydrophilic or hydrophobic? Explain why.

18.51 Is histidine hydrophilic or hydrophobic? Explain why.

ACID–BASE PROPERTIES OF AMINO ACIDS (SECTION 18.4)

18.52 At 5<pH<8, which of the following amino acids has a net positive charge, which has a net negative charge, and which is neutral? (Hint: Draw the various charged forms of each amino acid before deciding.)

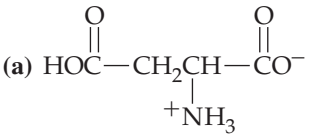
(a) Asparagine **(b)** Lysine **(c)** Proline

18.53 At neutral pH, which of the following amino acids has a net positive charge, which has a net negative charge, and which is neutral? (Hint: Draw the various charged forms of each amino acid before deciding.)

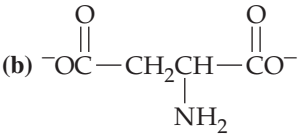
(a) Aspartic acid **(b)** Histidine **(c)** Valine

18.54 Which of the following forms of aspartic acid would you expect to predominate at low pH, neutral pH, and high pH?

(a)



(b)



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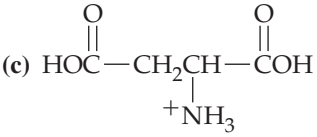
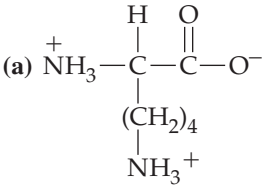


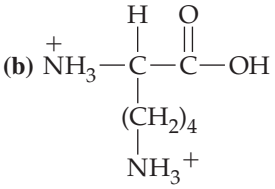
18.55 Which form of aspartic acid in Problem 18.54 is the zwitterion? What is the pI for the zwitterion?

18.56 Which of the following forms of lysine would you expect to predominate at low pH, neutral pH, and high pH?

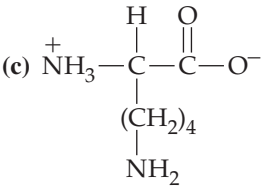
(a)



(b)



(c)



18.57 Which form of lysine in Problem 18.56 is the zwitterion? What is the pI for the zwitterion?

18.58 Proteins are usually least soluble in water at their isoelectric points. Explain.

18.59 How could you make the zwitterion of aspartic acid more soluble in water?

PEPTIDES (SECTION 18.5)

18.60 Use the three-letter abbreviations to name all tripeptides that contain valine, methionine, and leucine.

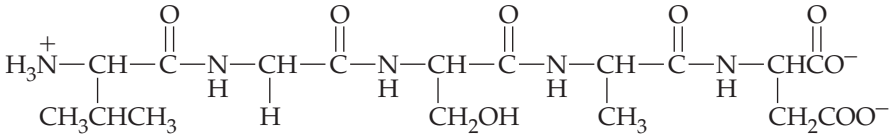
18.61 Write structural formulas for the two dipeptides that contain leucine and aspartate.

18.62 The *endorphins* are a group of naturally occurring neurotransmitters that act in a manner similar to morphine to control pain. Research has shown that the biologically active parts of the endorphin molecules are simple pentapeptides called *enkephalins.* Draw the structure of the methionine enkephalin with the sequence Tyr-Gly-Gly-Phe-Met. Identify the N-terminal and C-terminal amino acids.

18.63 Refer to Problem 18.62. Draw the structure of the leucine enkephalin with the sequence Tyr-Gly-Gly-Phe-Leu. Identify the N-terminal and C-terminal amino acids.

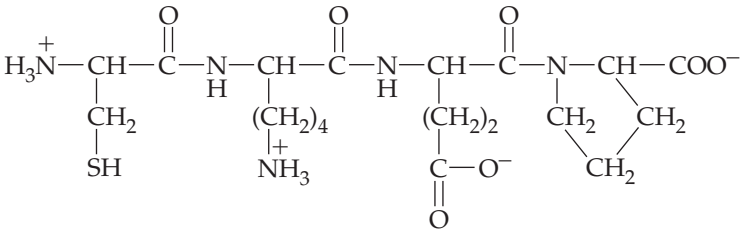
18.64 **(a)** Identify the amino acids present in the peptide shown and name the peptide using the three-letter abbreviations.

(b) Identify the N-terminal and C-terminal amino acids of the peptide.



18.65 **(a)** Identify the amino acids present in the peptide shown and name the peptide using the three-letter abbreviations.

(b) Identify the N-terminal and C-terminal amino acids of the peptide.



PROTEIN STRUCTURE: AN OVERVIEW AND PRIMARY PROTEIN STRUCTURE (1°) (SECTION 18.6)

18.66 What is the primary structure of a protein?

18.67 What is the sequence of atoms along the "backbone" of a protein?

18.68 Bradykinin, a peptide that helps to regulate blood pressure, has the primary structure Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg.

(a) Draw the complete structural formula of bradykinin.

(b) Bradykinin has a very kinked secondary structure. Why?

18.69 What effect on the overall structure of hemoglobin in the presence and absence of oxygen did the substitution of valine for glutamic acid have in the primary structure of hemoglobin?

SECONDARY PROTEIN STRUCTURE (2°) (SECTION 18.7)

18.70 Describe the specific bonding responsible for secondary structure in proteins, including which atoms are involved.

18.71 Is hydrogen bonding covalent or noncovalent?

18.72 How does the alpha-helix result from hydrogen bonding?

18.73 How does the beta-pleated sheet result from hydrogen bonding?

18.74 Give an example of a protein containing primarily alpha-helices. Is this a fibrous or globular protein?

18.75 Give an example of a protein containing primarily beta-pleated sheets. Is this a fibrous or globular protein?

TERTIARY PROTEIN STRUCTURE (3°) (SECTION 18.8)

18.76 What kind of bond would you expect between the side chains of the following amino acids?

(a) Cysteine and cysteine

(b) Alanine and leucine

(c) Aspartic acid and asparagine

(d) Serine and lysine

18.77 Is the bond formed between each pair in Problem 18.76 covalent or noncovalent?

18.78 What drives spontaneous folding into the correct tertiary structure for a newly synthesized protein?

18.79 What is the function of proteins that are called chaperone proteins?

18.80 What is the difference between a simple protein and a conjugated protein?

18.81 What kinds of molecules are found in the following classes of conjugated proteins in addition to the protein part?

(a) Metalloproteins **(b)** Hemoproteins

(c) Lipoproteins **(d)** Nucleoproteins

18.82 Why is cysteine such an important amino acid for defining the tertiary structure of some proteins?

18.83 What conditions are required for disulfide bonds to form between cysteine residues in a protein?

QUATERNARY PROTEIN STRUCTURE (4°) (SECTION 18.9)

18.84 What is meant by the following terms as they apply to protein structure, and what bonds or molecular interactions stabilize that level of structure?

(a) Primary structure **(b)** Secondary structure

(c) Tertiary structure **(d)** Quaternary structure

18.85 What level of protein structure is determined by the following:

(a) Peptide bonds between amino acids?

(b) Hydrogen bonds between backbone carbonyl oxygen atoms and hydrogen atoms attached to backbone nitrogen atoms?

(c) R group interactions that may involve Van der Waals forces, ionic interactions, or hydrogen bonds?

18.86 How do the following noncovalent interactions help to stabilize the tertiary and quaternary structure of a protein? Give an example of a pair of amino acids that could give rise to each interaction.

(a) Hydrophobic interactions

(b) Salt bridges (ionic interactions)

18.87 How do the following interactions help to stabilize the tertiary and quaternary structure of a protein? Give an example of a pair of amino acids that could give rise to each interaction.

(a) Side-chain hydrogen bonding

(b) Disulfide bonds

18.88 What is the minimum number of polypeptide chains necessary for quaternary structure to exist?

18.89 Give an example of a protein that has quaternary structure. How many polypeptide chains are present in this protein?

18.90 What is a conjugated protein? Give an example.

18.91 What kinds of molecules provide the nonprotein part of a conjugated protein? Give an example.

CHEMICAL PROPERTIES OF PROTEINS SECTION (18.10)

18.92 What kinds of changes take place in a protein when it is denatured?

18.93 Explain how a protein is denatured by the following:

(a) Heat

(b) Strong acids

(c) Organic solvents

18.94 What is the difference between protein digestion and protein denaturation? Both occur after a meal.

18.95 Why is hydrolysis of a protein not considered to be denaturation?

18.96 Fresh pineapple cannot be used in gelatin desserts because it contains an enzyme that hydrolyzes the proteins in gelatin, destroying the gelling action. Canned pineapple can be added to gelatin with no problem. Why?

18.97 As a chef, you prepare a wide variety of foods daily. The following dishes all contain protein. What method (if any) has been used to denature the protein present in each food?

(a) Charcoal-grilled steak

(b) Pickled pigs' feet

(c) Meringue

(d) Steak tartare (raw, chopped beef)

(e) Salt pork

CONCEPTUAL PROBLEMS

18.98 For each amino acid listed, tell whether its influence on tertiary structure is largely through hydrophobic interactions, hydrogen bonding, formation of salt bridges, covalent bonding, or some combination of these effects.

(a) Tyrosine **(b)** Cysteine

(c) Asparagine **(d)** Lysine

(e) Tryptophan **(f)** Alanine

(g) Leucine **(h)** Methionine

18.99 Oxytocin is a small peptide that is used to induce labor by causing contractions in uterine walls. It has the primary structure Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gln. This peptide is held in a cyclic configuration by a disulfide bridge. Draw a diagram of oxytocin, showing the disulfide bridge.

18.100 Methionine has a sulfur atom in its formula. Explain why methionine does not form disulfide bridges.

18.101 Four of the most abundant amino acids in proteins are leucine, alanine, glycine, and valine. What do these amino acids have in common? Would you expect these amino acids to be found on the interior or on the exterior of the protein?

18.102 Globular proteins are water-soluble, whereas fibrous proteins are insoluble in water. Indicate whether you expect the following amino acids to be on the surface of a globular protein or on the surface of a fibrous protein.

(a) Ala **(b)** Glu

(c) Leu **(d)** Phe

(e) Ser **(f)** Val

18.103 Figure 18.4 shows sharp directional changes in the path of the peptide chain. This can be seen in both the ribbon model and the space-filling rendering. These sharp directional changes connecting adjacent regions of secondary structure are often referred to either as "reverse turns" or as "bends." The two most common amino acids in reverse turns are glycine and proline. Use your knowledge of the structures of these two amino acids to speculate on why they might be found in reverse turns.

18.104 During sickle-cell anemia research to determine the modification involved in sickling, sequencing of the affected person's hemoglobin β-subunit reveals that the

sixth amino acid is valine rather than glutamate; thus, the replacement of glutamate by valine severely alters the three-dimensional structure of hemoglobin. Which amino acid, if it replaced the Glu, would cause the least disruption in hemoglobin structure? Why?

18.105 A family visits a pediatrician with their sick child. The four-month-old baby is pale, has obvious episodes of pain, and is not thriving. The doctor orders a series of blood tests, including a test for hemoglobin types. The results show that the infant is not only anemic but that the anemia is due to sickle-cell anemia. The family wants to know if their other two children have sickle-cell anemia, sickle-cell trait, or no sickle-cell gene at all.

(a) What test will be used?

(b) Sketch the expected results if samples for each child are tested at the same time.

(c) What is the difference between sickle-cell anemia and sickle-cell trait?

18.106 Why do you suppose individuals with diabetes must receive insulin subcutaneously by injection rather than orally?

18.107 Individuals with phenylketonuria (PKU) are sensitive to phenylalanine in their diet. Why is a warning on foods containing aspartame (L-aspartyl-L-phenylalanine methyl ester) of concern to individuals with PKU?

18.108 What could you prepare for dinner for a strict vegan that provides all of the essential amino acids in appropriate amounts? (Remember, strict vegans do not eat meat, eggs, milk, or products that contain those animal products.)

GROUP PROBLEMS

18.109 Which would you expect to be more soluble in water, a peptide containing mostly alanine and leucine or a peptide containing mostly lysine and aspartic acid? Explain. (Hint: Consider side-chain interactions with water.)

18.110 Which of the following amino acids is most likely to be found on the outside of a soluble protein, and which of them is more likely to be found on the inside? Explain each answer. (Hint: Consider the effect of the amino acid side chain in each case and that the protein is folded up into its globular form.)

(a) Valine **(b)** Aspartate

(c) Histidine **(d)** Alanine

18.111 Which of the following amino acids is most likely to be found on the outside of a soluble protein? Which is more likely to be found on the inside? Explain each answer. (Hint: Consider the effect of the amino acid side chain in each case and that the protein is folded up into its globular form.)

(a) Leucine **(b)** Glutamate

(c) Phenylalanine **(d)** Glutamine

18.112 List the amino acids with side chains that are capable of hydrogen bonding. Draw an example of two of these amino acids hydrogen bonding to one another. For each one, draw a hydrogen bond to water in a separate sketch. Refer to Section 8.2 for help with drawing hydrogen bonds.

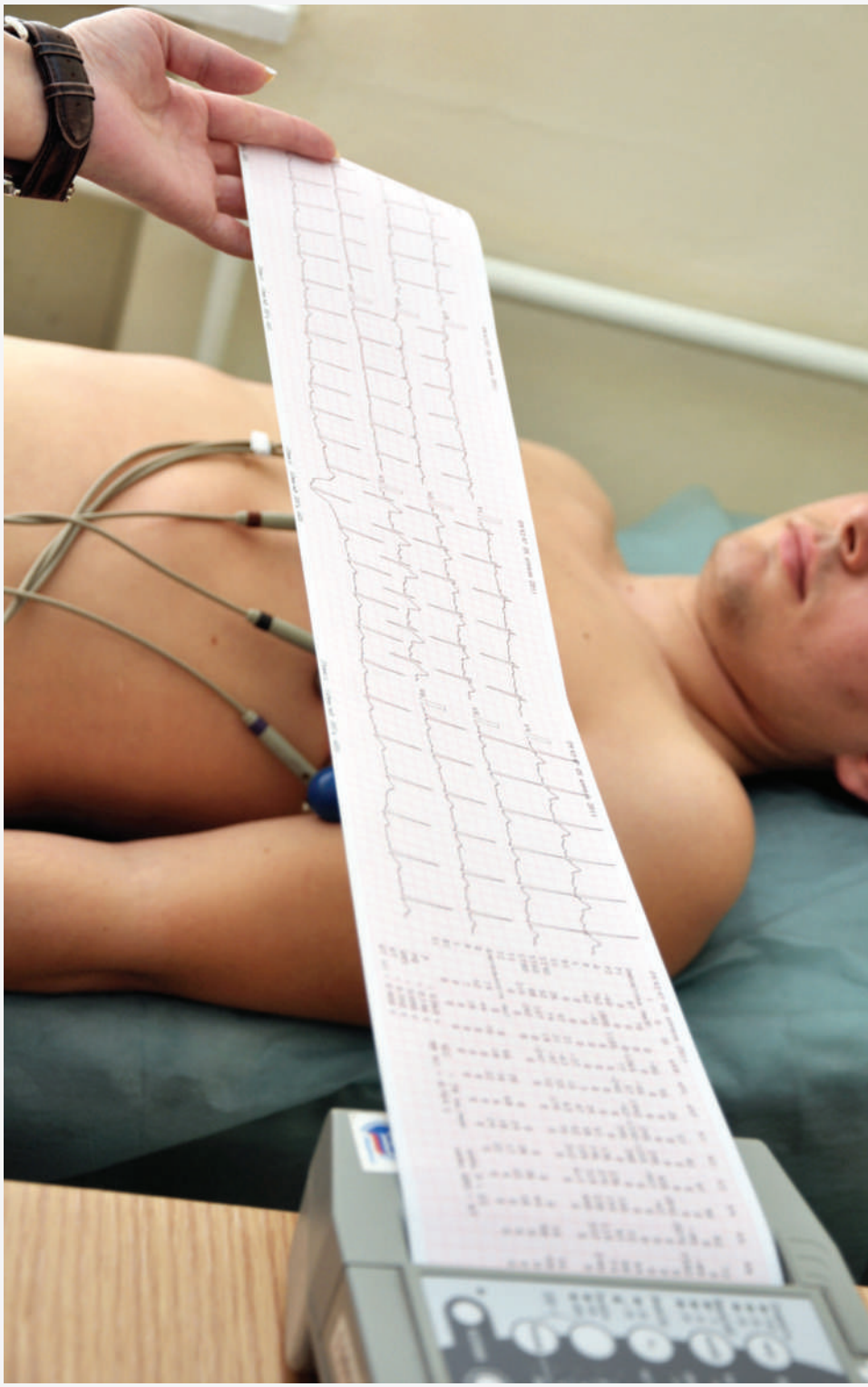
19

Enzymes and Vitamins

CONTENTS

CONCEPTS TO REVIEW

A. Coordinate covalent bonds (Section 4.4)
B. Reaction rates (Section 7.5)
C. pH (Section 10.5)
D. Effects of conditions on reaction rates (Section 7.6)
E. Tertiary protein structure (Section 18.8)



▲ The electrocardiogram (ECG) seen here is a recording of the electrical signals generated by the patient's beating heart. This recording helps the physician team determine what may be wrong with the patient's heart.

Ann, an emergency room (ER) nurse, is challenged with a variety of patients every shift. One night two patients required immediate, rapid care. The first, 52-year-old John Smith, arrived with central chest pain radiating to his left arm and difficulty breathing. These symptoms suggest heart attack as one diagnosis. A few minutes later, 75-year-old Brenda Givens arrived. She had

difficulty speaking and walking and one side of her face was droopy. Ann recognized these as signs of a stroke—brain damage usually caused by a blood clot in the brain. The ER doctor ordered continuous electrocardiogram (EKG) monitoring and several blood tests for both patients. Both Mr. Smith and Ms. Givens had their blood tested for enzymes and selected proteins that normally are found only inside intact cells. These tests helped in diagnosis by ruling out other possible problems and confirming the other symptoms. For a heart attack, Mr. Smith's damaged heart cells released several enzymes specific to the heart and a large quantity of troponins, small proteins intimately involved with muscle cell contraction. Blood lipid levels were also checked for both patients. Ms. Givens was treated intravenously with tissue plasminogen activator (tPA) to activate plasminogen, which acts on fibrin, the major protein in blood clots. This treatment dissolved the blood clot and restored blood flow to the affected part of the brain. Enzymes, the subject of this chapter, are used for both diagnosis and treatment of many medical conditions.

Animals and plants are composed of millions of cells organized into different functional types. Among the many thousands of protein molecules in each cell, there are more than 2000 different specialized proteins, called enzymes, each one used in a different reaction. Although enzymes—powerful and highly selective biological catalysts—carry out the chemical reactions in cells, how do cells organize so many different reactions so that all occur to the proper extent? The answer is that all enzyme reactions in living organisms are under tight regulation by a variety of mechanisms. An important difference between chemistry in a laboratory and chemistry in a living organism is control. In a laboratory, the speed of a reaction is controlled by adjusting experimental conditions such as temperature, solvent, and pH. In an organism, these conditions cannot be adjusted. The human body maintains a temperature near 37 °C (310.15 K), the solvent must be water, and the pH must be close to 7.4 in most body fluids.

In this chapter, the focus will be on enzymes and the regulation of enzymatic reactions. We will also look at *vitamins* and *minerals,* because they are essential to the function of certain enzymes. Chapter 28 is devoted to the role of *hormones* and *neurotransmitters* in keeping our biochemistry under control, which they do primarily by regulating the activity of enzymes.

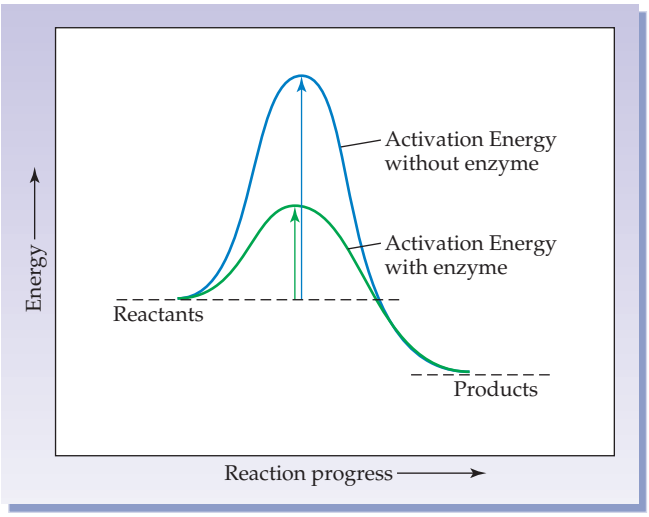
19.1 Catalysis by Enzymes

Learning Objective:

- Describe the function of enzymes in biochemical reactions.

Enzymes are catalysts that accelerate the rates of biochemical reactions but at the end of the reaction remain unchanged themselves. However, as catalysts, enzymes do change the molecules acted on by breaking existing bonds and forming new ones in the reaction products. Like all catalysts, an enzyme does not affect the equilibrium point of a reaction and cannot bring about a reaction that is energetically unfavorable. Rather, an enzyme decreases the time it takes for the reaction to reach equilibrium by lowering its activation energy.

Enzyme A protein or other molecule that acts as a catalyst for a biological reaction.



CONCEPTS TO REVIEW See Figure 7.4 for a visual representation of the effect of a catalyst on a reaction's activation energy.

Active site A pocket in an enzyme with the specific shape and chemical makeup necessary to bind a substrate.

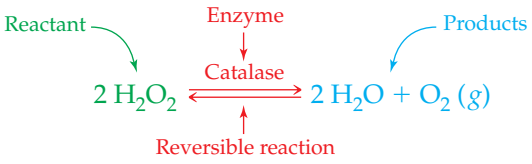
Substrate A reactant in an enzyme-catalyzed reaction.

Specificity (enzyme) The limitation of the activity of an enzyme to a specific substrate, specific reaction, or specific type of reaction.

Enzymes, with few exceptions, are water-soluble globular proteins (Section 18.9). As proteins, they are far larger and more complex molecules than simple inorganic catalysts. Because of their size and complexity, enzymes have more ways available in which to connect with reactants, speed up reactions, and be controlled by other molecules.

Within the folds of an enzyme's protein chain is the **active site**—the region where the reaction takes place. The active site has the specific shape and chemical reactivity needed to catalyze the reaction. One or more **substrates** (the substance the enzyme binds to and the reactants in an enzyme-catalyzed reaction) are held in place by intermolecular forces to groups that line the active site.

The extent to which an enzyme's activity is limited to a certain substrate and a certain type of reaction is referred to as the **specificity** of the enzyme. Enzymes differ greatly in their specificity. *Catalase,* for example, catalyzes one reaction: the decomposition of hydrogen peroxide (Figure 19.1). Catalase destroys hydrogen peroxide before it oxidizes essential biomolecules, damaging them.



HANDS-ON CHEMISTRY 19.1

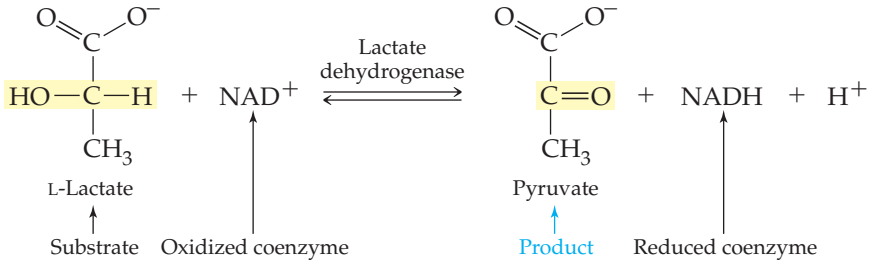
Do food items contain active catalase? You can test this at home with samples of raw meat and vegetables. You will need clear (not colored), transparent glasses, 3% (v/v) hydrogen peroxide (from a drugstore or grocery store), and a few 1 cm cubes of raw meat such as chicken liver or a bit of hamburger. Also cube some raw potato. Drop some of the raw meat in a glass with a few centimeters of hydrogen peroxide in it. Using a different glass of hydrogen peroxide, do the same thing with potato cubes. What happened with the meat? With the potato? Does the amount of meat or potato used matter? Repeat your experiment with cooked meat and cooked potato. What happened?

Evolution of bubbles means catalase present in the sample was converting hydrogen peroxide to water and oxygen; the enzyme was active, in its native state and not denatured. If no significant amount of bubbles appeared, catalase was either absent or inactive. Based on the results of the trials with raw and cooked samples, was catalase present, absent, or inactive? If inactive, why?

▲ **Figure 19.1**
Dilute hydrogen peroxide is frequently used to treat minor wounds. The bubbles produced are oxygen due to the action of the enzyme catalase released from injured tissue and bacteria.

Thrombin is specific for catalyzing hydrolysis of a peptide bond following the amino acid arginine and primarily acts on fibrinogen, a protein essential to blood clotting. When this bond breaks, the product (fibrin) proceeds to polymerize into a blood clot (Section 29.5). *Carboxypeptidase A* is less specific—it removes many different C-terminal amino acid residues from protein chains during digestion. And the enzyme *papain* from papaya fruit catalyzes the hydrolysis of peptide bonds in many locations. It is this ability to break down proteins that accounts for the use of papain in meat tenderizers, in contact-lens cleaners, and in cleansing dead or infected tissue from wounds *(debridement).*

Since the amino acids in enzymes are all L-amino acids, it should come as no surprise that enzymes are also specific with respect to stereochemistry. If a substrate is chiral, an enzyme usually catalyzes the reaction of only one of the pair of enantiomers because only one fits the active site in such a way that the reaction can occur. The enzyme lactate dehydrogenase (LDH), for example, catalyzes the removal of hydrogen from L-lactate but not from D-lactate.



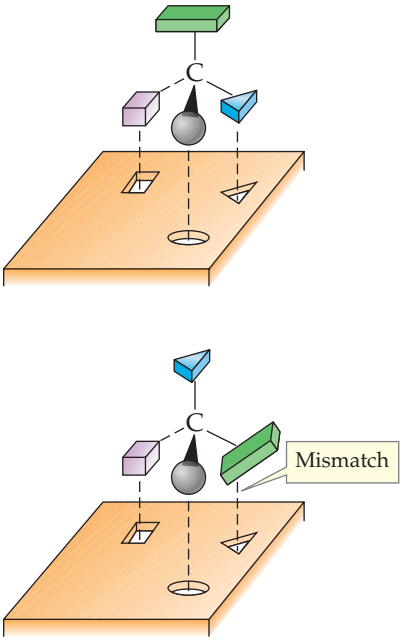
This is another example of the importance of molecular shape in biochemistry. The specificity of an enzyme for one of two enantiomers is a matter of fit. A left-handed enzyme cannot fit with a right-handed substrate any more than a left-handed glove fits on a right hand (Figure 19.2).

The catalytic activity of an enzyme is measured by its **turnover number,** the maximum number of substrate molecules acted upon by one molecule of enzyme per unit time (Table 19.1). Most enzymes turn over 10–1000 molecules per second, but some are much faster. Catalase, with its essential role in protecting against molecular damage, is one of the fastest—it can turn over 10 million molecules per second. This is the fastest reaction rate attainable in the body because it is the rate at which molecules collide.

Turnover number The maximum number of substrate molecules acted upon by one molecule of enzyme per unit time.

Table 19.1 Turnover Numbers for Some Enzymes (Maximum Number of Catalytic Events Per Second)

Enzyme	Reaction Catalyzed	Turnover Number
Papain	Hydrolysis of peptide bonds	10
Ribonuclease	Hydrolysis of phosphate ester link in ribonucleic acid (RNA)	10^2
Kinase	Transfer of phosphoryl group between substrates	10^3
Acetylcholinesterase	Deactivation of the neurotransmitter acetylcholine	10^4
Carbonic anhydrase	Converts CO_2 to HCO_3^-	10^6
Catalase	Decomposition of H_2O_2 to $H_2O + O_2$	10^7



▲ **Figure 19.2**
A chiral reactant and a chiral reaction site.
The enantiomer at the top fits the reaction site like a hand in a glove, but the enantiomer at the bottom does not fit and therefore cannot be a substrate for this enzyme.

PROBLEM 19.1

Which of the enzymes listed in Table 19.1 catalyzes a maximum of 1000 reactions per second?

PROBLEM 19.2

The enzyme LDH converts lactate to pyruvate. In mammals, this enzyme accepts only L-lactate as substrate, but the correct substrate in invertebrates such as oysters is D-lactate. Explain why LDH has two different forms, each accepting one of the enantiomers of the substrate, lactate, but not the other.

19.2 Enzyme Cofactors

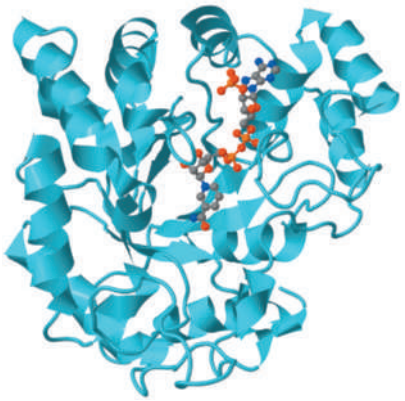
Learning Objective:

- Explain the role of cofactors in some enzymatic reactions.

Many enzymes are conjugated proteins that require nonprotein **cofactors** as part of their structure to function. Some cofactors are metal ions, while others are nonprotein organic molecules called **coenzymes.** To be active, an enzyme may require a metal ion, a coenzyme, or both. Some enzyme cofactors are tightly held by noncovalent intermolecular forces or are covalently bound to their enzymes; others are more loosely bound, entering and leaving the active site as needed.

Cofactor A nonprotein part of an enzyme that is essential to the enzyme's catalytic activity; a metal ion or a coenzyme.

Coenzyme An organic molecule that acts as an enzyme cofactor.



▲ The ribbon structure for aldose reductase, an oxidoreductase enzyme that reduces a C═O group in a sugar molecule to a —C—OH group with the aid of the coenzyme NADH. The sugar glucose (orange) and NADH (gray) are shown in the active site of the enzyme. Note the alpha helices in this enzyme.

Why are cofactors necessary? The functional groups in enzymes are limited to those of the amino acid side chains in the protein. By combining with cofactors, enzymes acquire chemically reactive groups not available in side chains. For example, as illustrated in the ribbon structure for aldose reductase, the nicotinamide adenine dinucleotide (NADH) molecule bound by intermolecular forces to aldose reductase (an enzyme) is a coenzyme and is the reducing agent that makes the reaction possible. (Vitamins that function as cofactors are discussed in Section 19.9.) Because many enzymes require metal ion cofactors, we need trace minerals in our diet. Table 19.2 shows the many different metal ions that function as enzyme cofactors.

Table 19.2 Inorganic Ion Cofactors

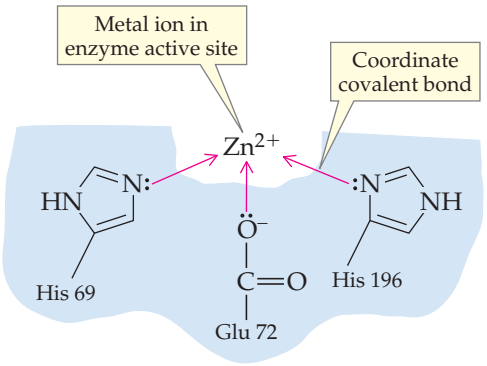
Ions	Enzyme Examples
Cu^{2+}*	Cytochrome oxidase
Fe^{2+} or Fe^{3+}*	Catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose-6-phosphatase
Mn^{2+}*	Arginase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se*	Glutathione peroxidase
Zn^{2+}*	Alcohol dehydrogenase

**Trace minerals*

Recall from Section 4.4 that a coordinate covalent bond is one that is formed when both electrons are donated by the same atom.

Review Lewis acids and bases from Sections 4.6 and 4.7

Metal ions are able to form coordinate covalent bonds and function as Lewis acids by accepting lone-pair electrons present on nitrogen or oxygen atoms in enzymes or substrates. This bonding may anchor a substrate in the active site and may also allow the metal ion to participate in the catalyzed reaction. For example, every molecule of the digestive enzyme carboxypeptidase A contains one Zn^{2+} ion that is essential for its catalytic action. We say that the zinc ion is "coordinated" to a nitrogen atom in each of two histidine side chains and one oxygen atom in a glutamate side chain in the active site. In this way, the ion is held in place in the active site of the enzyme.



Like the trace minerals that are our source of metal ion cofactors, certain vitamins are also a dietary necessity for humans because we cannot synthesize them in the body, yet they are critical building blocks for coenzymes. See Table 19.3 for examples.

Table 19.3 Some Important Coenzymes

Coenzyme	Type of Chemical Group Moved	Dietary Molecule
Coenzyme A	Acyl groups	Pantothenic acid
Coenzyme B_{12}	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide (FAD)	Electrons	Riboflavin (vitamin B_{12})
Nicotinamide adenine dinucleotide (NAD^+)	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxyl phosphate	Amino groups	Pyridoxine (vitamin B_6)

HANDS-ON CHEMISTRY 19.2

Check the label on a bottle of multivitamin/multimineral tablets and identify any metal ion cofactors listed in Table 19.2 that are included in the supplement. Identify the dietary molecules listed in Table 19.3 as well.

KEY CONCEPT PROBLEM 19.3

The cofactors NAD^+, Cu^{2+}, Zn^{2+}, coenzyme A, FAD, and Ni^{2+} are all needed by your body for enzymatic reactions.

(a) Which cofactors are coenzymes?

(b) What is the primary difference between coenzymes and cofactors?

19.3 Enzyme Classification

Learning Objectives:

- Give an enzyme the appropriate name given the substrate.
- Assign an enzyme to the correct class based on its reaction.

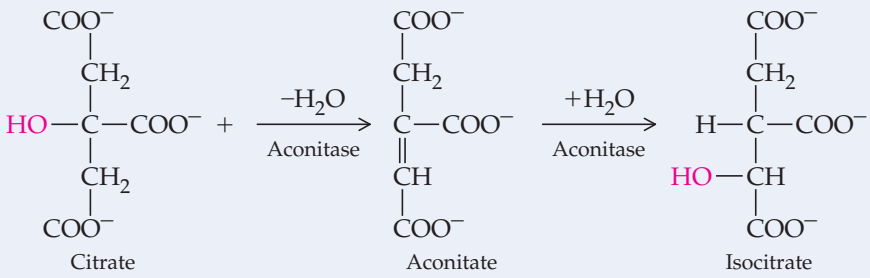
MASTERING REACTIONS

How to Read Biochemical Reactions

At first glance, biochemical reactions appear complicated. However, biochemical reactions are simply organic chemistry reactions inside living organisms. Let us look at the following reaction and dissect it for understanding.

Firstly, this is a one-way, two-step reaction catalyzed by the same enzyme for both steps where no helper molecules are needed. Like the reactions you have seen throughout the text, this reaction also occurs from left to right, with citrate as the first substrate and aconitate as the first product. Then aconitate becomes the second substrate and isocitrate forms the second (and final) product. We also see that H_2O is removed in the first step and added back in the second step. If you compare the initial substrate (citrate) to the final product (isocitrate), notice that they both have exactly the same number of C atoms, O atoms, and H atoms. Therefore, the atoms have been rearranged, but the number of atoms in product and substrate are exactly the same and of the same kind. Aconitate, however, has the same number of C atoms but one less O atom and two fewer H atoms than either citrate or isocitrate. Aconitase, then, must be an isomerase because citrate, the first substrate, and isocitrate, the final product, are isomers. Remember, only an isomerase can convert one molecule into its isomer, generally through an intermediate form as seen in this reaction.

You can use the same step-by-step process to read any biochemical reaction and identify the substrates and enzymes within the reaction.



Nomenclature of Enzymes

Most enzymes have the family-name ending *-ase*. Exceptions to this rule occur for enzymes such as papain and trypsin, which are still referred to by older common names. The more informative systematic names typically have two parts: the first identifies the substrate (reactant) on which the enzyme operates, and the second part is an enzyme class name that describes the reaction. For example, *pyruvate carboxylase* is a ligase that acts on the substrate *pyruvate* to add a *carboxyl group*. Some enzymes are named by dropping the terminal syllable and adding *-ase* to the substrate name. Fumarase, an enzyme that converts fumarate to succinate in the citric acid cycle, is one. The enzymes that act on a few other long-studied substrates such as urea and sucrose are named in the same way, that is, urease and sucrase. Note also that some enzymes are capable of catalyzing both forward and reverse reactions, and where both directions are of significance, the equations are written with double arrows.

Enzyme Classification

Thousands of enzymes keep our bodies running. Not every enzyme is found in every cell in the body; enzymes are specialists that are found only where needed. Enzymes are divided into six main classes according to the kind of reaction catalyzed, and each main class is further subdivided based on substrate specificity. Table 19.4 lists the main classes and subclasses with examples.

Table 19.4 Classification of Enzymes

	Examples
Main Class: **Oxidoreductases** catalyze oxidation–reduction reactions. **Subclasses:** *Oxidases* catalyze oxidation by addition of O_2 to a substrate. *Reductases* catalyze reduction of a substrate. *Dehydrogenases* catalyze the removal or addition of 2 H atoms and require a coenzyme.	Alcohol dehydrogenase, an *oxidoreductase,* is found in liver cells, and it oxidizes naturally occurring alcohols found in foods to aldehydes and ketones. In yeast, this enzyme provides the first step in metabolizing ethanol, a component of beer, wine, and distilled spirits. A(Reduced) + B(Oxidized) ⟶ A′(Oxidized) + B′(Reduced) $CH_3—CH_2—OH + NAD^+ \overset{\text{Alcohol dehydrogenase}}{\rightleftharpoons} CH_3—C(=O)—H + NADH + H^+$ Reduced substrate; Oxidized coenzyme; Oxidized product; Reduced coenzyme
Main Class: **Transferases** catalyze the transfer of a functional group between two different compounds. **Subclasses:** *Transaminases* catalyze the transfer of an amino group from one substrate to another using energy supplied by adenosine triphosphate (ATP). *Kinases* catalyze the transfer of phosphate groups from one substrate to another.	Phosphofructokinase, a *transferase,* transfers a phosphate group from ATP to fructose-6-phosphate to complete the energy priming process in the catabolism (degradation) of glucose. Glucose catabolism is an important energy source for our bodies and is examined in depth in Chapter 22. Glycolysis occurs in brain and muscle tissue. A + B—C ⟷ A—B + C Fructose 6-phosphate + Adenosine triphosphate $\overset{\text{Phospho-fructokinase}}{\rightleftharpoons}$ Fructose 1,6-*bis*phosphate + Adenosine diphosphate

Main Class:

Hydrolases catalyze bond breaking with the addition of water as H and OH to the fragments.

Subclasses:

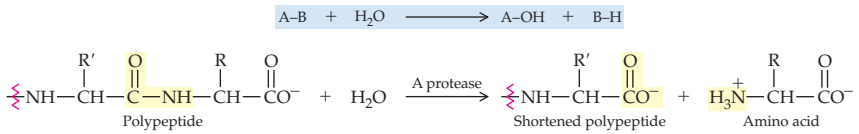
Lipases break glycerides (fats) into glycerol and fatty acids.

Proteases break proteins into peptides and amino acids.

Amylases break starch into sugars.

Nucleases break deoxyribonucleic acid (DNA) and RNA into nucleic acids.

Hydrolases are particularly important during digestion. Proteins are hydrolyzed into amino acids by various proteases, and carbohydrates such as starch, lactose, and sucrose are hydrolyzed to glucose, fructose, and galactose by specific enzymes. Hydrolases are essential to provide amino acids for protein synthesis and glucose for use in energy generating pathways.

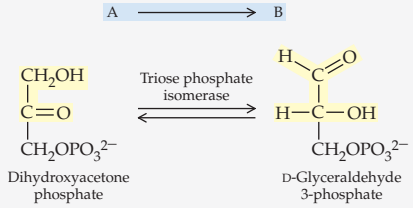


Main Class:

Isomerases catalyze the rearrangement of atoms in a substrate.

No Subclasses

During glycolysis (the breakdown of glucose to produce energy) the enzyme triose phosphate isomerase ensures that both of the products of an intermediate step can be further used. It does so by converting dihydroxyacetone phosphate, which otherwise cannot be further metabolized, to D-glyceraldehyde 3-phosphate, the substrate for the next enzyme in the glycolysis reaction sequence. Because of *isomerases,* maximum energy can be obtained from glucose metabolism. Glycolysis occurs in all cells but primarily in red blood cells, kidney, brain, and muscle tissue.



Main Class:

Lyases catalyze the addition or elimination of a functional group from a substrate without hydrolysis.

Subclasses:

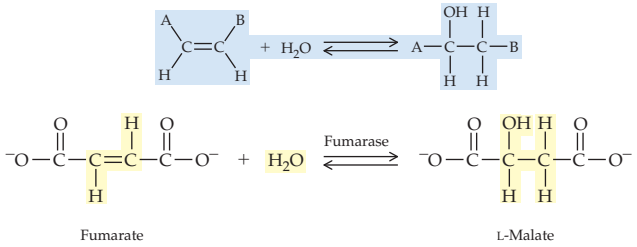
Decarboxylases catalyze the removal of CO_2.

Deaminases catalyze the removal of NH_3.

Dehydratases catalyze the removal of H_2O.

Hydratases catalyze the addition of H_2O.

Fumarase, an enzyme found in the citric acid cycle, is a *lyase.* The citric acid cycle occurs in the mitochondria of cells. Plant lyases are responsible for fruit softening and ripening by degrading pectin, a structural component of plant cell walls.



Main Class:

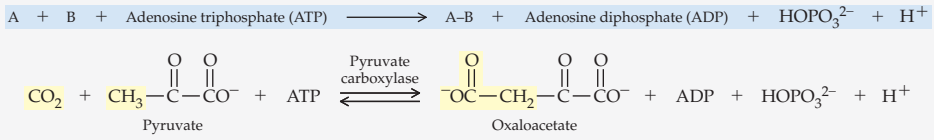
Ligases catalyze the bonding of two substrate molecules.

Subclasses:

Synthetases catalyze the formation between two substrates using ATP energy.

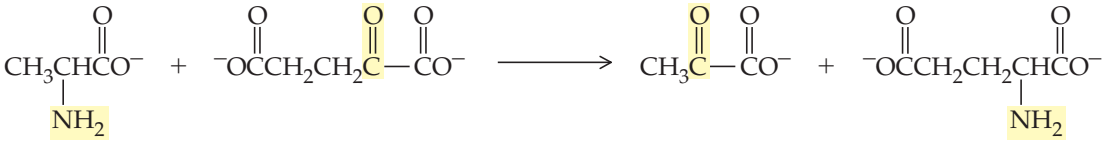
Carboxylases catalyze the formation of a bond between CO_2 and a substrate using ATP energy.

Ligases are involved in synthesis of biological polymers such as proteins and DNA. DNA ligase both repairs DNA in response to environmental damage such as ultraviolet (UV) rays from the sun or exposure to chemical carcinogens and links nucleic acids during DNA replication, which occurs in cell division during development and tissue regeneration. Protein and DNA ligases are found in nearly all cells.



Worked Example 19.1 Classifying Enzymes

To what class does the enzyme that catalyzes the following reaction belong?



ANALYSIS First, identify the type of reaction that has occurred by "reading" the chemical reaction to find what has changed. An amino group and a carbonyl keto oxygen atom have been exchanged between the two molecules, forming two different molecules. Then, determine what class of enzyme catalyzes a functional group exchange.

SOLUTION

Because the amino group and carbonyl keto oxygen atom (highlighted in yellow) have changed places, the reaction is a transfer of an amino functional group; therefore, the enzyme is a transferase.

PROBLEM 19.4

Describe the reactions that you would expect these enzymes to catalyze.

(a) Alcohol dehydrogenase
(b) Aspartate transaminase
(c) Tyrosine-tRNA synthetase
(d) Phosphohexose isomerase

PROBLEM 19.5

Name the enzyme whose substrate is

(a) Urea
(b) Cellulose

PROBLEM 19.6

To what class of enzymes does hexokinase belong? Describe in general the reaction it catalyzes.

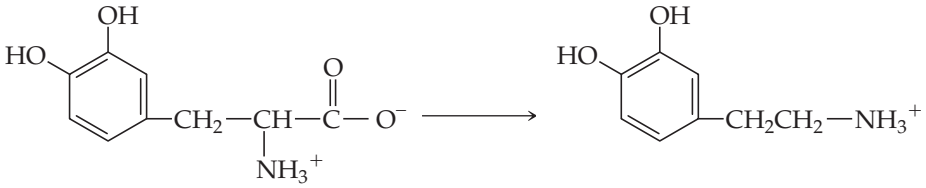
PROBLEM 19.7

Identify and describe the chemical change in the lyase-catalyzed reaction in Table 19.4 that involves fumarate and malate. Identify the substrate(s) and product(s).

PROBLEM 19.8

Which of the following reactions can be catalyzed by a decarboxylase?

(a)



(b)

19.4 How Enzymes Work

Learning Objectives:

- Explain the two models of enzyme catalysis.
- Describe how an enzyme and substrate combine to facilitate a reaction.

Enzyme *specificity* is determined by the active site, which provides the exact right environment for the reaction to take place. There, amino acid side-chain groups from the enzyme attract and hold the substrate or substrates in position through noncovalent, intermolecular forces and sometimes by temporary covalent bonding. The active site also may contain acidic or basic side chains needed for catalysis of the reaction.

Descriptions of catalysis reactions are often written in general symbols: E (enzyme), S (substrate), P (product), [P] (concentration of product), ES (enzyme–substrate complex), and EP (enzyme–product complex). A reaction is written as

$$E + S \longrightarrow ES \longrightarrow EP \longrightarrow E + P$$

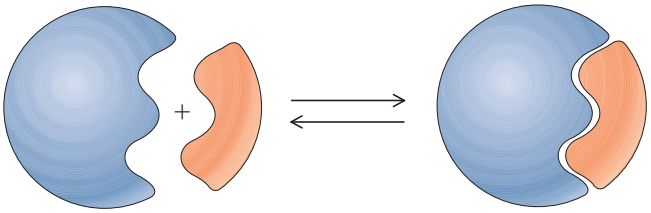
Instead of

$$\text{Enzyme} + \text{Substrate} \longrightarrow \text{Enzyme–substrate complex} \longrightarrow \text{Enzyme–product complex} \longrightarrow \text{Enzyme} + \text{Product}$$

Two Models of Enzyme–Substrate Interaction

Two models explain the interaction between substrates and enzymes. Historically, the **lock-and-key model** came first; it was proposed when the need for a spatial fit between substrates and enzymes was first recognized. The substrate is described as fitting into the active site as a key fits into a lock; the fit is rigid and unchanging, and only one substrate fits one specific enzyme, just like a key for a lock.

Lock-and-key model A model of enzyme action in which the enzyme is a rigid lock that exactly fits the substrate, the key for the reaction.



When it became possible to study enzyme–substrate interaction more closely, experimental results suggested the *lock-and-key model* was incorrect. Modern understanding of molecular structure makes it clear that enzyme molecules are not totally rigid, like locks. The **induced-fit model** accounts for changes in the shape of the enzyme active site that accommodates the substrate (and other, similar substrates) and facilitates the reaction. As an enzyme and substrate come together, their interaction induces exactly the right fit for catalysis of the reaction.

Induced-fit model A model of enzyme action in which the enzyme has a flexible active site that changes shape to best fit the substrate and catalyze the reaction.

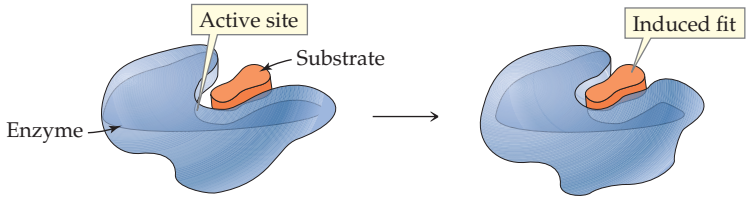
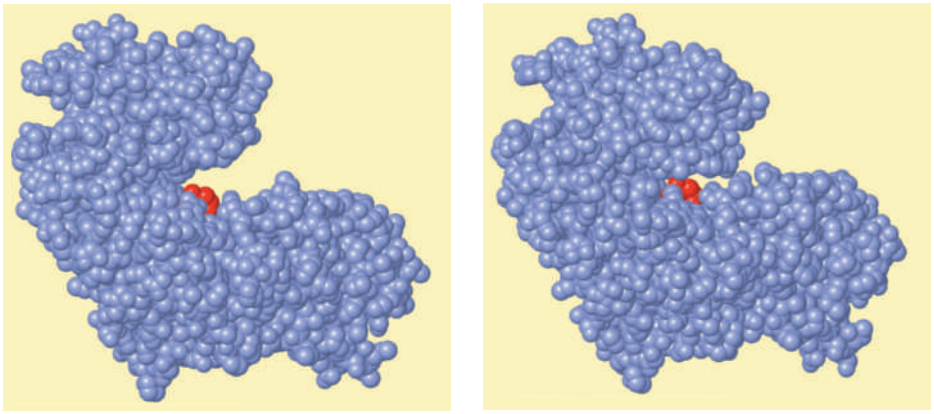


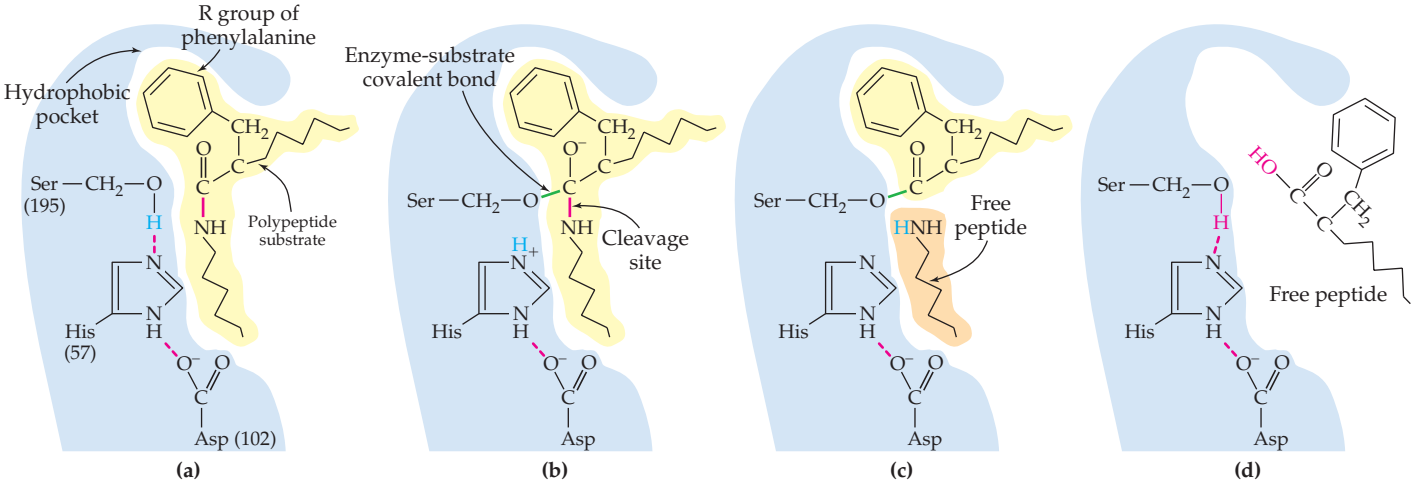
Figure 19.3 illustrates a well-studied example of induced fit, the interaction between glucose (a hexose) and hexokinase. The transferase reaction is a phosphorylation—the addition of a phosphoryl group to a —OH group—catalyzed by a kinase. The reaction is the first step in glucose metabolism (Section 22.3). Notice in Figure 19.3 on the following page how the enzyme closes in once the glucose molecule has entered the active site—this is the induced fit.



▶ **Figure 19.3**
A space-filling model showing the induced fit of hexokinase (blue) and its substrate, glucose (red).
(a) The active site is a groove in the hexokinase molecule. (b) When glucose enters the active site, the enzyme changes shape, wrapping itself more closely around the substrate.

Enzyme-catalyzed reactions begin with migration of the substrate (S) or substrates into the active site of the enzyme (E) to form an *enzyme–substrate complex* (ES). The substrate is first drawn into position by the same kinds of noncovalent forces that govern the shapes of protein molecules (see Figure 19.4).

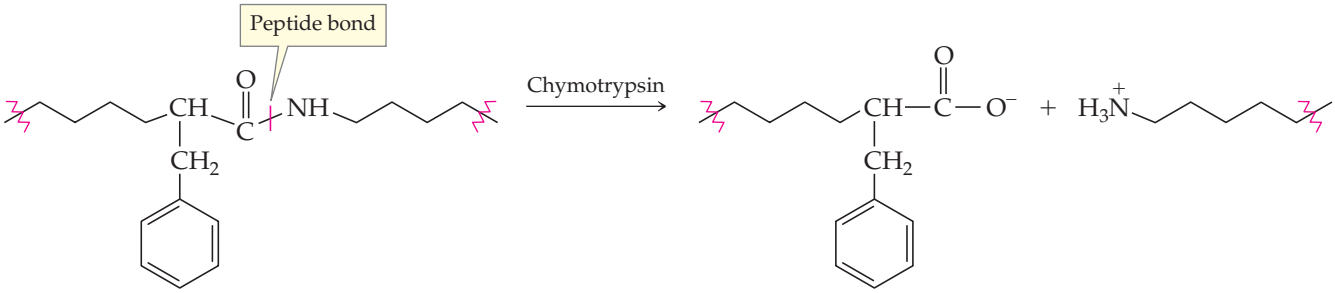
Before forming an enzyme–substrate complex, the substrate molecule is in its most stable, lowest-energy shape. Within the enzyme–substrate complex, the substrate is forced into a less stable shape, and bonding electrons may be drawn away from some bonds in preparation for breaking them and forming new bonds. The result is that the *activation energy barrier between substrate and product is lowered* without the need for a large energy input. This is shown in the energy diagram on page 625 comparing the energy input needed for a purely chemical reaction with the same reaction catalyzed by an enzyme.



▲ **Figure 19.4**
Hydrolysis of a peptide bond by chymotrypsin.
(a) The polypeptide enters the enzyme active site with its hydrophobic side chain (the aromatic ring) in the hydrophobic pocket and the peptide bond to be broken (red) opposite serine and histidine residues. (b) H^+ transfer from serine to histidine allows formation of a strained intermediate in which the serine side chain bonds to the peptide bond carbon (green). (c) The peptide bond is broken and the segment with the new terminal $—NH_2$ group leaves the active site. (d) In subsequent steps, a water molecule enters the active site; its H atom restores the serine side chain and its —OH bonds to the other piece of the substrate protein to give a new terminal —COOH group so that this piece can also leave the active site.

Within the enzyme–substrate complex, atoms that will form new bonds must connect with each other. The new bonds might be with a second substrate or temporary bonds with atoms in the enzyme. Also, groups needed for catalysis must be close to the correct locations in the substrate. Many organic reactions, for example, require acidic, basic, or metal ion catalysts. An enzyme's active site can provide acidic and basic groups without disrupting the constant-pH environment in body fluids, while the necessary metal ions are present as cofactors. Once the chemical reaction is completed, enzyme and product molecules separate from each other and the enzyme, restored to its original condition, becomes available for another substrate molecule.

The hydrolysis of a peptide bond by chymotrypsin, shown in Figure 19.4, illustrates how an enzyme functions. Chymotrypsin is one of several enzymes active in the digestion of proteins by breaking them down to smaller molecules. It cleaves polypeptide chains by breaking the peptide bond on the carbonyl side of amino acid residues that include an aromatic ring.



The enzyme–substrate complex forms (Figure 19.4a and b) due to stabilization of a substrate hydrophobic side chain (here, the aromatic ring) in a hydrophobic pocket in the enzyme active site by intermolecular forces and the subsequent formation of a covalent bond (green) to the substrate. The result is to position the substrate with the peptide bond to be broken (red) next to the amino acid side chains that function as catalysts. The enzyme has not only bound to the substrate (the *proximity effect*) but has done so in such a way as to bring the groups that must connect close to each other (the *orientation effect*). Aspartate, histidine, and serine provide functional groups needed for catalysis within the active site (the *catalytic effect*). As an illustration of the critical nature of protein folding, note that in the 241-amino-acid primary structure of chymotrypsin, aspartate is number 102, histidine is number 57, and serine is number 195. These amino acids are distant from each other along the linear backbone but are brought close together by backbone folding so that their side chains are in exactly the positions needed in the active site.

With the peptide bond carbon atom temporarily bonded to serine in the active site, it is easier for the peptide bond to break because the activation energy barrier has been lowered (the *energy effect*). As the bond breaks, nitrogen picks up a hydrogen atom (blue) from histidine to form the new terminal amino group and this portion of the substrate is set free (Figure 19.4c). Reaction with a water molecule restores the hydrogen to serine and supplies an OH group to form the new terminal carboxyl group of the shortened peptide. This part of the substrate is set free and the enzyme is restored to its original state (Figure 19.4d).

In summary, enzymes act as catalysts because of their following abilities to:

- Bring substrates and catalytic sites together *(proximity effect)*
- Hold substrates at the exact distance and in the exact orientation necessary for reaction *(orientation effect)*
- Provide acidic, basic, or other types of groups required for catalysis *(catalytic effect)*
- Lower the energy barrier by inducing strain in bonds in the substrate molecule *(energy effect)*

Worked Example 19.2 Identifying active site side-chain functions

Look at the hydrolysis of a peptide bond by chymotrypsin in Figure 19.4.

(a) Which amino acids have side chains that could provide stabilization to the aromatic ring shown in the substrate?

(b) What does the serine side chain do in the reaction and why can it do this?

(c) What does the histidine side chain do in the reaction and why can it do this?

ANALYSIS Look critically at the diagrams of the reaction in Figure 19.4 to follow the movement of atoms. Consider each part of the question separately, using the diagrams as an aid.

(a) Note that the aromatic ring of phenylalanine fits into a "hydrophobic pocket." Therefore, the side chains of the amino acids surrounding this pocket in chymotrypsin must be nonpolar.

(b) In the second diagram, note that serine has donated a hydrogen ion to histidine. Remember that acids are proton donors.

(c) Also in the second diagram, note that histidine has accepted a proton from serine. Remember that bases are proton acceptors.

SOLUTION

(a) Any of the following nonpolar amino acids could be part of the hydrophobic pocket in chymotrypsin: alanine, leucine, isoleucine, methionine, proline, valine, phenylalanine, or tryptophan (see Table 18.3).

(b) Serine is a polar amino acid and can donate a proton from the —OH group on the side chain, functioning as an acid. The RO^- remaining can interact with the substrate, initiating cleavage of the substrate.

(c) Histidine is a basic amino acid and can accept a proton until needed to complete the cleavage reaction.

In this example, nonpolar amino acids held the substrate in place via weak intermolecular forces while amino acids that could act as acids or bases carried out the reaction.

KEY CONCEPT PROBLEM 19.9

The active sites of enzymes usually contain amino acids with acidic, basic, and polar side chains. Some enzymes also have amino acids with nonpolar side chains in their active sites. Which types of side chains would you expect to participate in holding the substrate in the active site? Which types would you expect to be involved in the catalytic activity of the enzyme?

19.5 Factors Affecting Enzyme Activity

Learning Objective:

- Describe the changes in enzyme activity that result when substrate concentration, enzyme concentration, temperature, or pH change.

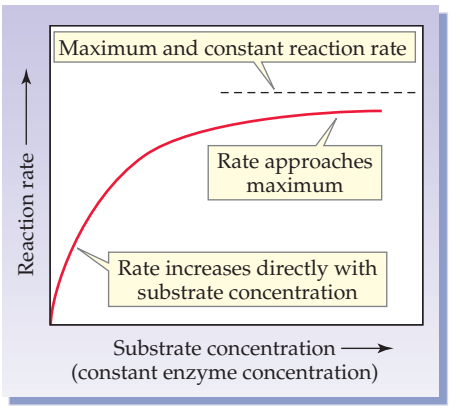
For a reaction to occur, the enzyme and substrate molecules must come together and form the enzyme–substrate complex. There are several factors that affect enzyme activity and cause a variation in the reaction rate. Substrate concentration, enzyme concentration, temperature, and pH all affect reaction rates. Enzymes have been finely tuned through evolution so that their maximum catalytic activity is dependent on these four factors. As you might expect, optimum conditions vary for each enzyme.

Substrate Concentration

Frequently, in cells, the substrate concentration varies while the enzyme concentration remains unchanged. If the substrate concentration is low relative to that of the enzyme, not all the enzyme molecules are in use. The reaction rate will increase as the concentration of substrate increases because more of the enzyme molecules are put to work. In this situation, shown at the far left of the curve in Figure 19.5, the rate increases as the available substrate increases. Initially, this is a directly proportional relationship, so if the substrate concentration doubles, the reaction rate doubles. However, as the substrate concentration continues to increase, the increase in the rate begins to level off as more of the active sites are occupied. (Think of people waiting in line to take their seats in a theater. The line moves more slowly as more seats fill and it becomes more difficult to find an empty one.) Eventually, the substrate concentration reaches a point at which none of the available active sites are free; the enzyme is saturated with substrate. The reaction rate is now determined by how fast the enzyme–substrate complex is converted to product. Since the maximum number of enzyme molecules are converting substrate to product at the same time, the rate of conversion from substrate to product occurs at the maximum rate for that reaction.

Once the enzyme is saturated, increasing substrate concentration has no effect on the rate. In the absence of a change in the concentration of the enzyme, the rate when the enzyme is saturated is determined by the efficiency of the enzyme, the pH, and the temperature.

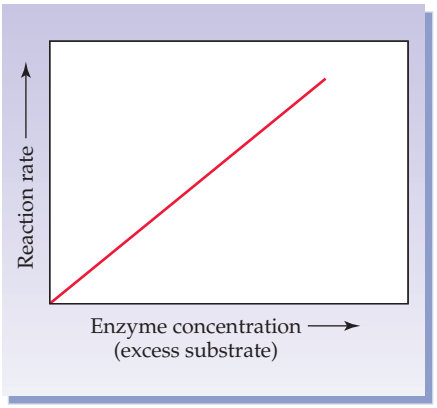
Under most conditions, an enzyme is not likely to be saturated. Therefore, at a given pH and temperature, the reaction rate is controlled by the amount of substrate and the overall efficiency of the enzyme. If the enzyme–substrate complex is rapidly converted to product, the rate at which enzyme and substrate combine to form the complex becomes the limiting factor. Calculations show an upper limit to this rate: enzyme and substrate molecules moving at random in solution can collide with each other no faster than 10^8 collisions per mole per liter per second. Remarkably, a few enzymes actually operate close to this efficiency—every one of the collisions results in the formation of product! We saw an example of such an efficient enzyme earlier in catalase, the enzyme that breaks down hydrogen peroxide at the rate of 10^7 catalytic events per second (see Table 19.1).



▲ **Figure 19.5**
Change of reaction rate with substrate concentration when enzyme concentration is constant.
At low substrate concentration, the reaction rate is directly proportional to the substrate concentration (at constant pH and temperature). With increasing substrate concentration, the increase in rate slows as more of the active sites are occupied. Eventually, with all active sites occupied, the rate reaches a maximum and constant rate.

Enzyme Concentration

It is possible for the concentration of an active enzyme to vary according to our metabolic needs. So long as the concentration of substrate does not become a limitation, the reaction rate varies directly with the enzyme concentration (Figure 19.6). If the enzyme concentration doubles, the rate doubles; if the enzyme concentration triples, the rate triples; and so on.



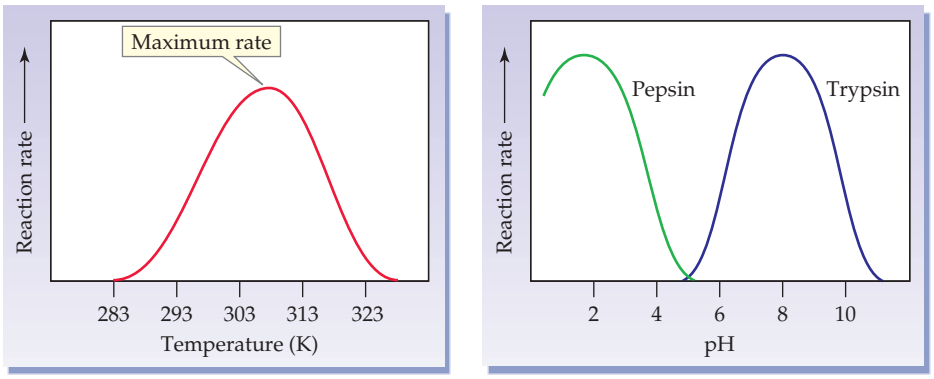
▲ **Figure 19.6**
Change of reaction rate with enzyme concentration in the presence of excess substrate.

Effect of Temperature on Enzyme Activity

An increase in temperature increases the rate of most chemical reactions, and enzyme-catalyzed reactions are no exception. Unlike many simple reactions, however, the rates of enzyme-catalyzed reactions do not increase continuously with rising temperature. Instead, the rates reach a maximum and then begin to decrease, as shown in Figure 19.7a on the following page. This falloff in rate occurs because enzymes begin to denature when heated too strongly. The noncovalent attractions between protein side chains are disrupted, the delicately maintained three-dimensional shape of the enzyme begins to come apart, and as a result, the active site needed for catalytic activity is destroyed.

Most enzymes denature and lose their catalytic activity above 323–333 K (50–60 °C), a fact that explains why medical instruments and laboratory glassware are sterilized by heating with steam in an autoclave. The high temperature of the steam permanently denatures the enzymes of any bacteria present, killing them.

◀◀ Review the chemical properties of proteins in Section 18.12.



▶ Figure 19.7
Effect of temperature (a) and pH (b) on reaction rate.
(a) The reaction rate increases with increasing temperature until a temperature is reached at which the enzyme begins to denature; then the rate decreases rapidly. (b) The optimum activity for an enzyme occurs at the pH where it acts, as illustrated for two protein hydrolysis enzymes—pepsin, which acts in the highly acidic environment of the stomach, and trypsin, which acts in the small intestine, an alkaline environment.

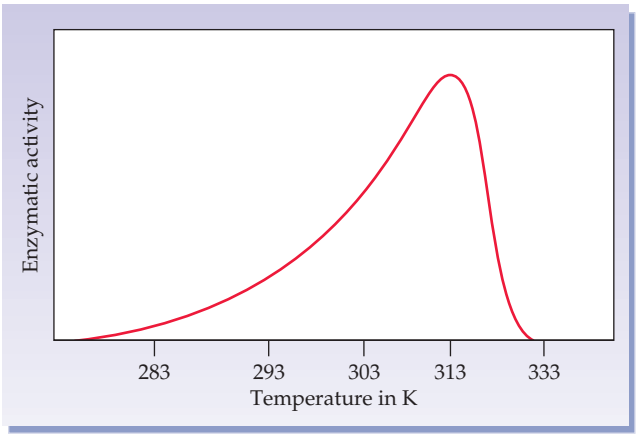
A severe drop in body temperature creates the potentially fatal condition of hypothermia, which is accompanied by a slowdown in metabolic reactions. This effect is used to advantage by cooling the body during cardiac surgery. Upon gentle warming, enzymatic reaction rates return to normal because cooling does not denature proteins.

Effect of pH on Enzyme Activity

The catalytic activity of many enzymes depends on pH and usually has a well-defined optimum point at the normal, buffered pH of the enzyme's environment. For example, pepsin, which initiates protein digestion in the highly acidic environment of the stomach, has its optimum activity at pH 2 (Figure 19.7b). By contrast, trypsin—like chymotrypsin, an enzyme that aids digestion of proteins in the small intestine—has optimum activity at pH 8. Most enzymes have their maximum activity between the pH values of 5–9. Eventually, both extremes of pH will denature a protein. The "typical" body pH is the pH of the blood, pH 7.4. pH extremes that change the pH of the blood significantly are highly damaging to body tissues; that is why swallowing concentrated HCl (pH 1 or less) or drain cleaner (mostly NaOH, pH 14 or more) is often fatal.

Worked Example 19.3 Enzymatic Activity: Determining Optimum Temperature

Consider the following temperature activity curve. Enzymatic activity is shown for muscle LDH from 273 K (0 °C) to 333 K (60 °C), Suppose you wish to test a sample for LDH activity; what is the best temperature for the test?

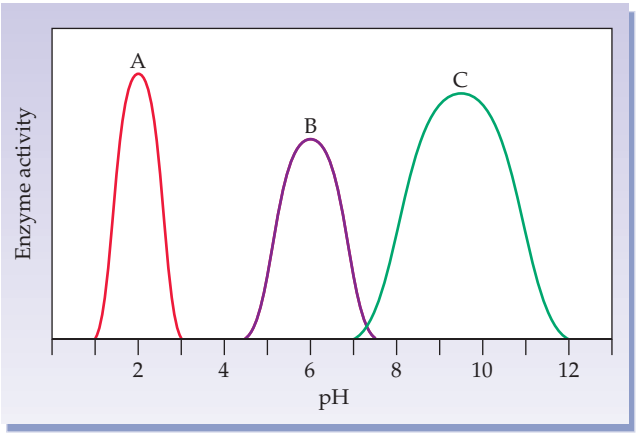


ANALYSIS An enzyme shows its highest catalytic activity at a certain temperature, with less activity at temperatures below and above the optimum temperature. Look at the curve of activity versus temperature and find the highest point on the curve—that point represents the optimum activity.

SOLUTION
From the highest point on the curve of activity versus temperature, drop a vertical line down to the *x*-axis (the one that reads "Temperature") to find the optimum temperature. The temperature optimum for LDH is 313 K (40 °C).

Worked Example 19.4 Enzymatic Activity: Determining Optimum pH

Enzymatic activity is shown for three different enzymes as a function of pH in the following graph. What is the optimum pH for pepsin (curve A), for urease (curve B), and for alanine dehydrogenase (curve C)?



ANALYSIS Recall that the optimum pH is the pH at which the enzyme shows the highest activity; therefore, the highest point on the curve, representing maximum activity, is the optimum pH for the enzyme.

SOLUTION
Find the correct curve for each enzyme and the peak of each activity curve. Drop a vertical line to the pH axis and read the optimum pH directly from the axis scale. The optimum pH for pepsin is approximately 2.0, that for urease approximately 6.0, and that for alanine dehydrogenase approximately 9.5.

KEY CONCEPT PROBLEM 19.10

What do we mean when we say an enzyme is saturated with substrate? When an enzyme is saturated with substrate, how does adding more (a) substrate and (b) enzyme affect the rate of the reaction?

PROBLEM 19.11

Will the reaction catalyzed by the enzyme represented in Figure 19.7a have a higher rate of reaction at 298 K (25 °C) or at 308 K (35 °C)? Will it have a higher rate of reaction at 308 K (35 °C) or at 318 K (45 °C)?

PROBLEM 19.12

How will the rates of the reaction catalyzed by pepsin (Figure 19.7b) compare at pH 2 and pH 4?

19.6 Enzyme Regulation: Inhibition

Learning Objectives:

- Define and identify reversible and irreversible inhibition.
- Define and identify uncompetitive and competitive inhibition.

In the body, the concentrations of thousands of different compounds must vary continuously to meet changing conditions as we eat, sleep, exercise, or fall ill. Enzymes do more than just speed up reactions; at a moment's notice, they turn some reactions off, slow some down, or quickly accelerate others to their maximum possible rate. Clearly, then, the enzymes themselves must be regulated. How is this regulation achieved?

A variety of strategies adjust the rates of enzyme-catalyzed reactions. Any process that starts or increases the action of an enzyme is **activation.** Conversely, any process that slows or stops the action of an enzyme is **inhibition.** Although we will describe the strategies of enzyme control one by one, keep in mind that several strategies usually operate together. Considering that a cell contains thousands of proteins—many molecules of some proteins and only a few molecules of other proteins—and hundreds of

Activation (of an enzyme) Any process that initiates or increases the action of an enzyme.

Inhibition (of an enzyme) Any process that slows or stops the action of an enzyme.

other kinds of biomolecules, all in concentrations required to maintain constant conditions, the achievement of enzyme control by the body is awe-inspiring.

The inhibition of an enzyme can be *reversible* or *irreversible*. In reversible inhibition, the inhibitor can leave, restoring the enzyme to its uninhibited level of activity. In irreversible inhibition, the inhibitor remains permanently bound and the enzyme is permanently inhibited. The inhibition can also be *competitive, uncompetitive,* or *mixed,* depending on whether the inhibitor binds to the active site, the substrate, or some combination of enzyme and substrate.

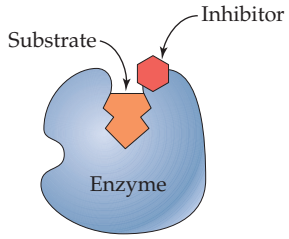
Uncompetitive (enzyme) inhibition Enzyme regulation in which an inhibitor binds reversibly to the enzyme–substrate complex, blocking the binding of the second substrate to the active site.

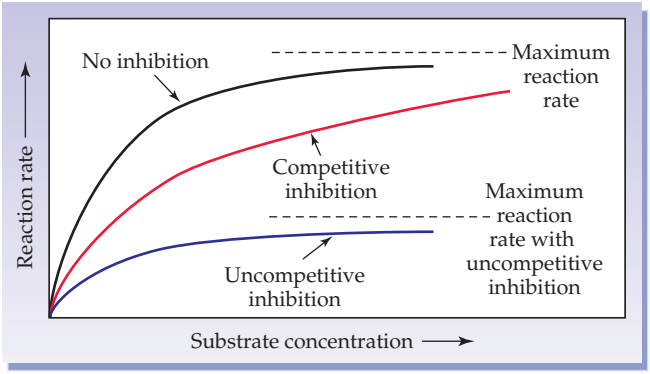
Reversible Uncompetitive Inhibition

In **uncompetitive inhibition,** the inhibitor does not compete with the substrate for the active site and cannot bind to enzyme alone. An uncompetitive inhibitor exerts control by binding to the enzyme–substrate complex so that the reaction occurs less efficiently or not at all. This type of inhibition is reversible and often occurs in reactions where two substrates are involved.

In Figure 19.8, reaction rates with and without an uncompetitive inhibitor are compared in the bottom and top curves. With the inhibitor, the reaction rate increases with increasing substrate concentration more gradually than when no inhibitor is present. The maximum rate is lowered, and once that rate is reached, no amount of substrate can increase it further. As long as the inhibitor is present at constant concentration, this upper limit does not change.

Uncompetitive inhibition





▸ Figure 19.8
Enzyme inhibition. The top curve and dashed line show the reaction rate and maximum rate with no inhibitor. With a competitive inhibitor (middle curve), the maximum rate is unchanged, but a higher substrate concentration is required to reach it. With an uncompetitive inhibitor (bottom curve), the maximum rate (bottom dashed line) is lowered.

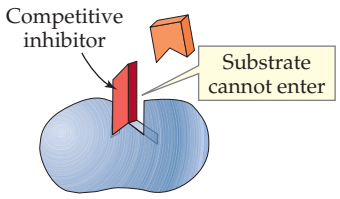
Reversible Competitive Inhibition

What happens if an enzyme encounters a molecule very much like its normal substrate in shape, size, and functional groups? The impostor molecule enters the enzyme's active site, binds to it, and thereby prevents the usual substrate molecule from binding to the same site. Consequently, the enzyme is tied up, making it unavailable as a catalyst. This situation is called **competitive inhibition**—the inhibitor *competes* with substrate for binding to the active site. A competitive inhibitor binds reversibly to an active site through noncovalent interactions but undergoes no reaction. While it is there, it prevents the substrate from entering the active site.

Competitive (enzyme) inhibition Enzyme regulation in which an inhibitor competes with a substrate for binding to the enzyme active site.

$$\text{Substrate} + \text{Enzyme} \rightleftharpoons \text{Substrate–enzyme complex}$$
$$\text{Inhibitor} + \text{Enzyme} \rightleftharpoons \text{Inhibitor–enzyme complex}$$

Competitive inhibition



Whether the substrate or the inhibitor occupies the active site depends on their relative concentrations. A substrate in relatively high concentration occupies more of the active sites, so the reaction is less inhibited. An inhibitor in relatively high concentration occupies more of the active sites, so the reaction is more inhibited.

The middle curve in Figure 19.8 shows that in the presence of a competitive inhibitor at constant concentration, the reaction rate increases more gradually with increasing substrate concentration than when there is no inhibitor present. Unlike uncompetitive inhibition, however, the maximum reaction rate is unchanged. Eventually, all of an enzyme's active sites can be occupied by substrate, but a higher substrate concentration is required to reach that condition.

The product of a reaction may be a competitive inhibitor for the enzyme that catalyzes that reaction. For example, glucose 6-phosphate is a competitive inhibitor for hexokinase, which catalyzes formation of this phosphorylated form of glucose. Thus, when supplies of glucose 6-phosphate are ample, glucose is available for other reactions.

A competitive inhibitor is sometimes used in treating an unhealthy condition because the inhibitor mimics the structure of the substrate and fits into the enzyme's active site. For example, competitive inhibition is used to good advantage in the treatment of methanol poisoning. Although not harmful itself, methanol (wood alcohol) is oxidized in the body to formaldehyde, which is highly toxic ($CH_3OH \longrightarrow H_2C{=}O$). Because of its molecular similarity to methanol, ethanol acts as a competitive inhibitor of alcohol dehydrogenase. With the oxidation of methanol blocked by ethanol, methanol is excreted without causing harm. Thus, the medical treatment of methanol poisoning includes administering ethanol, to avoid blindness or death of the patient.

Another example of reversible inhibition involves lead poisoning. Lead can poison animals, including humans, in two ways. One way is by displacing an essential metal cofactor from the active site of an enzyme. When lead displaces zinc in an enzyme essential to the synthesis of heme, the oxygen-carrying part of hemoglobin, the enzyme becomes inactive and anemia can result. Physicians treat this sort of lead poisoning with chelation therapy. Ethylenediaminetetraacetic acid (EDTA) forms coordinate covalent bonds preferentially with lead in the body, and lead is then excreted in the urine as a chelated compound.

The second way lead can poison involves the process known as irreversible inhibition, the topic we look at next.

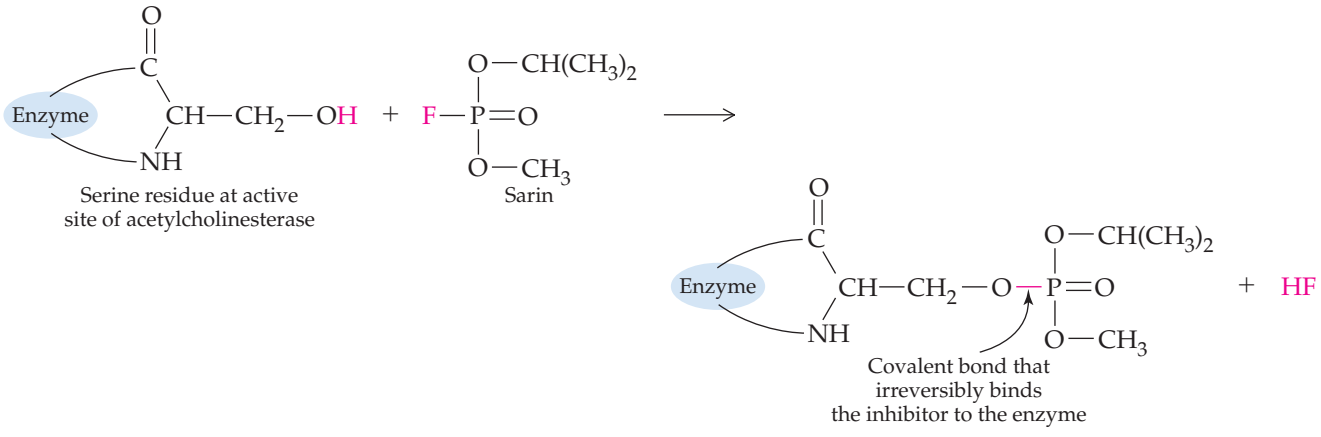
Irreversible Inhibition

If an inhibitor forms a bond that is not easily broken with a group in an active site, the result is **irreversible inhibition.** The enzyme's reaction cannot occur because the substrate cannot connect appropriately with the active site. Many irreversible inhibitors are poisons as a result of their ability to completely shut down the active site. Heavy metal ions, such as mercury (Hg^{2+}) and lead (Pb^{2+}), are irreversible inhibitors that form covalent bonds to the sulfur atoms in the —SH groups of cysteine residues.

Irreversible (enzyme) inhibition
Enzyme deactivation in which an inhibitor forms covalent bonds to the active site, permanently blocking it.

Often, heavy metal ions like lead and mercury affect enzymes that function in the nervous system. At low levels, lead can cause decreased attention span and mental difficulties. These symptoms are noticed in children who eat flakes of lead-containing paint, which have a sweet taste. Primarily, for this reason, lead-containing paint has not been used since the 1950s, but it is often still present in older homes. Small amounts of mercury in the diet cause similar problems. For this reason, children and pregnant women are advised to severely limit their intake of fish, particularly large deep-sea fish such as tuna. Tuna accumulate mercury in their tissues; the mercury is absorbed from our digestive system and remains in our bodies.

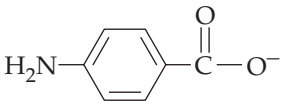
Organophosphorus insecticides, such as parathion and malathion, and nerve gases, such as Sarin, are irreversible inhibitors of the enzyme acetylcholinesterase, which breaks down a chemical messenger *(acetylcholine)* that transmits nerve impulses (Section 28.7). The acetylcholinesterase inhibitors bond covalently to a serine residue in the enzyme's active site.



Normally, acetylcholinesterase breaks down acetylcholine immediately after that molecule transmits a nerve impulse. Removal of acetylcholine "resets" the receiving cells, getting them ready to receive further signals. Without acetylcholinesterase activity, accumulating acetylcholine blocks transmission of further nerve impulses, resulting in paralysis of muscle fibers and death from respiratory failure. Sarin, one of the most toxic nerve agents, is now classified by the United Nations as a weapon of mass destruction, as exposure can be fatal. There is no effective treatment to counteract this irreversible inhibitor of acetylcholinesterase.

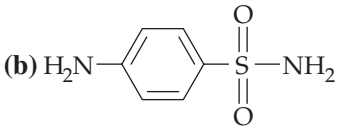
PROBLEM 19.13

Could either of the following molecules be a competitive inhibitor for the enzyme that has *p*-aminobenzoate as its substrate? If so, why?



p-Aminobenzoate, the substrate

(a) $H_2NCH_2CH_3$



(b)

PROBLEM 19.14

What kind of reaction product might be a competitive inhibitor for the enzyme that catalyzes its formation?

19.7 Enzyme Regulation: Allosteric Control and Feedback Inhibition

Learning Objectives:

- Define and identify allosteric control.
- Define feedback control and explain how it regulates enzyme catalysis.

In Section 19.6, we explored enzyme regulation by inhibition of activity, both reversible and irreversible, which required specific kinds of binding of substrate and inhibitor to the enzyme. Now, we look at two other common methods of enzyme regulation: allosteric control and feedback control. Both of these enzyme regulation methods also require the regulators to bind to the enzyme, but differently from inhibition regulation.

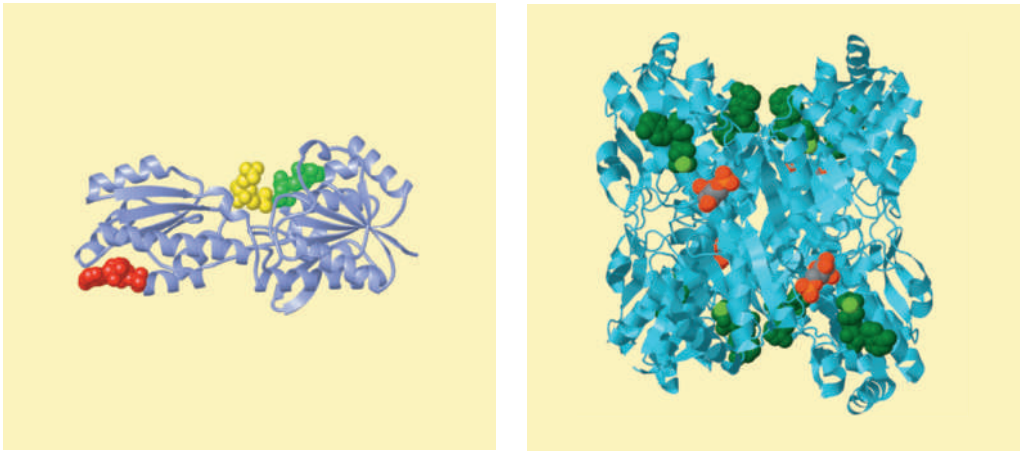
Allosteric Control

Allosteric control An interaction in which the binding of a regulator at one site on a protein affects the protein's ability to bind another molecule at a different site.

Allosteric enzyme An enzyme whose activity is controlled by the binding of an activator or inhibitor at a location other than the active site.

Many enzymes are regulated by *allosteric* control (from the Greek *allos,* meaning "other" and *steros,* meaning "space"). In **allosteric control,** the binding of a molecule (an *allosteric regulator* or *effector*) at one site on a protein affects the binding of another molecule at a different site. Most **allosteric enzymes** have more than one protein chain and two kinds of binding sites—those for substrates and those for regulators (Figure 19.9). Binding of a regulator, usually by noncovalent intermolecular forces, changes the shape of the enzyme. This change alters the shape of the active site, affecting the ability of the enzyme to bind its substrate and catalyze its reaction. One advantage of allosteric enzyme control is that the regulators need not be structurally similar to the substrate because they do not bind to the active site.

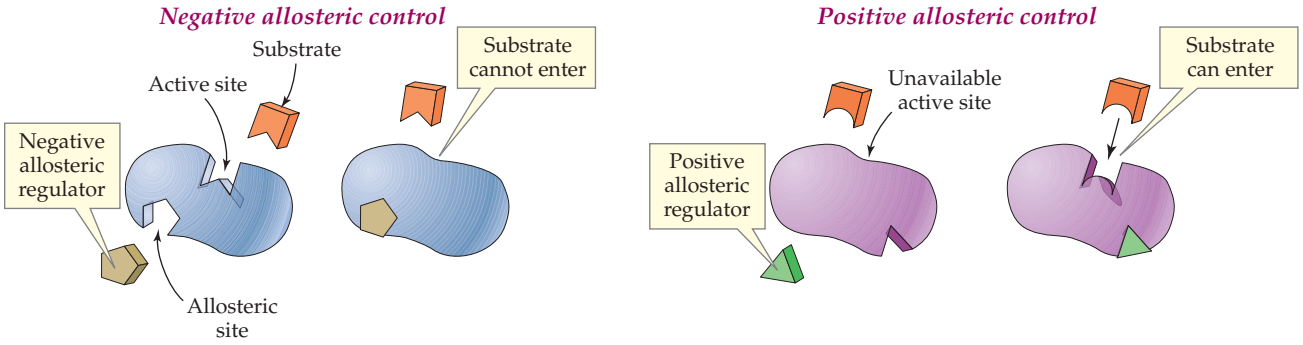
Allosteric control of an enzyme by regulator molecules can be either positive or negative but always involves subtle shape changes in the enzyme. Binding a positive regulator changes an unavailable active site so that the substrate can fit into the active site and the reaction occurs. The presence of positive allosteric regulator molecules increases the reaction rate. Conversely, binding a negative regulator changes the active site so that the enzyme can no longer bind substrate to the active site, slowing the



(a) (b)

▲ **Figure 19.9**
An allosteric enzyme
(a) One of the four identical subunits in phosphofructokinase, an enzyme that catalyzes transfer of a phosphoryl group from ATP to fructose 6-phosphate (see transferase reaction in Section 19.3). The subunit is shown after the reaction has occurred and contains the reaction product fructose-1, 6-bisphosphate; a molecule formed in the third step of glycolysis. The diphosphate portion of the phosphorylated substrate (yellow) and adenosine diphosphate (ADP) (green) are in the active site and the allosteric activator (red, also ADP) in the regulatory site. (b) The four subunits of the complete enzyme are shown in blue. ADP (green), the cofactor, is shown in the active site and ADP (red) that acts as the allosteric activator is shown in the regulatory site. Note that there is one cofactor and one regulator molecule per protein chain.

reaction. Because allosteric enzymes can have several substrate binding sites and several regulator-binding sites and because there may be interaction among them, very fine control is achieved.



Feedback Control

As you will see in subsequent chapters, biochemical reaction pathways are dependent on a series of consecutive reactions in which the product of one reaction is the reactant for the next. Such pathways are subject to *feedback control,* which occurs when the result of a process feeds information back to affect the beginning of the process. Any device that maintains a constant temperature, such as an oven, is regulated by feedback control. Ovens have sensors that detect temperature and feed back that information to turn heating elements on or off.

Consider a biochemical pathway in which A is converted to B, then B is converted to C, and so on, with each reaction catalyzed by its own enzyme:

$$A \xrightarrow{\text{Enzyme 1}} B \xrightarrow{\text{Enzyme 2}} C \xrightarrow{\text{Enzyme 3}} D$$

Feedback control Regulation of an enzyme's activity by the product of a reaction later in a pathway.

What happens if product D inhibits enzyme 1? This inhibition causes the amount of A converted to B to decrease, so the synthesis of B and C decrease in turn. The effect of this **feedback control** mechanism is to control the concentration of D. When more D is present than is needed for other biochemical pathways, enzyme 1 is inhibited and its reaction is slowed or stopped. By inhibiting the first enzyme in the pathway, no energy is wasted making the unneeded intermediates B and C. When the amount of available D decreases as it is used up in other reactions, any D bound to enzyme 1 dissociates. Soon, there is no D available for feedback control. As a result, enzyme 1 is no longer inhibited and the production of D accelerates.

Feedback control typically occurs at points in a pathway where control is critical. In the pathway above, this point is the conversion of A to B by enzyme 1. The intermediates B and C are not used in other metabolic pathways (the pathway is unbranched); B and C are made only in order to convert A to D, so it is not important for the cell to continue to synthesize either of the intermediates. Thus, from an energetic standpoint, it makes the most sense for product D to regulate the first step in the pathway. Pyruvate dehydrogenase and citrate synthase, enzymes involved in sugar metabolism, and aspartate transcarboxylase, the first enzyme in the pyrimidine synthesis pathway, are examples of enzymes regulated by feedback control.

Worked Example 19.5 Determining Feedback Control Points

Look at the three-step pathway (reaction route) for the conversion of 3-phosphoglycerate to serine:

$$\text{3-phosphoglycerate} \xrightarrow{1} \text{3-phosphohydroxypyruvate} \xrightarrow{2} \text{3-phosphoserine} \xrightarrow{3} \text{serine}$$

When the cell has plenty of serine available, which enzyme in the pathway, 1, 2, or 3, is most likely to be inhibited?

ANALYSIS This is a simple, linear pathway. The pathway is most likely controlled by feedback control of the final product.

SOLUTION
Assuming that feedback control is the simplest control mechanism for this linear pathway, serine, the product of the pathway, will inhibit the first enzyme in the pathway when sufficient serine is available in the cell.

PROBLEM 19.15

(a) L-Threonine is converted to L-isoleucine in a linear pathway involving five separate enzymes. Which of the enzymes in the following pathway is most likely inhibited by the product of the pathway, L-isoleucine?

$$\text{L-threonine} \xrightarrow{E1} A \xrightarrow{E2} B \xrightarrow{E3} C \xrightarrow{E4} D \xrightarrow{E5} \text{L-isoleucine}$$

(b) If product A inhibited the first enzyme in the pathway (E1), could this be called feedback control? Explain.

19.8 Enzyme Regulation: Covalent Modification and Genetic Control

Learning Objectives:

- Define and identify inhibition by covalent modification.
- Define and identify inhibition by genetic control of enzymes.

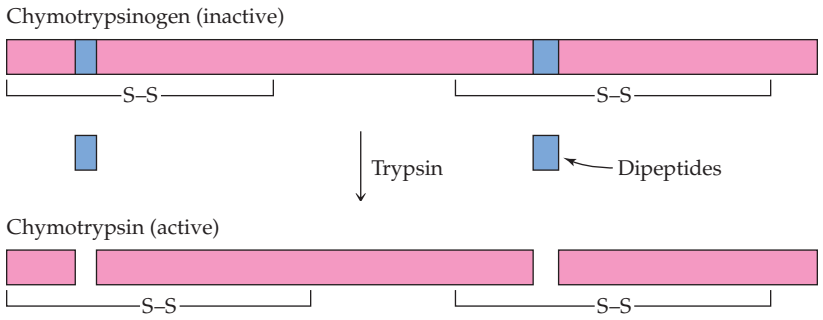
Covalent Modification

There are two modes of enzyme regulation by covalent modification—removal of a covalently bonded portion of an enzyme or addition of a group. Some enzymes are synthesized in inactive forms that differ from the active forms in composition. Activation

of such enzymes, known as **zymogens** or *proenzymes,* requires a chemical reaction that splits off part of the molecule. Blood clotting, for example, is initiated by activation of zymogens.

Zymogen A compound that becomes an active enzyme after undergoing a chemical change.

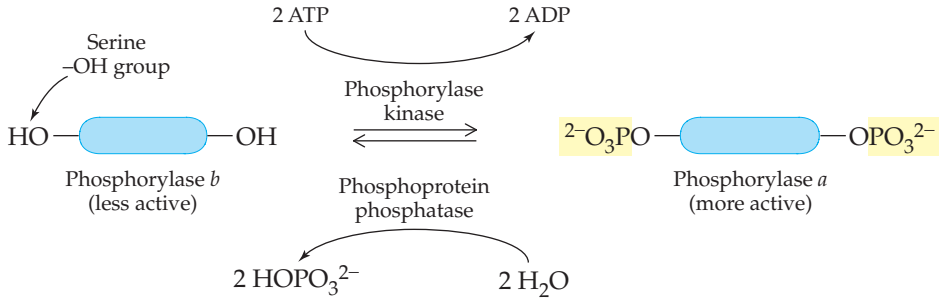
Other examples of zymogens include *trypsinogen, chymotrypsinogen,* and *proelastase,* precursors of enzymes that digest proteins in the small intestine. Produced in the pancreas, these enzymes must be inactive when they are synthesized so that they do not immediately digest the pancreas. Each zymogen has a polypeptide segment at one end that is not present in the active enzymes. The extra segments are snipped off to produce trypsin, chymotrypsin, and elastase, the active enzymes, when the zymogens reach the small intestine, where protein digestion occurs.



▲ Chymotrypsinogen (a zymogen) at top, and the active enzyme chymotrypsin at bottom.

One danger of traumatic injury to the pancreas or the duct that leads to the small intestine is premature activation of these zymogens inside pancreatic cells, resulting in acute pancreatitis, a painful and potentially fatal condition in which the activated enzymes attack the pancreas.

Another mode of covalent modification is the reversible addition of phosphoryl groups ($-PO_3^{2-}$) to a serine, tyrosine, or threonine residue. *Kinase* enzymes catalyze the addition of a phosphoryl group supplied by ATP *(phosphorylation). Phosphatase enzymes* catalyze the removal of the phosphoryl group *(dephosphorylation).* This control strategy swings into action, for example, when glycogen stored in muscles must be hydrolyzed to glucose that is needed for quick energy, a process known as glycogenolysis. Two serine residues in glycogen phosphorylase, the enzyme that initiates glycogen breakdown, are phosphorylated. Only with these phosphoryl groups in place is glycogen phosphorylase active. The groups are removed, changing both the shape and charge on the enzyme, once the need to break down glycogen for quick energy has passed.



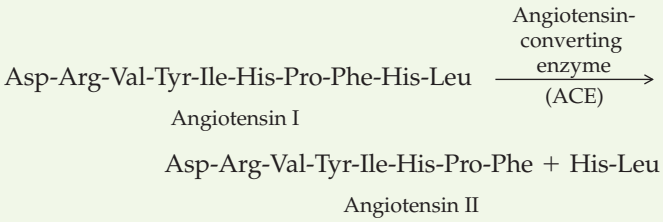
The curved arrows shown above are used frequently in biochemical equations in later chapters. While the focus of the main reaction arrow is on changes in the major biomolecule reactant, the participation of other reactants needed to accomplish the chemical change is shown by the curved arrows adjacent to the main reaction arrow. Coenzymes and energy-providing molecules like ATP are often included in this manner. Here, the top curved arrow shows that the reaction in the forward direction requires ATP to supply the phosphoryl groups and produces ADP. The bottom curved arrow shows that water is needed for the reverse reaction, the hydrolysis that removes the phosphoryl groups as hydrogen phosphate anions.

CHEMISTRY IN ACTION

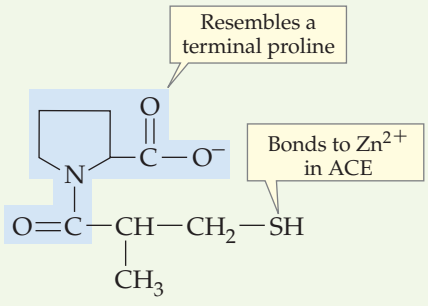
Enzyme Inhibitors as Drugs

Consider the medical possibilities when the chemical structures of a substrate and the active site to which it binds are known. A drug designer can create a molecule similar in structure to the substrate so that it binds to the active site and acts as an inhibitor. Inhibiting a particular enzyme can help treat a variety of medical conditions.

The family of drugs known as angiotensin-converting enzyme (ACE) inhibitors is a good example of enzyme inhibitors that help treat a medical condition. Angiotensin II, the octapeptide illustrated next, is a potent *pressor*—it elevates blood pressure, in part by causing contraction of blood vessels. Angiotensin I, is an inactive precursor of angiotensin II. To become active, two amino acid residues—His and Leu—must be cut off the end of angiotensin I, a reaction catalyzed by ACE. This reaction is part of a normal pathway for blood pressure control and is accelerated when blood pressure drops because of bleeding or dehydration. Inhibition of ACE activity lowers high blood pressure to more normal levels.

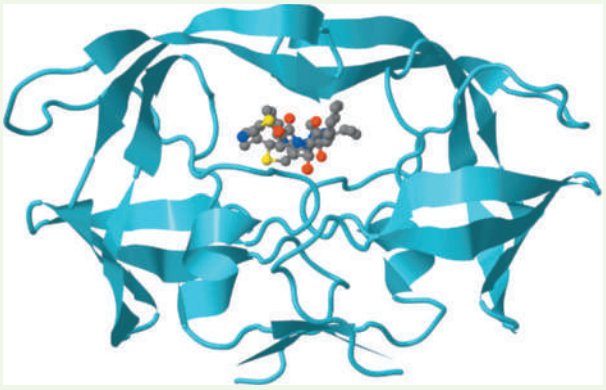


The first ACE inhibitor on the market, *captopril,* was developed by experimenting with modifications of the proline-like structure. Success was achieved by introducing an —SH group that binds to the zinc ion in the active site.



Several other ACE inhibitors have subsequently been developed, and they are now common medications for patients with high blood pressure.

The development of enzyme inhibitors also plays a continuing, major role in the battle against *acquired immunodeficiency syndrome* (AIDS). The battle is far from won, but two important AIDS-fighting drugs are enzyme inhibitors. The first, known as AZT *(azidothymidine,* also called *zidovudine),* resembles in structure a molecule essential to reproduction of the AIDS-causing *human immunodeficiency virus (HIV).* Because AZT is accepted by an HIV enzyme as a substrate, it prevents the virus from producing duplicate copies of itself.



▲ Ritonavir, an enzyme inhibitor, in the active site of HIV protease.

The most successful AIDS drug thus far inhibits a *protease,* an enzyme that cuts a long protein chain into smaller pieces needed by the HIV. *Protease inhibitors,* such as ritonavir, cause dramatic decreases in the virus population and AIDS symptoms. The success is only achieved, however, by taking a "cocktail" of several drugs, including AZT. The cocktail is expensive and requires precise adherence to a schedule of taking 20 pills a day. These conditions make it unavailable or too difficult for many individuals to use.

Many drugs are enzyme inhibitors. For example, topiramate, a carbonic anhydrase inhibitor, is prescribed to treat seizure disorders and also to prevent migraines. Sildenafil (Viagra) inhibits a specific phophodiesterase responsible for some forms of erectile dysfunction. And most antibiotics inhibit enzymes involved in microbial growth and reproduction.

CIA Problem 19.1 The primary structure of angiotensin II has Pro-Phe at the C-terminal end of the octapeptide. An ACE inhibitor from the South American pit viper is a pentapeptide with a C-terminal proline and is a mild ACE inhibitor. Captopril has a modified proline structure and is also a mild ACE inhibitor.

(a) Why do you suppose that a mild ACE inhibitor is more valuable for the treatment of high blood pressure than a very potent ACE inhibitor? (Hint: How much should blood pressure change at once?)

(b) What structural modifications to the pit viper peptide might make it a more powerful ACE inhibitor? (Hint: Compare protein structures at C-terminal end.)

CIA Problem 19.2 AZT (zidovudine) inhibits the synthesis of the HIV virus RNA because AZT resembles substrate molecules. Which kind of inhibition is most likely taking place in this reaction?

CIA Problem 19.3 Ritonavir inhibits the action of HIV protease. What kind of inhibition is imposed on HIV protease by ritonavir?

Genetic Control

The synthesis of all proteins, including enzymes, is regulated by genes (Chapter 27) and is a strategy that controls enzyme availability. **Genetic control** is especially useful for enzymes needed only at certain stages of development. Mechanisms controlled by hormones (Section 28.2) can accelerate or decelerate enzyme synthesis. For example, lactase, needed to digest lactose is not synthesized in most adults because adults have a more varied diet than infants and do not need to digest milk sugar. Conversely, fetuses and infants do not metabolize ethanol because alcohol dehydrogenase, the necessary enzyme, is under genetic control and does not appear until later in life.

Genetic (enzyme) control Regulation of enzyme activity by control of the synthesis of enzymes.

In summary, we have described the most important strategies that control the activity of enzymes. In any given biochemical pathway in a healthy individual, several of these strategies are likely occurring simultaneously at any given moment.

Summary: Mechanisms of Enzyme Control

- *Inhibition,* which is either *reversible* or *irreversible*. *Reversible inhibition* that occurs away from the active site is termed uncompetitive inhibition, while reversible inhibition that occurs at the active site and often involves molecules that mimic substrate structure is termed competitive inhibition. *Irreversible inhibition* occurs due to covalent bonding of the inhibitor to the enzyme. Competitive inhibition is a strategy often utilized in medications, and irreversible inhibition is a mode of action of many poisons.
- *Feedback control* is exerted on an earlier reactant by a later product in a reaction pathway and is made possible by *allosteric control.* The feedback molecule binds to a specific enzyme early in the pathway in a way that alters the shape and therefore the efficiency of the enzyme.
- *Production of inactive enzymes (zymogens),* which must be activated by cleaving a portion of the molecule.
- *Covalent modification of an enzyme by addition and removal of a phosphoryl group,* with the phosphoryl group supplied by ATP.
- *Genetic control,* whereby the amount of enzyme available is regulated by limiting its synthesis.

PROBLEM 19.16

Which type of enzyme regulation is best for the following situations?

(a) An enzyme that becomes overactive during a disease

(b) An enzyme needed only when there is low blood glucose

(c) An enzyme that springs into action when a traumatic injury occurs

(d) An enzyme needed only during adolescence

19.9 Vitamins, Antioxidants, and Minerals

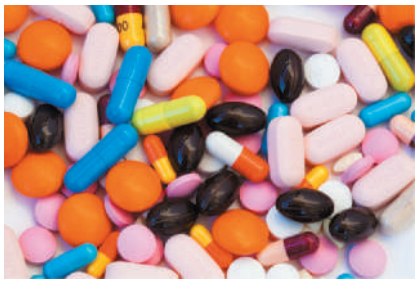
Learning Objectives:

- Describe the two classes of vitamins, the reasons vitamins are necessary in the diet, and the results of vitamin excesses or deficiencies.
- Identify antioxidants and explain their function.
- Identify essential minerals, explain why minerals are necessary in the diet, and explain the results of mineral deficiencies.

The role of vitamin C in collagen synthesis was examined in Section 18.11.

Long before the reasons were understood, people knew that lime and other citrus juices cure scurvy, meat and milk cure pellagra, and cod-liver oil prevents rickets. Eventually, researchers discovered that these diseases are caused by deficiencies of **vitamins**—organic molecules required in only trace amounts that must be obtained through the diet. Vitamins are a dietary necessity for humans because our bodies do not have the ability to synthesize them.

Vitamin An organic molecule, essential in trace amounts that must be obtained in the diet because it is not synthesized in the body.

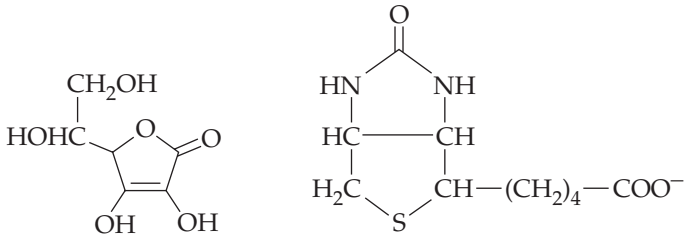


▲ A myriad of vitamin pills in capsule and tablet form.

Water-Soluble Vitamins

Vitamins are grouped by solubility into two classes: water-soluble and fat-soluble. The water-soluble vitamins, listed in Table 19.5, are found in the aqueous environment inside cells, where most of them are needed as components of coenzymes. Over time, an assortment of names, letters, and numbers for designating vitamins have accumulated. Structurally, the water-soluble vitamins have —OH, —COOH, or other polar groups that make them water soluble, but otherwise they range from simple molecules like vitamin C to large, complex structures like vitamin B_{12}.

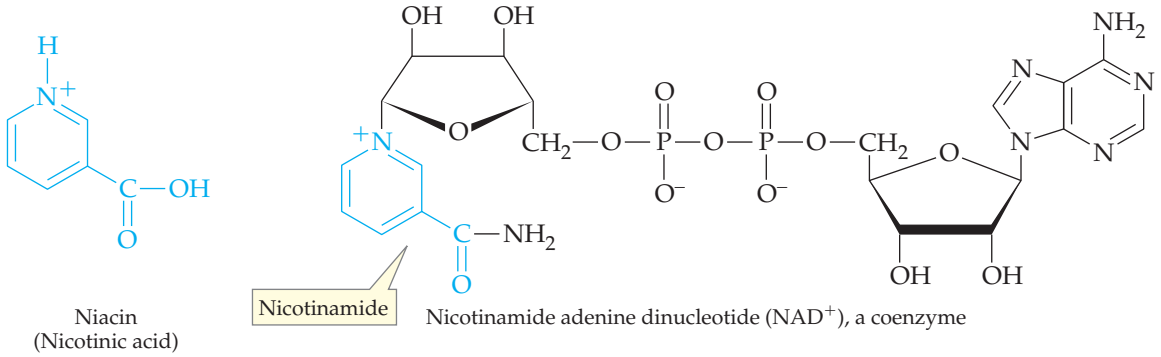
Most vitamins are components of coenzymes, but some function as coenzymes themselves. *Vitamin C* is biologically active without any change in structure from the molecules present in foods. Similarly, *biotin* is connected to enzymes by an amide bond at its carboxyl group but otherwise undergoes no structural change from dietary biotin.



Vitamin C (Ascorbic acid)

Biotin

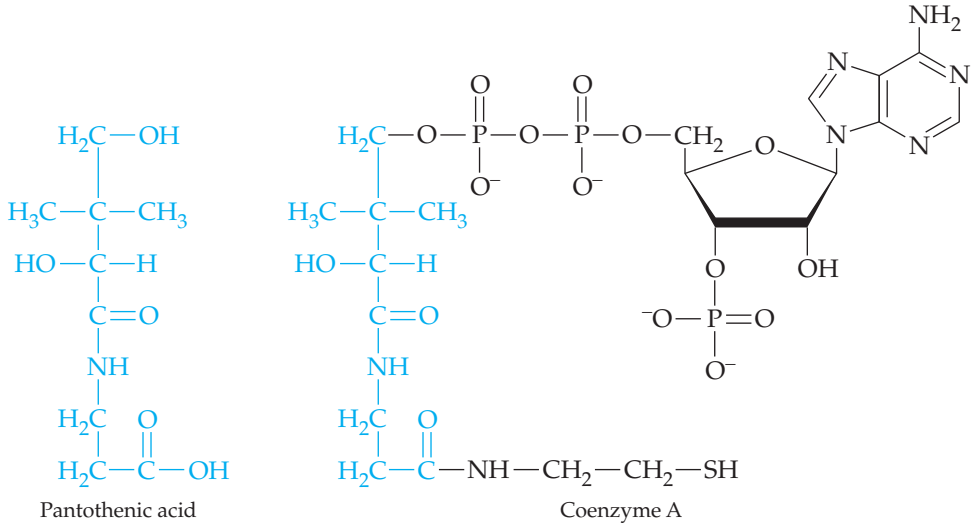
Other water-soluble vitamins are incorporated into coenzymes. The vitamin-derived portions of two of the most important coenzymes, NAD^+ and coenzyme A, are illustrated in Figure 19.10. Table 19.5 includes the functions, deficiency symptoms, and major dietary sources of water-soluble vitamins.



Niacin (Nicotinic acid)

Nicotinamide

Nicotinamide adenine dinucleotide (NAD^+), a coenzyme



Pantothenic acid

Coenzyme A

▲ **Figure 19.10**
The vitamin-derived portions of NAD^+ and coenzyme A.

Table 19.5 The Water-Soluble Vitamins*

Vitamin	Significance	Sources	Reference Daily Intake (RID)**	Effects of Deficiency	Effects of Excess
Thiamine (B_1)	In coenzyme for decarboxylation reactions	Milk, meat, bread, legumes	1.2 mg	Muscle weakness, and cardiovascular problems including heart disease, causes beriberi	Low blood pressure
Riboflavin (B_2)	In coenzymes flavin mononucleotide (FMN) and FAD	Milk, meat	1.3 mg	Skin and mucous membrane deterioration	Itching, tingling sensations
Niacin (nicotinic acid, nicotinamide,B_3)	In coenzyme NAD^+	Meat, bread, potatoes	16 mg	Nervous system, gastrointestinal, skin, and mucous membrane deterioration, causes pellagra	Itching, burning sensations, blood vessel dilation, death after large dose
B_6 (pyridoxine)	In coenzyme for amino acid and lipid metabolism	Meat, legumes	1.3 mg	Retarded growth, anemia, convulsions, epithelial changes	Central nervous system alterations, perhaps fatal
Folic acid	In coenzyme for amino acid and nucleic acid metabolism	Vegetables, cereal, bread	0.4 mg	Retarded growth, anemia, gastrointestinal disorders, neural tube defects	Few noted except at massive doses
B_{12} (cobalamin)	In coenzyme for nucleic acid metabolism	Milk, meat	2.4 μg	Pernicious anemia	Excess red blood cells
Biotin	Coenzyme for carboxylation reactions	Eggs, meat, vegetables	0.3 mg	Fatigue, muscular pain, nausea, dermatitis	None reported
Pantothenic acid (B_5)	In coenzyme A	Milk, meat	5 mg	Retarded growth, central nervous system disturbances	None reported
C (ascorbic acid)	Coenzyme; delivers hydride ions; antioxidant	Citrus fruits, broccoli, greens	90 mg	Epithelial and mucosal deterioration, causing scurvy	Kidney stones

Adapted in part from Frederic H. Martini, Fundamentals of Anatomy and Physiology, 4th edition (Prentice Hall, 1998).
**RDI values are the basis for information on the Nutrition Facts Label included on most packaged foods. The values are based on the Recommended Dietary Intake Reports (2006–2011). See www.nap.edu.*

Worked Example 19.6 Identifying Coenzymes

Identify the substrate, product, and coenzyme in the reaction shown. The reaction is catalyzed by the enzyme alcohol dehydrogenase.

$$\text{Ethanol} + NAD^+ \longrightarrow \text{Acetaldehyde} + NADH + H^+$$

ANALYSIS Identify which molecules have been changed and how, starting from the left side of the arrow (the beginning of the reaction) to the right side of the arrow (the end of the reaction). In this case, ethanol is oxidized to acetaldehyde and NAD^+ is reduced to $NADH/H^+$. Recognize that nicotinamide adenine dinucleotide (NAD^+) is a coenzyme involved in oxidation/reduction reactions.

SOLUTION
Since NAD^+ is a coenzyme involved in oxidation/reduction reactions, ethanol (the other molecule on the left side of the equation) is the substrate and acetaldehyde (on the right side of the arrow) is the product of the reaction. $NADH + H^+$ is the reduced form of NAD^+ and is considered to be reduced coenzyme only—not a product of the reaction.

PROBLEM 19.17 Does the enzyme described in each of the following statements require a cofactor to be active?

(a) Ni^{2+} is present in the active site.
(b) Addition of FAD allows the reaction to occur.
(c) The presence of K^+ does not affect the reaction.

PROBLEM 19.18 Which vitamin provides us with each of the following?

(a) NAD^+ **(b)** Coenzyme A

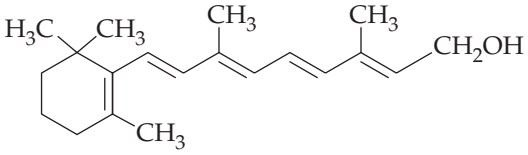
▲ Deeply pigmented vegetables and fruits contain vitamins.

Fat-Soluble Vitamins

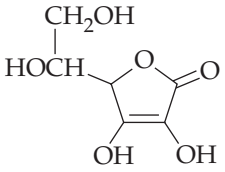
Fat-soluble vitamins A, D, E, and K are stored in the body's fat deposits. Although the clinical effects of deficiencies of these vitamins are well documented, the molecular mechanisms by which they act are not nearly as well understood as those of the water-soluble vitamins. None have been identified as a coenzyme. Table 19.6 summarizes the functions, sources, and deficiency symptoms of fat-soluble vitamins. The hazards of overdosing on fat-soluble vitamins are greater than the hazards of overdosing on water-soluble vitamins because the fat-soluble vitamins accumulate in body fats. Excesses of the water-soluble vitamins are more likely to be excreted in the urine.

PROBLEM 19.19

Compare the structures of vitamin A and vitamin C. Which one is water-soluble and which is fat-soluble? What structural features does each have that make one water-soluble and the other fat-soluble?



Vitamin A
(Retinol)



Vitamin C
(Ascorbic acid)

Table 19.6 The Fat-Soluble Vitamins*

Vitamin	Significance	Sources	Reference Daily Intake**	Effects of Deficiency	Effects of Excess
A	Essential for night vision, healthy eyes, and normal development of epithelial tissue; antioxidant	Leafy green and yellow vegetables	900 μg	Retarded growth, night blindness, deterioration of epithelial membranes	Liver damage, skin peeling, central nervous system effects (nausea, anorexia)
D	Required for normal bone growth, calcium and phosphorus absorption at gut, and retention in kidneys	Synthesized in skin exposed to sunlight	15 μg	Rickets, skeletal deterioration	Calcium deposits in many tissues, disrupting functions
E	Prevents breakdown of vitamin A and fatty acids; antioxidant	Meat, milk, vegetables	15 mg	Anemia, other problems suspected	None reported
K	Essential for liver synthesis of prothrombin and other clotting factors	Vegetables; production by intestinal bacteria	120 μg	Bleeding disorders	Liver dysfunction, jaundice

Adapted in part from Frederic H. Martini, Fundamentals of Anatomy and Physiology, 4th edition (Prentice Hall, 1998).

***RDI values are the basis for information on the Nutrition Facts Label included on most packaged foods. The values are based on the Recommended Dietary Intake Reports (2006–2011). See www.nap.edu. RDIs for fat-soluble vitamins are often reported in International Units (IU), which are defined differently for each vitamin. The values given here are approximate equivalents in mass units.*

PROBLEM 19.20

Based on the structure shown for retinol (vitamin A) and the names of the two related forms of vitamin A, retinal and retinoic acid, what do you expect to be the structural differences among these three compounds?

Antioxidants

Antioxidant A substance that prevents oxidation by reacting with an oxidizing agent.

Free radical An atom or molecule with an unpaired electron.

An **antioxidant** is a substance that prevents oxidation. The food industry uses antioxidants to combat oxidation of unsaturated fats by air, which causes deterioration of baked goods. In the body, we need similar protection against active oxidizing agents that are byproducts of normal metabolism.

Our principal dietary antioxidants are vitamin C, vitamin E, β-carotene, and the mineral selenium. They work together to defuse the potentially harmful action of **free radicals,** highly reactive molecular fragments with unpaired electrons (e.g., superoxide ion, $\cdot O_2^-$). Free radicals quickly gain stability by picking up electrons from nearby molecules, which are left damaged.

Vitamin E is unique in having antioxidant activity as its principal biochemical role. It acts by giving up the hydrogen from its —OH group to oxygen-containing free radicals. The hydrogen is then restored by reaction with vitamin C. Selenium joins the list of important antioxidants because it is a cofactor in an enzyme that converts hydrogen peroxide (H_2O_2) to water before the peroxide can go on to produce free radicals.

LOOKING AHEAD The role of vitamins as antioxidants is explored further in the discussion of elimination of cellular damaging reactive oxygen species in the Chemistry in Action "Harmful Oxygen Species and Antioxidant Vitamins," page 703.

KEY CONCEPT PROBLEM 19.21

Vitamins are a diverse group of compounds that must be present in the diet. List four functions of vitamins in the body.

PROBLEM 19.22

See the Chemistry in Action "Vitamins, Minerals, and Food Labels" below. Which vitamin listed on the label functions as an antioxidant in the body? Why is this important?

CHEMISTRY IN ACTION

Vitamins, Minerals, and Food Labels

It is not uncommon to encounter incomplete or incorrect information about vitamins and minerals. We have been frightened by the possibility that aluminum causes Alzheimer's disease and tantalized by the possibility that vitamin C defeats the common cold. Sorting out fact from fiction or distinguishing preliminary research results from scientifically proven relationships is especially difficult in this area of nutrition.

One consistent source of information on nutrition is the Food and Nutrition Board of the National Academy of Sciences-National Research Council. They periodically survey the latest nutritional information and publish Recommended Dietary Allowances (RDAs) that are "designed for the maintenance of good nutrition of the majority of healthy persons in the United States." Another source is the U.S. Food and Drug Administration (FDA), which sets the guidelines for food labeling.

Since 1994, as mandated by the FDA, most packaged food products carry standardized *Nutrition Facts* labels. The nutritional value of a food serving of a specified size is reported as *% Daily Value.* For vitamins and minerals, these percentages are calculated from RDI values published in 1968. RDIs are averages for adults and children over 4 years of age. The values for vitamins are included in Tables 19.5 and 19.6. For minerals, they are listed in the accompanying table.

Nutrition Facts
Serving Size 55 pieces (30g)
Servings Per Container About 6

Amount Per Serving
Joules 585 Joules from Fat 188

	% Daily Value*
Total Fat 5g	**8%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Polyunsaturated Fat 1.5g	
Monounsaturated Fat 2.5g	
Cholesterol Less than 5mg	**1%**
Sodium 250mg	**10%**
Total Carbohydrate 19g	**6%**
Dietary Fiber 2g	**7%**
Sugars Less than 1g	
Protein 4g	

Vitamin A 0% • Vitamin C 0%
Calcium 4% • Iron 6%

*Percent Daily Values are based on a 8350 joules diet. Your daily values may be higher or lower depending on your caloric needs:

Energy (J):		8350	10,500
Total Fat	Less than	65g	80g
Sat. Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

All vitamins and minerals are important and essential, but in choosing which vitamins and minerals *must* be listed on the new labels, the government has focused on those currently of greatest importance in maintaining good health. The choices reflect a new emphasis on preventing disease rather than preventing deficiencies. The *mandatory* listings are for vitamin A, vitamin C, calcium, and iron. These recommendations are based on evidence for the benefits of high dietary levels of the antioxidants vitamin A (or the related compound, β-carotene) and vitamin C. Calcium deficiencies are related to osteoporosis, and iron deficiencies are a special concern for women because of their menstrual blood loss.

Reference Daily Intake Values* for Minerals

Mineral	RDI	Mineral	RDI
Calcium	1.0 g	Selenium	70 μg
Iron	18 mg	Manganese	2 mg
Phosphorus	1.0 g	Fluoride	2.5 mg
Iodine	150 μg	Chromium	120 μg
Magnesium	400 mg	Molybdenum	75 μg
Zinc	15 mg	Chloride	3.4 g
Copper	2 mg		

**On Nutrition Facts labels, calcium and iron must be listed; phosphorus, iodine, magnesium, zinc, and copper listings are optional; by law, the others cannot be listed.*

CIA Problem 19.4 Which vitamins and minerals are listed on the food label and in what amount? Is this a good nutritional choice for consuming these vitamins and minerals?

CIA Problem 19.5 Read the labels on foods that you eat for a day, or look up the foods in a nutrition table and determine what percent of your daily dosage of vitamins and minerals you get from each. Are you getting the recommended amounts from the food you eat, or should you be taking a vitamin or mineral supplement?

CIA Problem 19.6 For what reasons are listings for vitamin A, vitamin C, iron, and calcium mandatory on food labels?

CIA Problem 19.7 In addition to the four nutrients named in CIA Problem 19.6, what other nutrients may be listed on food labels? (Hint: Look at all the ingredients that have amounts listed on the label shown.)

Minerals

The other important group of micronutrients is minerals, some of which are transition group elements. Table 19.7 lists the essential minerals, their sources and functions. A balanced diet supplies sufficient amounts of each of these micronutrients. Many of the transition elements are necessary for proper functioning of enzymes, since these elements are used as cofactors. Other minerals are used as building blocks for the body and some exist as ions, called electrolytes, in our body fluids. The RDI for most of these minerals is listed in the Chemistry in Action "Vitamins, Minerals, and Food Labels."

Dietary minerals are divided into macrominerals, those with required daily amounts greater than 100 mg per day, and microminerals, those needed in lesser quantities. The macrominerals listed in Table 19.7 do not include sulfur because it is an integral part of the amino acids cysteine and methionine, which are taken in sufficient amounts in the diet. Adequate, regular intake of calcium and phosphorus is necessary for formation and maintenance of bone. Magnesium is also necessary for bone metabolism and is stored in bone tissue; it is also a cofactor in many different enzymes ranging from glucose and lipid metabolism to protein synthesis.

We generally do not think of the other three macrominerals as essential, since deficiencies are rare. Rather, we often consume too much sodium, chloride, and potassium by eating processed food. These macronutrients function as electrolytes, maintaining

Table 19.7 Macro and Trace Minerals

Mineral	Significance	Sources	Effects of Deficiency	Effects of Excess
Macrominerals				
Calcium	Bone formation, muscle contraction	Dairy, eggs, beans	Osteoporosis, muscle cramps	Kidney stones, heart arrhythmias
Phosphorus	Bone formation, component of DNA and energy molecules	Any protein	Muscle weakness	Impaired calcium metabolism
Potassium	Osmotic balance inside cells	Fruit, vegetables, meat	Loss of appetite, muscle cramps	Inhibited heart function
Chloride	Primary negative ion in extracellular fluid	All foods, especially processed	Convulsions (rare)	Hypertension
Sodium	Nerve impulse conduction, electrolyte (osmotic balance)	All foods, especially processed	Muscle cramps, nausea	Hypertension
Magnesium	Protein synthesis, glucose metabolism	Dairy, whole grains, plants	Muscle weakness	Nausea
Microminerals				
Iron	Hemoglobin and cytochrome component	Meat, whole grains, legumes	Fatigue, anemia	Hemochromatosis
Fluoride	Part of vitamin B_{12}	Milk, eggs, seafood	Dental cavities	Discolored teeth
Zinc	Enzyme cofactor, smell and taste functions	Meat, dairy, whole grains	Poor immune function, slow wound healing	Poor immune system, increased low-density lipoprotein (LDL) cholesterol
Copper	Enzymes for oxidations and connective tissue formation	Meat, nuts, eggs, bran cereal	Anemia	Nausea
Selenium	Cofactor for glutathione peroxidase	Meat, whole grains	Cardiac muscle damage	Nausea, hair loss
Manganese	Coenzyme for many enzymes in energy metabolism	Whole grains, legumes	Poor growth	Weakness, mental confusion
Iodine	Production of thyroid hormones	Iodized salt, seafood	Goiter	Depressed thyroid activity
Molybdenum	Coenzyme	Meat, whole grains, legumes	Not found	Not found
Chromium	Enhances insulin function	Meat, whole grains	Glucose intolerance	Rare from diet

CHEMISTRY IN ACTION

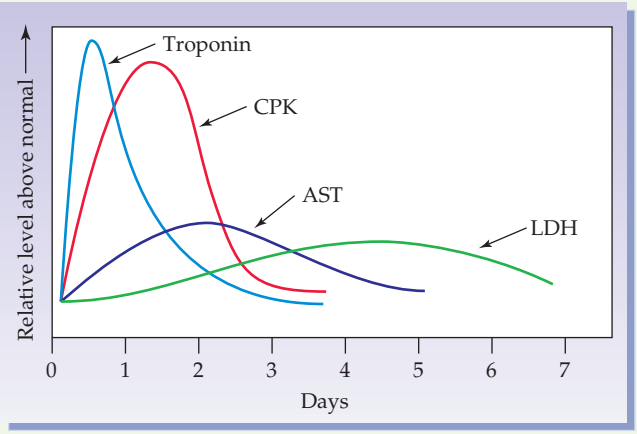
Enzymes in Medical Diagnosis

In a healthy person, certain enzymes, such as those responsible for forming and dissolving blood clots, are normally present in high concentrations in blood serum. Enzymes that function within cells are found normally in low concentrations in blood serum due to normal degeneration of healthy cells. However, when tissue is injured, large quantities of cellular enzymes are released into the blood from dying cells, with the distribution of enzymes and other proteins dependent on the identity of the injured cells. Measurement of blood levels of specific molecules is therefore a valuable diagnostic tool. For example, higher-than-normal activities of the enzymes included in a routine blood analysis indicate the following conditions:

Enzyme	Diagnosis
Aspartate transaminase (AST)	Damage to heart or liver
Alanine transaminase (ALT)	Damage to heart or liver
Lactate dehydrogenase (LDH)	Damage to heart, liver, or red blood cells
Alkaline phosphatase (ALP)	Damage to bone and liver cells
γ-Glutamyl transferase (GGT)	Damage to liver cells; alcoholism
Creatine phosphokinase (CPK-2)	Damage to heart
Acid phosphatase	Prostate cancer

Enzyme analysis measures the activity of an enzyme rather than its concentration. Because activity is influenced by pH, temperature, and substrate concentration, it is measured in IU at standard conditions. One IU is defined as the amount of an enzyme that converts 1 μmol of its substrate to product per minute under defined standard conditions of pH, temperature, and substrate concentration. The analytical results are reported in units per liter (U/L).

Enzyme assays are done to diagnose heart attacks *(myocardial infarctions, MI),* like in Mr. Smith's case at the beginning of the chapter, and differentiate them from other conditions like liver disease. CPK has three isomeric forms: CPK-1 is found in brain tissue, CPK-2 is found in heart tissue, and CPK-3 is found in skeletal muscle. After an MI, CPK-2 values rise rapidly within 6 hours and peak around 12 hours after the event, then decrease. AST and ALT blood levels are also measured to help in diagnosis but are also indicators of liver disease. LDH, which has five isomeric forms, one of which is found only in heart muscle, formerly was used as an MI indicator. Currently



▲ Blood levels of troponins, CPK-2, AST, and LDH in the days following a heart attack.

the levels of troponin proteins are measured in blood samples over 18 hours. There are several troponin isomers; cardiac troponin is specific to heart muscle cells and is associated with actin and myosin in cells; troponins are not enzymes but are a reliable marker for an MI. Troponin levels rise rapidly immediately and dramatically after an MI, decreasing over several days post event rise.

What happened to Mr. Smith and Ms. Givens from the beginning of the chapter? Physicians determined from elevated CPK and AST levels (both enzymes), the characteristic rise in troponin levels (determined in an assay involving enzymes), and other tests that Mr. Smith had a heart attack. His blood lipids were also elevated, and he was placed on a heart-healthy diet along with appropriate medications. Ms. Givens, indeed, had suffered an ischemic stroke, blocking blood circulation in part of her brain. She was promptly treated with an intravenous infusion of tPA, an enzyme obtained from recombinant DNA technology. Early treatment with tPA results in clot dissolution and better recovery from a stroke. Ms. Givens was also given diet recommendations and medications before discharge from the hospital.

CIA Problem 19.8 Enzyme levels in blood are often elevated in various disease states. Which enzyme or other blood marker gives the earliest indication of a heart attack? Which test is used to confirm a heart attack, after several tests over several days?

CIA Problem 19.9 Why must enzyme activity be monitored under standard conditions?

osmotic balance in both intracellular and extracellular spaces. They also help in the production of electrical signals throughout the nervous system; potassium ions are important in regulating heartbeat.

Magnesium and selenium, along with the transition elements chromium, copper, manganese, molybdenum, and zinc, are classed as micronutrients. Our bodies need only tiny amounts of these elements to supply enough cations to function as cofactors for enzymes. Some of these elements, such as copper and selenium, are highly toxic if ingested in high amounts. Each of these transition elements exists as a cation that can form covalent-coordinated bonds with specific, charged residues in the protein structure of their respective enzymes. Because these are transition element cations, with variable oxidation states, they can also serve as transient holders of electrons during enzymatic reactions.

Vitamins and micronutrient minerals serve complementary functions. Both serve as cofactors for enzymatic reactions. Minerals serve directly, whereas vitamins may be modified into other organic molecules in order to participate in a reaction. The other essential minerals are used as building material or to maintain electrolyte balance.

PROBLEM 19.23

Which micronutrient mineral do you think is the most toxic in excess? Why is it necessary if it is toxic?

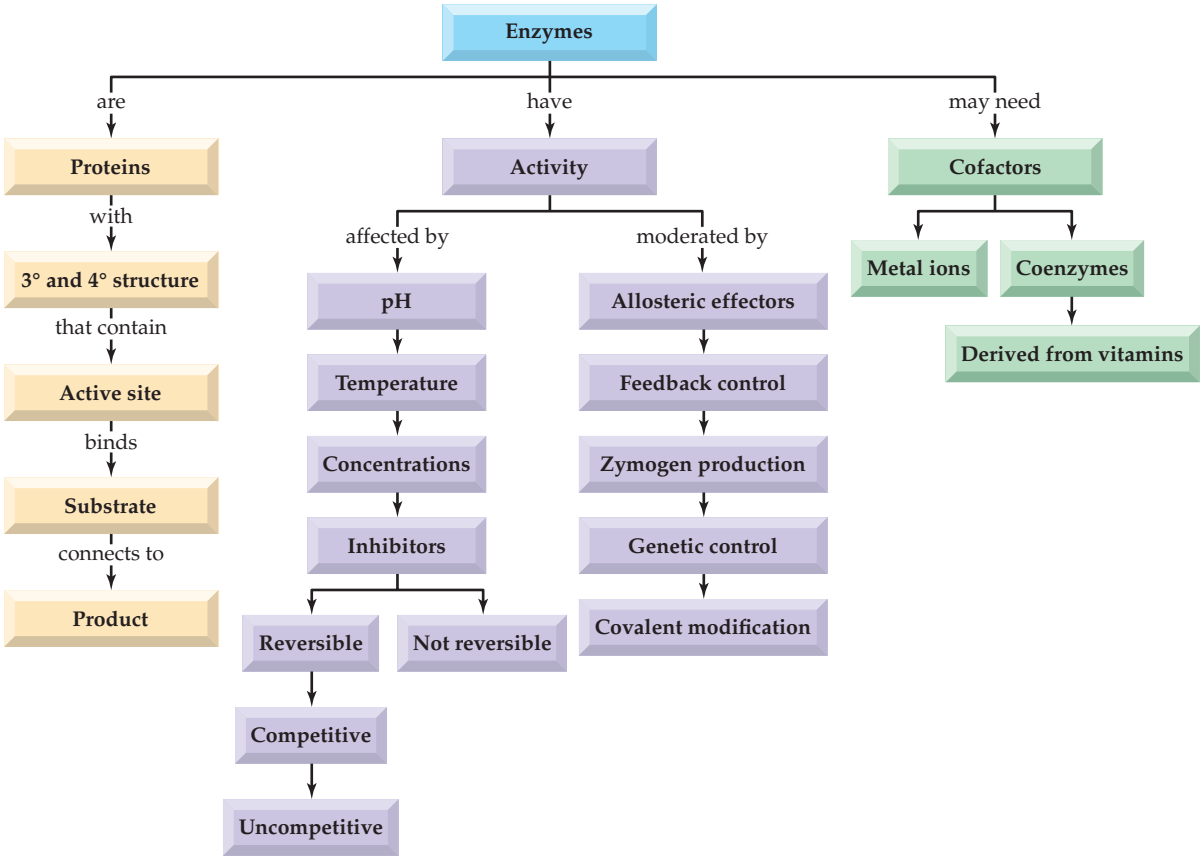
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Describe the function of enzymes in biochemical reactions.** *Enzymes* are the catalysts for biochemical reactions, acting by lowering the activation energy needed for the reaction. They are mostly water-soluble, globular proteins *(see Problems 84 and 85).*
- **Explain the role of cofactors in some enzymatic reactions.** Some enzymes require *cofactors,* which are either metal ions or the nonprotein organic molecules known as *coenzymes,* for activity. These cofactors facilitate electron transfer and chemical group movement during the reaction *(see Problems 25, 27, and 32–35).*
- **Give an enzyme the appropriate name given the substrate.** Enzymes are named for the substrate (first part of the name) and type of reaction involved (second part of the name) with the suffix *-ase* attached. Some enzymes retain classical names and do not follow these rules *(see Problems 25, 36, and 37).*
- **Assign an enzyme to the correct class based on its reaction.** There are six major classes of reactions that are catalyzed by enzymes. Each major class encompasses subclasses of similar reactions (Table 19.2) *(see Problems 25, 36, 37, and 41–46).*
- **Explain the two models of enzyme catalysis.** In the *lock-and-key model* of catalysis, the substrate fits the active site of the enzyme like a key fits a lock. It is a rigid model. In the *induced-fit model,* substrate is drawn into the active site by noncovalent interactions. As the substrate enters the active site, the enzyme shape adjusts to best accommodate the substrate and catalyze the reaction *(see Problems 40, 41, 48, and 49).*
- **Describe how an enzyme and substrate combine to facilitate a reaction.** Within the *enzyme–substrate complex,* the substrate is held in the best orientation for reaction and in a strained condition that allows the activation energy to be lowered. When the reaction is complete, the product is released and the enzyme returns to its original condition. The *specificity* of each enzyme is determined by the presence within the active site of catalytically active groups, hydrophobic pockets, and ionic or polar groups that exactly fit the chemical makeup of the substrate *(see Problems 24, 30, 50–53, 81, and 82).*
- **Describe the changes in enzyme activity that result when substrate concentration, enzyme concentration, temperature, or pH change.** With fixed enzyme concentration, reaction rate first increases with increasing substrate concentration and then approaches a fixed maximum at which all active sites are occupied. In the presence of excess substrate, reaction rate is directly proportional to enzyme concentration. With increasing temperature, reaction rate increases to a maximum and then decreases as the enzyme protein denatures. Reaction rate is maximal at a pH that reflects the pH of the enzyme's site of action in the body *(see Problems 54–57 and 82).*
- **Define and identify reversible and irreversible inhibition.** The effectiveness of enzymes is controlled by a variety of *activation* and *inhibition* strategies. *Competitive inhibitors* are *reversible inhibitors* that typically resemble the substrate and reversibly block the active site; they slow the reaction rate but do not change the maximum rate. *Irreversible inhibitors* form covalent bonds to an enzyme that permanently inactivate it; most are poisons *(see Problems 30, 62, 64, and 65).*
- **Define and identify uncompetitive and competitive inhibition.** *Uncompetitive inhibitors* act on the enzyme–substrate complex, blocking a second substrate from entering the active site; they lower the maximum reaction rate. *Competitive inhibitors* are molecules similar to the substrate that fit the active site and slow the reaction rate *(see Problems 28 and 58–61).*
- **Define and identify allosteric control.** Allosteric control is achieved by an enzyme regulator molecule that can exercise control over an enzyme by binding to a site different from the active site. Binding a regulator induces a change of shape in the active site, increasing or decreasing the efficiency of the enzyme. The regulator molecule does not need to resemble the reaction substrate *(see Problems 29, 30, 66, and 67).*
- **Define feedback control and explain how it regulates enzyme catalysis.** Feedback control acts through *allosteric control* of enzymes that have regulatory sites separate from their active sites. When enough product of a series of reactions is present, the excess inhibits

the activity of the first enzyme in the reaction series preventing more product from accumulating *(see Problems 29, 30, 68, and 69).*

- **Define and identify inhibition by covalent modification.** Enzyme activity is also regulated by *reversible* phosphorylation and dephosphorylation and by synthesis of inactive *zymogens* that are later activated by removal of part of the molecule *(see Problems 29, 71, and 73).*
- **Define and identify inhibition by genetic control of enzymes.** *Genetic control* is exercised by regulation of the synthesis of enzymes specific to the stage of life and need of the organism *(see Problems 29, 30, 70, and 72).*
- **Describe the two classes of vitamins, the reasons vitamins are necessary in the diet, and the results of vitamin excesses or deficiencies.** *Vitamins* are organic molecules required in small amounts in the body that must be obtained from the diet. The water-soluble vitamins (Table 19.5) are coenzymes or parts of coenzymes. The fat-soluble vitamins (Table 19.6) have diverse and less well-understood functions. In general, excesses of water-soluble vitamins are excreted and excesses of fat-soluble vitamins are stored in body fat, making excesses of the fat-soluble vitamins potentially more harmful *(see Problems 80, 81, and 88).*
- **Identify antioxidants and explain their function.** Vitamin C, β-carotene (a precursor of vitamin A), vitamin E, and selenium work together as *antioxidants* to protect biomolecules from damage by free radicals.
- **Identify essential minerals, explain why minerals are necessary in the diet, and explain the results of mineral deficiencies.** Minerals are chemical elements needed in small amounts in the diet. Minerals function as macronutrients (calcium and phosphorus for bone), electrolytes, and micronutrients used primarily as enzyme cofactors.

CONCEPT MAP: ENZYMES



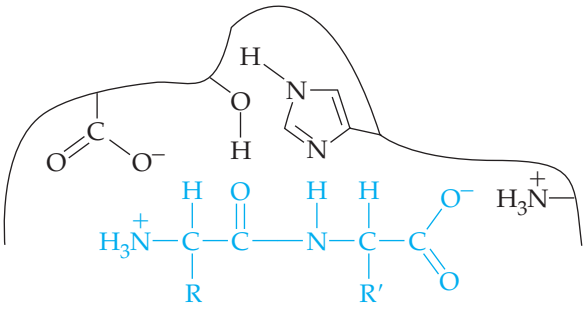
▲ **Figure 19.11 Concept Map.** Protein tertiary and quaternary structures provide active sites where biochemical reactions occur in enzymes. Activity is affected by several physical factors and can be affected by inhibitory molecules. Several different forms of control, depending on the enzyme, control activity. Some enzymes require cofactors, either metal ions or coenzymes, for activity.

KEY WORDS

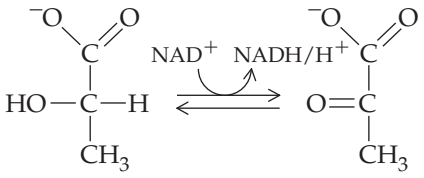
Activation (of an enzyme), *p. 639*
Active site, *p. 626*
Allosteric control, *p. 642*
Allosteric enzyme, *p. 642*
Antioxidant, *p. 650*
Coenzyme, *p. 627*
Cofactor, *p. 627*
Competitive (enzyme) inhibition, *p. 640*
Enzyme, *p. 625*
Feedback control, *p. 644*
Free radical, *p. 650*
Genetic (enzyme) control, *p. 647*
Induced-fit model, *p. 633*
Inhibition (of an enzyme), *p. 639*
Irreversible (enzyme) inhibition, *p. 641*
Lock-and-key model, *p. 633*
Specificity (enzyme), *p. 626*
Substrate, *p. 626*
Turnover number, *p. 627*
Uncompetitive (enzyme) inhibition, *p. 640*
Vitamin, *p. 647*
Zymogen, *p. 645*

UNDERSTANDING KEY CONCEPTS

19.24 On the following diagram, indicate with dotted lines the bonding between the enzyme (a dipeptidase; several amino acid residues in black) and the substrate (in blue) that might occur to form the enzyme–substrate complex. What are the two types of bonding likely to occur?



19.25 Answer questions (a)–(e) concerning the following reaction:



(a) The enzyme involved in this reaction belongs to what class of enzymes?

(b) Since hydrogens are removed, the enzyme belongs to what subclass of the enzyme class from part (a)?

(c) What is the substrate for the reaction as written?

(d) What is the product for the reaction as written?

(e) The enzyme name is derived from the substrate name and the subclass of the enzyme and ends in the family-name ending for an enzyme. Name the enzyme.

19.26 In the reaction shown in Problem 19.25, will the enzyme likely also use D-lactate as a substrate? Explain your answer. If D-lactate binds to the enzyme, how is it likely to affect the enzyme?

19.27 In the reaction shown in Problem 19.25, identify the coenzyme required for catalytic activity. Is the coenzyme an oxidizing agent or a reducing agent? What vitamin is a part of the coenzyme for this reaction?

19.28 Explain how the following changes affect the rate of an enzyme-catalyzed reaction in the presence of an uncompetitive inhibitor: (a) increasing the substrate concentration at a constant inhibitor concentration, (b) decreasing the inhibitor concentration at a constant substrate concentration.

19.29 Explain how the following mechanisms regulate enzyme activity.

(a) Covalent modification **(b)** Genetic control

(c) Allosteric regulation **(d)** Feedback inhibition

19.30 What type of enzyme regulation occurs in the following situations?

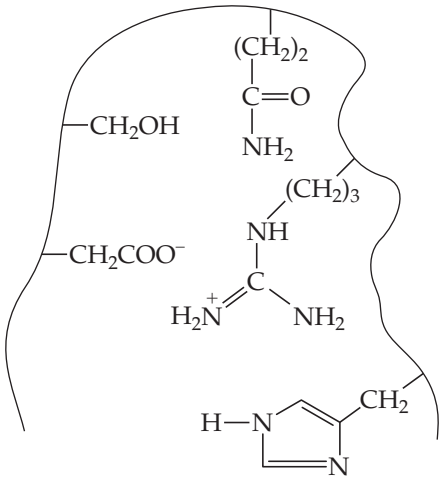
(a) Buildup of the product of the pathway that converts glucose to pyruvate stops at the first enzyme in the multistep process.

(b) Sarin, a nerve gas, covalently binds to acetylcholinesterase, stopping nerve signal transmission.

(c) Lactase is not produced in the adult.

(d) Conversion of isocitrate to α-ketoglutarate is inhibited by high levels of ATP. (Hint: ATP is neither a product nor a substrate in this reaction.)

19.31 Acidic and basic groups are often found in the active sites of enzymes. Identify the acidic and basic amino acids in the active site in the following diagram. (Hint: Consult Table 18.3 and Chapter 10 for the definition of acids and bases.)



ADDITIONAL PROBLEMS

ENZYME COFACTORS (SECTION 19.2)

19.32 Name the vitamin to which each of these coenzymes is related.

(a) FAD **(b)** Coenzyme A

(c) NAD^+

19.33 Which of the following is a cofactor and which is a coenzyme?

(a) Cu^{2+} **(b)** Tetrahydrofolate

(c) NAD^+ **(d)** Mg^{2+}

19.34 Which of these vitamins can serve as a cofactor?

(a) Vitamin A **(b)** Vitamin C

(c) Vitamin D

19.35 Which of the following is a cofactor and which is a coenzyme?

(a) Fe^{2+} **(b)** Pyridoxyl phosphate

(c) FAD **(d)** Ni^{2+}

STRUCTURE AND CLASSIFICATION OF ENZYMES (SECTION 19.3)

19.36 What general kinds of reactions do the following types of enzymes catalyze?

(a) Dehydrogenases **(b)** Decarboxylases

(c) Lipases

19.37 What general kinds of reactions do the following types of enzymes catalyze?

(a) Kinases **(b)** Isomerases

(c) Synthetases

19.38 Name an enzyme that acts on each molecule.

(a) Amylose **(b)** Peroxide **(c)** DNA

19.39 Name an enzyme that acts on each molecule.

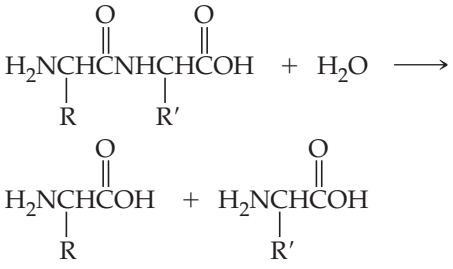
(a) Lactose **(b)** Protein **(c)** RNA

19.40 What features of enzymes make them so specific in their action?

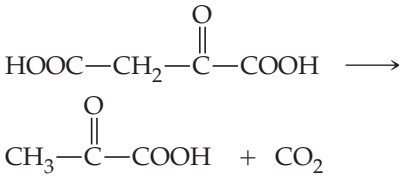
19.41 Describe in general terms how enzymes act as catalysts.

19.42 What classes of enzymes would you expect to catalyze the following reactions?

(a)



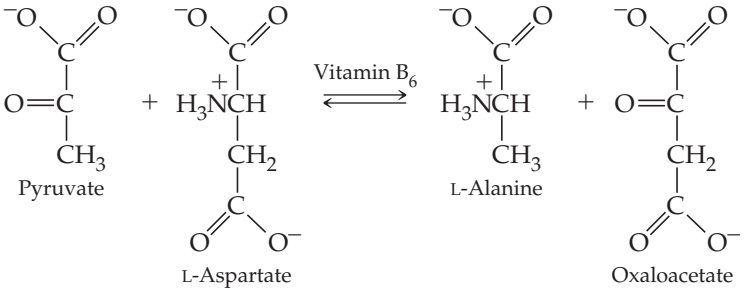
(b)



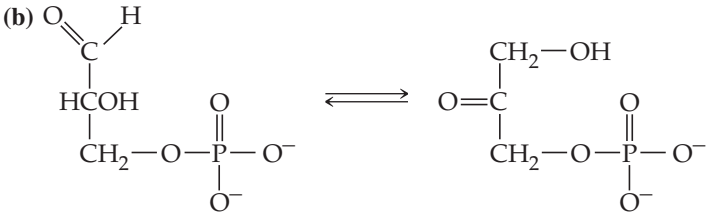
(c)

19.43 What classes of enzymes would you expect to catalyze the following reactions?

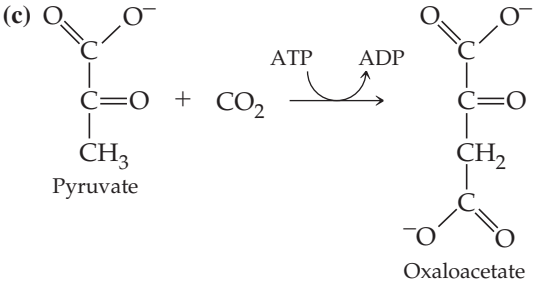
(a)



(b)



(c)



19.44 What kind of reaction does each of these enzymes catalyze?

(a) A ligase

(b) A transmethylase

(c) A reductase

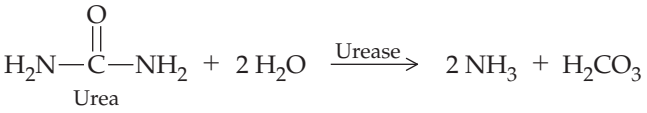
19.45 What kind of reaction does each of these enzymes catalyze?

(a) A dehydrase

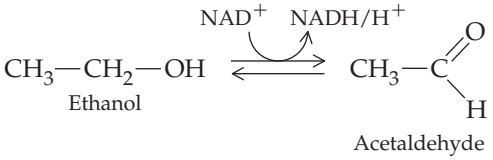
(b) A carboxylase

(c) A protease

19.46 The following reaction is catalyzed by the enzyme urease. To what class of enzymes does urease belong?



19.47 Alcohol dehydrogenase (ADH) catalyzes the following reaction. To what class of enzymes does ADH belong?



HOW ENZYMES WORK (SECTION 19.4)

19.48 What is the difference between the lock-and-key model of enzyme action and the induced-fit model?

19.49 Why is the induced-fit model a more likely model than the lock-and-key model?

19.50 Must the amino acid residues in the active site be near each other along the polypeptide chain? Explain.

19.51 The active site of an enzyme is a small portion of the enzyme molecule. What is the function of the rest of the huge molecule?

19.52 How do you explain the observation that pepsin, a digestive enzyme found in the stomach, has a high catalytic activity at pH 1.5, while trypsin, an enzyme of the small intestine, has no activity at pH 1.5?

19.53 Amino acid side chains in the active sites of enzymes can act as acids or bases during catalysis. List the amino acid side chains that can accept H^+ and those that can donate H^+ during enzyme-catalyzed reactions.

FACTORS AFFECTING ENZYME ACTIVITY (SECTION 19.5)

19.54 If the rate of an enzymatic reaction doubles when the amount of enzyme is doubled, what do you expect the rate of reaction to be if the amount of enzyme is tripled? Why?

19.55 What happens to the rate of an enzymatic reaction if the amount of substrate is doubled? Why?

19.56 What general effects would you expect the following changes to have on the rate of an enzyme-catalyzed reaction for an enzyme that has its maximum activity at body temperature (about 37 °C/310.15 K)?

(a) Raising the temperature from 310 K (37 °C) to 343 K (70 °C)

(b) Lowering the pH from 7 to 3

(c) Adding an organic solvent, such as methanol

19.57 What general effects would you expect the following changes to have on the rate of an enzyme-catalyzed reaction for an enzyme that has its maximum activity at body temperature (about 37 °C/310.15 K)?

(a) Lowering the reaction temperature from 313 K (40 °C) to 283 K (10 °C)

(b) Adding a drop of a dilute $HgCl_2$ solution

(c) Adding an oxidizing agent, such as hydrogen peroxide

ENZYME REGULATION: INHIBITION (SECTION 19.6)

19.58 The text discusses three forms of enzyme inhibition: uncompetitive inhibition, competitive inhibition, and irreversible inhibition.

(a) Describe how an enzyme inhibitor of each type works.

(b) What kinds of bonds are formed between an enzyme and each of these three kinds of inhibitors?

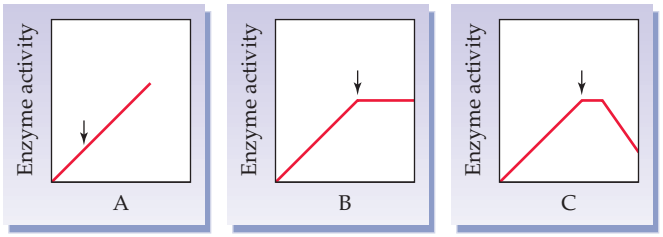
19.59 What kind of inhibition (uncompetitive, competitive, or irreversible) is present in each of the following:

(a) Penicillin is used to treat certain bacterial infections. Penicillin is effective because it binds to the enzyme glycopeptide transpeptidase and does not dissociate.

(b) Accidental methanol consumption is fairly common. The treatment includes the ingestion of ethanol. Both molecules can be converted to aldehydes by alcohol dehydrogenase. Ethanol is the true substrate.

(c) The antibiotic deoxycycline inhibits the bacterial enzyme collagenase, slowing bacterial growth. Deoxycycline does not fit into the active site of collagenase and binds elsewhere on the enzyme.

19.60 EcoRI, an enzyme that hydrolyzes DNA strands, requires Mg^{2+} as a cofactor for activity. EDTA chelates divalent metal ions in solution. In the graphs shown here, the arrow indicates the point at which EDTA is added to a reaction mediated by EcoRI. Which graph represents the activity curve you would expect to see? (Activity is shown as total product from the reaction as time increases.)



19.61 The enzyme lactate dehydrogenase converts lactic acid to pyruvate with the aid of the coenzyme NAD^+. In the graphs of Problem 19.60, the arrow indicates the point at which EDTA is added to a reaction mixture of lactic dehydrogenase and lactic acid. Which graph represents the activity curve you would expect to see? (Activity is shown as total product from the reaction as time increases.)

19.62 Lead exerts its poisonous effect on enzymes by two mechanisms. Which mechanism is irreversible and why?

19.63 One mechanism by which lead exerts its poisonous effect on enzymes can be stopped by chelation therapy with EDTA. Describe this type of lead poisoning and explain why it is reversible.

19.64 The meat tenderizer used in cooking is primarily papain, a protease enzyme isolated from the fruit of the papaya tree. Why do you suppose papain is so effective at tenderizing meat?

19.65 Bumblebee venom contains several related heptadecapeptides from the bomditin family. Papain can be used to help relieve the pain of bee stings. Why do you suppose it works?

ENZYME REGULATION: ALLOSTERIC CONTROL AND FEEDBACK (SECTION 19.7)

19.66 Why do allosteric enzymes have two types of binding sites?

19.67 Discuss the purpose of positive and negative regulation.

19.68 What is feedback inhibition?

19.69 What are the cellular advantages to feedback inhibition?

ENZYME REGULATION: COVALENT MODIFICATION AND GENETIC CONTROL (SECTION 19.8)

19.70 What is a zymogen? Why must some enzymes be secreted as zymogens?

19.71 Activation of a zymogen is by covalent modification. How might phosphorylation or dephosphorylation (also covalent modification) modify an enzyme to make it more active (or more inactive)?

19.72 Why are the protein-digesting enzymes trypsin and chymotrypsin secreted as the zymogen chymotrypsinogen?

19.73 Infants do not have the ability to metabolize ethanol and are assumed to lack the enzyme alcohol dehydrogenase? What kind of regulation is this?

VITAMINS, ANTIOXIDANTS, AND MINERALS (SECTION 19.9)

19.74 What criteria make a compound a vitamin?

19.75 What is the relationship between vitamins and enzymes?

19.76 Why is daily ingestion of vitamin C more critical than daily ingestion of vitamin A?

19.77 List the four fat-soluble vitamins. Why is excess consumption of three of these vitamins of concern?

19.78 Why is it important that the macronutrients calcium and phosphorus be ingested in approximately equal amounts?

19.79 Most of the micronutrients are transition elements. What property of the transition elements makes them especially suitable for their roles in the body?

CONCEPTUAL PROBLEMS

19.80 Look up the structures of vitamin C and vitamin E on the Web, and identify the functional groups in these vitamins.

19.81 What is the relationship between vitamin A and β-carotene? (Hint: Look up the structures on the Web.)

19.82 Many vegetables are "blanched" (dropped into boiling water) for a few minutes before being frozen. Why is blanching necessary?

19.83 How can you distinguish between a competitive inhibitor and an uncompetitive inhibitor experimentally?

19.84 What is the activation energy for a reaction? Why is activation energy necessary?

19.85 Does an enzyme-mediated reaction need the same, more, or less activation energy than the same reaction occurring without the presence of the enzyme? Explain why.

19.86 How will changing the conditions in an enzymatic reaction affect the rate of that reaction? Explain why in each case.

(a) Lowering the temperature from 37 °C (310 K) to 15 °C (288 K)

(b) Raising the temperature from 37 °C (310 K) to 60 °C (333 K)

(c) Lowering the pH from 7.4 to 3.0

(d) Raising the pH from 7.4 to 10

(e) Doubling the amount of substrate

(f) Decreasing the amount of substrate by half

19.87 Why are irreversible enzyme inhibitors referred to as poisons?

GROUP PROBLEMS

19.88 The adult RDA of riboflavin is 1.3 mg. If one glass (100 mL) of apple juice contains 0.014 mg of riboflavin, how much apple juice would an adult have to consume to obtain the RDA?

19.89 The ability to change a selected amino acid residue to another amino acid is referred to as "point mutation" by biochemists. Referring to the reaction for peptide bond hydrolysis in Figure 19.4, speculate on the effects that the following point mutations might have on the chymotrypsin mechanism shown in Figure 19.4: serine to valine; aspartate to glutamate.

19.90 Trypsin is an enzyme that cleaves on the C-terminal side (i.e., to the right of) all basic amino acids in a protein or peptide. (Consult Table 18.3 to identify basic amino acids.) Consider the following peptide. Predict the fragments that would be formed by treatment of this peptide with trypsin.

N-terminal end-Leu-Gly-Arg-Ile-Met-His-Tyr-Trp-Ala-C-terminal end

19.91 Apple slices and peeled potatoes rapidly brown in open air due to the presence of phenolases. Phenolases cause the oxidation of phenolic molecules like tyrosine to quinones, colored molecules responsible for the brown colors seen. An experiment comparing the time it took for a change to occur in the color of apple slices versus potato slices was done to test for phenolase activity. Then, a second experiment was done with new apple and potato slices with H_2O_2 measuring time until bubbles appeared.

Enzyme	Apple	Potato
Phenolase	130 sec.	180 sec.
Catalase	20 sec.	10 sec.

(a) Which sample contains more phenolase? Why?

(b) Which sample contains more catalase? Why?

(c) What variables in the experiment would affect your answers to (a) and (b)?

(d) Which enzyme has the higher turnover rate?

20

Carbohydrates

CONTENTS

CONCEPTS TO REVIEW

A. **Molecular Shape** (Section 4.8)

B. Chirality (Section 14.10)

C. Oxidation–Reduction Reactions (Sections 5.5, 5.6, 14.4, 15.5, and 15.6)

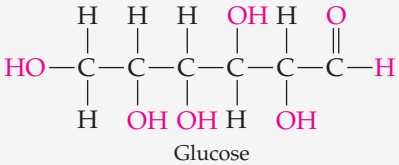
D. Acetal Formation (Section 15.7)

▲ Carbohydrates are found in many of the foods available at this picnic as well as in the table, plates, and clothing.

Imagine for a moment, Sarah and Jacob, two college students, discussing diets over lunch. Sarah makes a healthy choice to order vegetable soup and a salad while Jacob orders a juicy bacon cheeseburger with fries and lots of ketchup. They finish their meal with a stop for ice cream. Sarah claims the vegetables in her soup and her salad had fewer carbohydrates than Jacob's lunch, but Jacob disagrees, arguing that the only food he ate that had carbohydrates was the hamburger bun. Who is right? And how can they find out? There

are many resources available to find the carbohydrate, fiber, and sugar values for all food items, which will be discussed in more detail in the Chemistry in Action "Carbohydrates and Fiber in the Diet" later in chapter. Knowing these values in the foods you eat is important for maintaining a healthy lifestyle. This chapter explains carbohydrates, which are present in many of the foods you eat every day so that you can decide their place in your diet.

The word *carbohydrate* originally described glucose, the simplest and most readily available sugar. Because glucose has the formula $C_6H_{12}O_6$, it was once thought to be a "hydrate of carbon," $C_6(H_2O)_6$. Although this view has been abandoned, the name "carbohydrate" persisted, and we now use it to refer to a large class of biomolecules with similar structures. Carbohydrates have in common many hydroxyl groups on adjacent carbons together with either an aldehyde or ketone group. Glucose, for example, has five hydroxyl (—OH) groups and one aldehyde (—CHO) group:



Glucose

Carbohydrates are synthesized by plants and stored as starch, a polymer of glucose. When starch is eaten and digested, the freed glucose becomes a major source of the energy required by living organisms. Thus, carbohydrates are intermediaries by which energy from the sun is made available to animals.

20.1 An Introduction to Carbohydrates

Learning Objective:

- Classify carbohydrates by functional group and number of carbon atoms and label them accordingly.

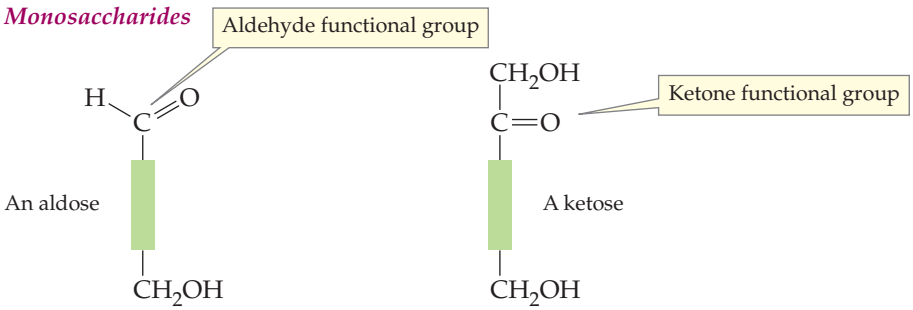
Carbohydrates are a large class of naturally occurring polyhydroxy aldehydes and ketones. **Monosaccharides,** sometimes known as **simple sugars,** are the simplest carbohydrates. They have from three to seven carbon atoms, and each contains one aldehyde or one ketone functional group. If the sugar has an aldehyde group, it is classified as an **aldose.** If it has a ketone group, the sugar is classified as a **ketose.** The aldehyde group is always at the end of the carbon chain, and the ketone group is always on the second carbon of the chain. In either case, there is a $-CH_2OH$ group at the other end of the chain.

Carbohydrate A member of a large class of naturally occurring polyhydroxy aldehydes and ketones.

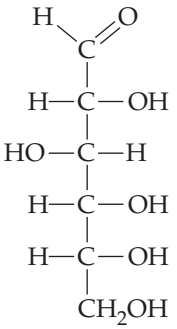
Monosaccharide (simple sugar) A carbohydrate with three to seven carbon atoms.

Aldose A monosaccharide that contains an aldehyde carbonyl group.

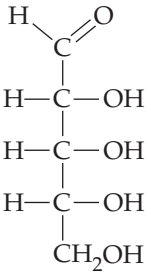
Ketose A monosaccharide that contains a ketone carbonyl group.



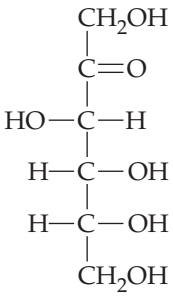
There are hydroxyl groups on all the carbon atoms between the carbonyl carbon atom and the $-CH_2OH$ at the other end and also on the end carbon next to a ketone group, as illustrated in the following three structures. The family-name ending *-ose* indicates a carbohydrate, and simple sugars are known by common names like *glucose*, *ribose*, and *fructose* rather than systematic names.



Glucose, an aldohexose (monomer for starch and cellulose; major source of energy)



Ribose, an aldopentose (a component of ATP, coenzymes, and RNA)



Fructose, a ketohexose (present in corn syrup and fruit)

The number of carbon atoms in an aldose or ketose is specified by the prefixes *tri-*, *tetr-*, *pent-*, *hex-*, or *hept-*. Thus, glucose is an aldo*hex*ose (*aldo* = aldehyde; *-hex* = six carbons; *-ose* = sugar); fructose is a keto*hex*ose (a 6-carbon ketone sugar); and ribose is an aldo*pent*ose (a five-carbon aldehyde sugar). Most naturally occurring simple sugars are aldehydes with either five or six carbon atoms.

Because of their many functional groups, monosaccharides undergo a variety of structural changes and chemical reactions. They react with each other to form **disaccharides** and **polysaccharides** (also known as **complex carbohydrates**), which are polymers of monosaccharides. Their functional groups are involved in reactions with alcohols, lipids, or proteins to form biomolecules with specialized functions. These and other carbohydrates are introduced in later sections of this chapter. First, we are going to discuss two important aspects of carbohydrate structure:

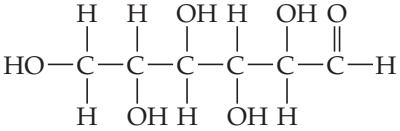
Disaccharide A carbohydrate composed of two monosaccharides.

Polysaccharide (complex carbohydrate) A carbohydrate that is a polymer of monosaccharides.

- Monosaccharides are chiral molecules (Section 20.2).
- Monosaccharides exist mainly in cyclic forms rather than the straight-chain forms shown earlier (Section 20.3).

Worked Example 20.1 Classifying Monosaccharides

Classify the monosaccharide shown as an aldose or a ketose, and label it according to its number of carbon atoms.



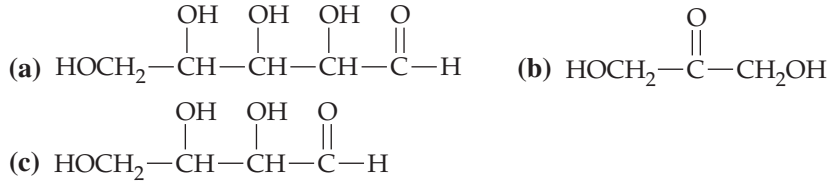
ANALYSIS First, determine if the monosaccharide is an aldose or a ketose. Then determine the number of carbon atoms present. This monosaccharide is an aldose because an aldehyde group is present. It contains 6 carbon atoms.

SOLUTION

The monosaccharide is a 6-carbon aldose, so we refer to it as an aldohexose.

PROBLEM 20.1

Classify the following monosaccharides as an aldose or a ketose, and label each according its number of carbon atoms.



PROBLEM 20.2

Draw the structures of an aldopentose and a ketohexose.

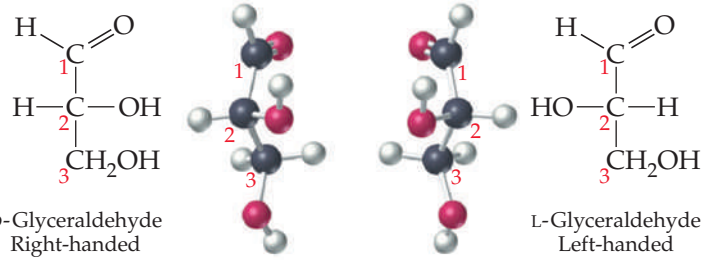
20.2 Handedness of Carbohydrates and Fischer Projections

Learning Objectives:

- Identify D and L enantiomers and any diastereomers of a monosaccharide from the Fischer projection.
- Draw the Fischer projection for a monosaccharide.

You learned that amino acids are chiral because they contain carbon atoms bonded to four different groups. Glyceraldehyde, an aldotriose and the simplest naturally occurring carbohydrate, has the structure shown next. Because four different groups are bonded to the number 2 carbon atom (—CHO, —H, —OH, and —CH_2OH), glyceraldehyde is also chiral.

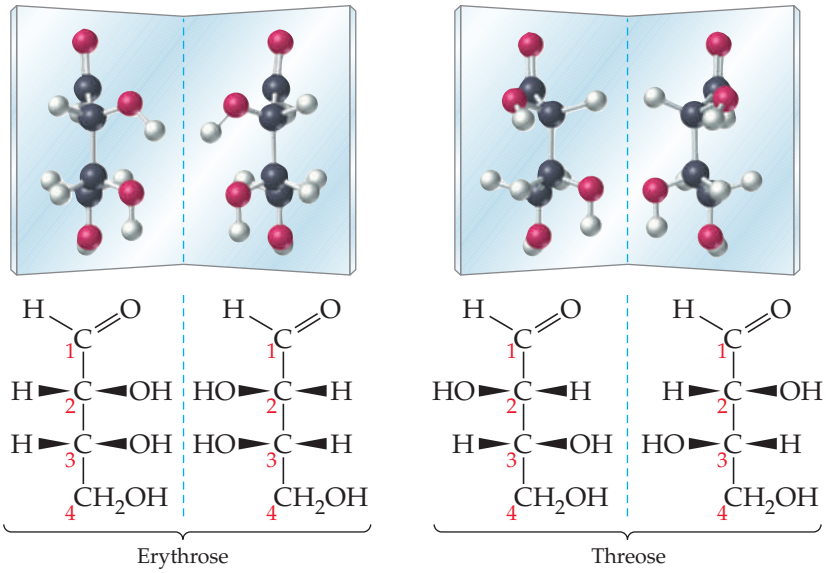
CONCEPTS TO REVIEW Chiral molecules are not superimposable on their mirror images (see Section 14.10).



Chiral compounds lack a plane of symmetry and exist as a pair of enantiomers in either a "right-handed" D form or a "left-handed" L form. Like all enantiomers, the two forms of glyceraldehyde have the same physical properties except for the way in which they affect polarized light. When polarized light is passed separately through a pair of enantiomers, each one rotates the light by the same amount, but the directions of rotation are *opposite*. If one enantiomer rotates the plane of the light to the left, the other rotates it to the right. But *the direction of rotation cannot be predicted*. There are D isomers that rotate polarized light to the left and L isomers that rotate it to the right. Recall from Section 14.10 that lower case d and l are used to indicate right and left light rotation but are unrelated to D and L absolute conformation (structure).

Compounds like glyceraldehyde that have *one* chiral carbon atom can exist as two enantiomers. But what about compounds with more than one chiral carbon atom? How many isomers are there for compounds that have two, three, four, or more chiral carbons? Aldotetroses, for example, have two chiral carbon atoms and can exist in the four isomeric forms shown in Figure 20.1. These four aldotetrose stereoisomers consist of two mirror-image pairs of enantiomers, one pair named *erythrose* and one pair named *threose*. Because erythrose and threose are stereoisomers but not mirror images of each other, they are described as **diastereomers.**

Diastereomers Stereoisomers that are not mirror images of each other.

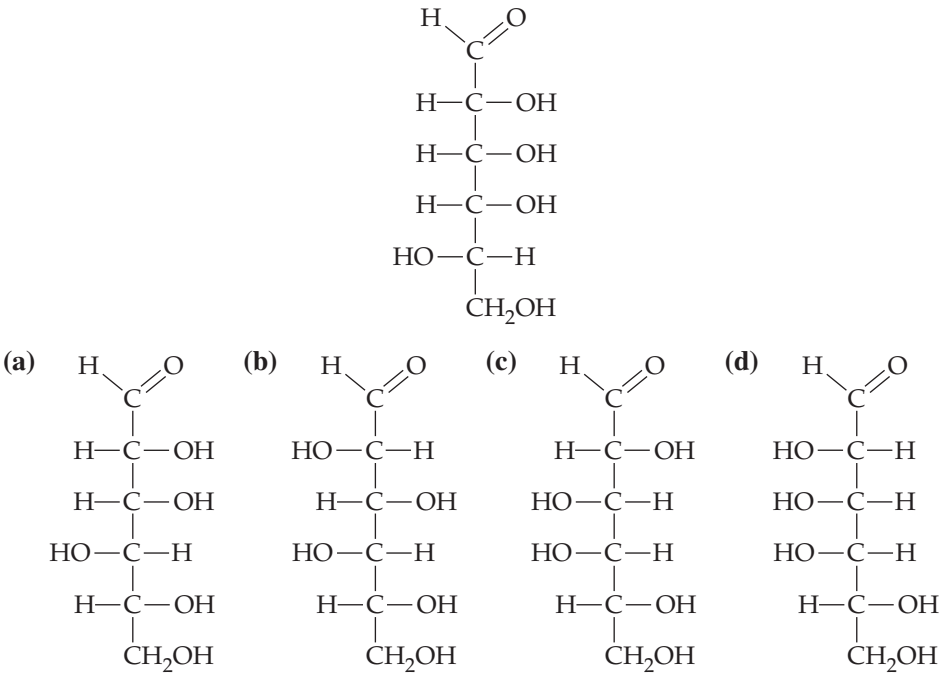


▶ **Figure 20.1**
Two pairs of enantiomers: The four isomeric aldotetroses (2,3,4-trihydroxybutanals). Carbon atoms 2 and 3 are chiral. Their —H atoms and —OH groups are written here to show their mirror-image relationship. Erythrose and threose exist as enantiomeric pairs.

By convention, the carbonyl group and the terminal CH_2OH are drawn pointing to the right. It is understood that the bonds between those carbon atoms and the other carbon atoms freely rotate and do not affect the symmetry of the molecule.

PROBLEM 20.3

Notice in the following structures (a)–(d) that the bottom carbon and its substituents are written as CH_2OH in every case. How does the C in this group differ in each case from the C atoms above it? Why must the locations of the H atoms and —OH groups attached to the carbons between this one and the carbonyl group be shown?



PROBLEM 20.4

From monosaccharides (a)–(d) in Problem 20.3, choose the one that is the enantiomer of the unlabeled monosaccharide shown.

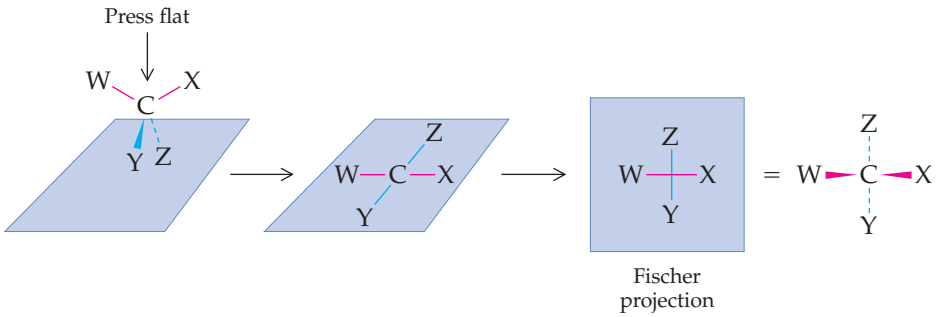
PROBLEM 20.5

Aldoheptoses have five chiral carbon atoms. What is the maximum possible number of aldoheptose stereoisomers? Draw all of the aldoheptose stereoisomers.

Drawing Sugar Molecules: Fischer Projections

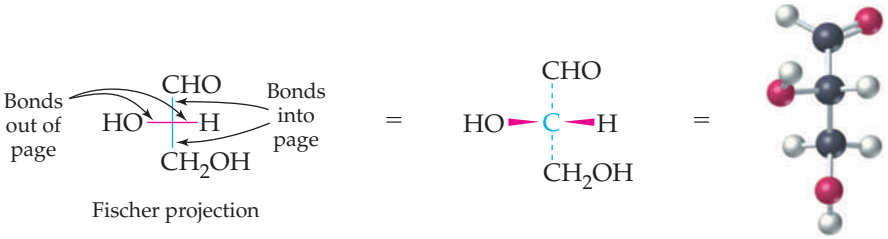
A standard method of representation called a **Fischer projection** has been adopted for drawing stereoisomers on a flat page so that we can tell one from another. A chiral carbon atom is represented in a Fischer projection as the intersection of two crossed lines, and this carbon atom is considered to be on the printed page. Bonds that point towards you are shown as horizontal lines, and bonds that point away from you are shown as vertical lines. Until now, we have used solid wedges and dashed lines to represent bonds above and behind the printed page, respectively, with ordinary solid lines for bonds in the plane of the page. The relationship between such a structure and a Fischer projection is as follows:

Fischer projection Structure that represents chiral carbon atoms as the intersections of two lines, with the horizontal lines representing bonds pointing out of the page and the vertical lines representing bonds pointing behind the page. For sugars, the aldehyde or ketone is at the top.

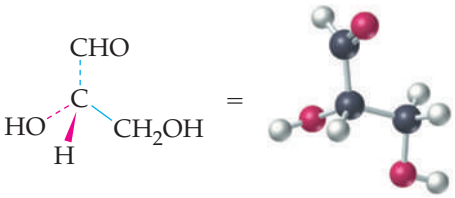


In a Fischer projection, the aldehyde or ketone carbonyl group of a monosaccharide is always placed at the top. The result is that —H and —OH groups projecting above the page are on the left and right of the chiral carbons, and groups projecting behind the page are above and below the chiral carbons. The Fischer projection of one of the enantiomers of glyceraldehyde is therefore interpreted as follows:

Fischer projection of a glyceraldehyde enantiomer



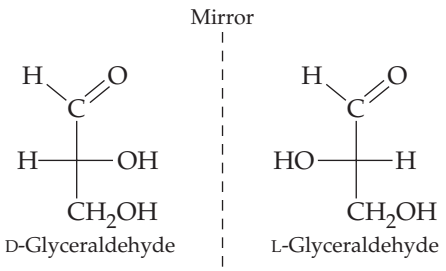
For comparison, the same glyceraldehyde enantiomer is represented next in the conventional manner, showing the tetrahedral arrangement of bonds to the chiral carbon.



Monosaccharides are divided into two families—the **D sugars** and the **L sugars**—based on their structural relationships to glyceraldehyde. Consistently writing monosaccharide formulas as Fischer projections allows us to identify the D and L forms at a glance. Look again at the structural formulas of the D and L forms of glyceraldehyde.

D Sugar Monosaccharide with the —OH group on the chiral carbon atom farthest from the carbonyl group pointing to the right in a Fischer projection.

L Sugar Monosaccharide with the —OH group on the chiral carbon atom farthest from the carbonyl group pointing to the left in a Fischer projection.



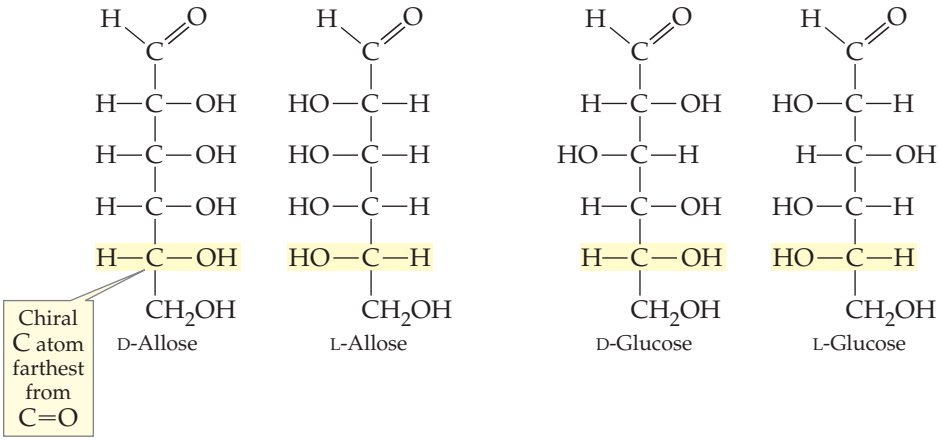
▲ Nature's preference. Snail shells have a preferred handedness, as do many molecules.

In the D form, the —OH group on carbon 2 comes out of the plane of the paper and points to the *right;* in the L form, the —OH group at carbon 2 comes out of the plane of the paper and points to the *left*. If you mentally place a mirror plane between these Fischer projections, you can see that they are mirror images.

Nature has a strong preference for one type of handedness in carbohydrates, just as it does in amino acids and in snail shells. It happens, however, that carbohydrates and amino acids have opposite handedness. Most naturally occurring α-amino acids belong to the L family, but most carbohydrates belong to the D family.

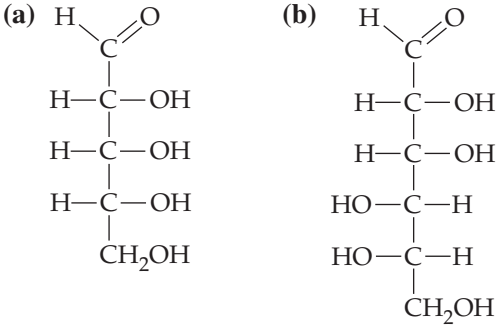
Fischer projections of molecules with more than one chiral carbon atom are written with the chiral carbons one above the other in a vertical line. To simplify visualizing the structures, we often include the C's for the chiral carbons in the plane of the page. Otherwise, the structures are interpreted like Fischer projections. Two pairs of aldohexose enantiomers are represented next in this manner. Given the Fischer projection of one enantiomer, you can draw the other by reversing the substituents on the left and right of each chiral atom. Note that each pair of enantiomers has a different name.

Two pairs of aldohexose enantiomers



Worked Example 20.2 Identifying D and L Isomers

Identify the following monosaccharides as (a) D-ribose or L-ribose and (b) D-mannose or L-mannose.



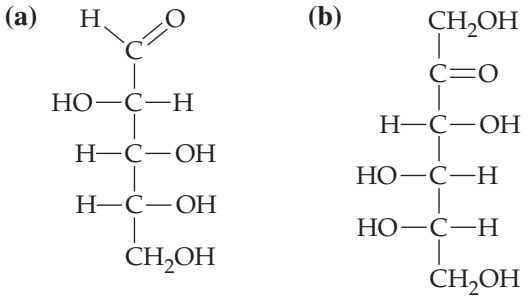
ANALYSIS To identify D or L isomers, you must check the location of the —OH group on the chiral carbon atom farthest from the carbonyl group. In a Fischer projection, this is the carbon atom above the bottom one. The —OH group points left in an L enantiomer and right in a D enantiomer.

SOLUTION

In (a), the —OH group on the chiral carbon above the bottom of the structure points to the right, so this is D-ribose. In (b), this —OH group points to the left, so this is L-mannose.

PROBLEM 20.6

Draw the enantiomer of the following monosaccharides, and in each pair identify the D sugar and the L sugar.



20.3 Structure of Glucose and Other Monosaccharides

Learning Objectives:

- Convert five- and six-carbon monosaccharides from the Fischer projection to the Haworth projection.
- Identify the anomeric carbon and the alpha (α) or beta (β) form of the monosaccharide and describe the role of mutarotation in cyclic structure.

D-Glucose, also called *dextrose* or *blood sugar,* is the most abundant of all monosaccharides and has the most important function. In nearly all organisms, D-glucose serves as a source of energy to fuel biochemical reactions. It is stored as starch in plants and glycogen in animals (Section 20.7). The structure of D-glucose illustrates a major point about the structure of monosaccharides: Although they can be written with the carbon atoms in a straight chain, monosaccharides with five or six carbon atoms exist primarily in their cyclic forms when in solution, as they are found in living organisms. These cyclic structures, represented by *Haworth projections,* formed by internal reactions to give hemiacetals or hemiketals, are shown in Figure 20.2.

Recall from Section 15.7 that the key to recognizing the hemiacetal is a carbon atom bonded to both an —OH group and an —OR group.

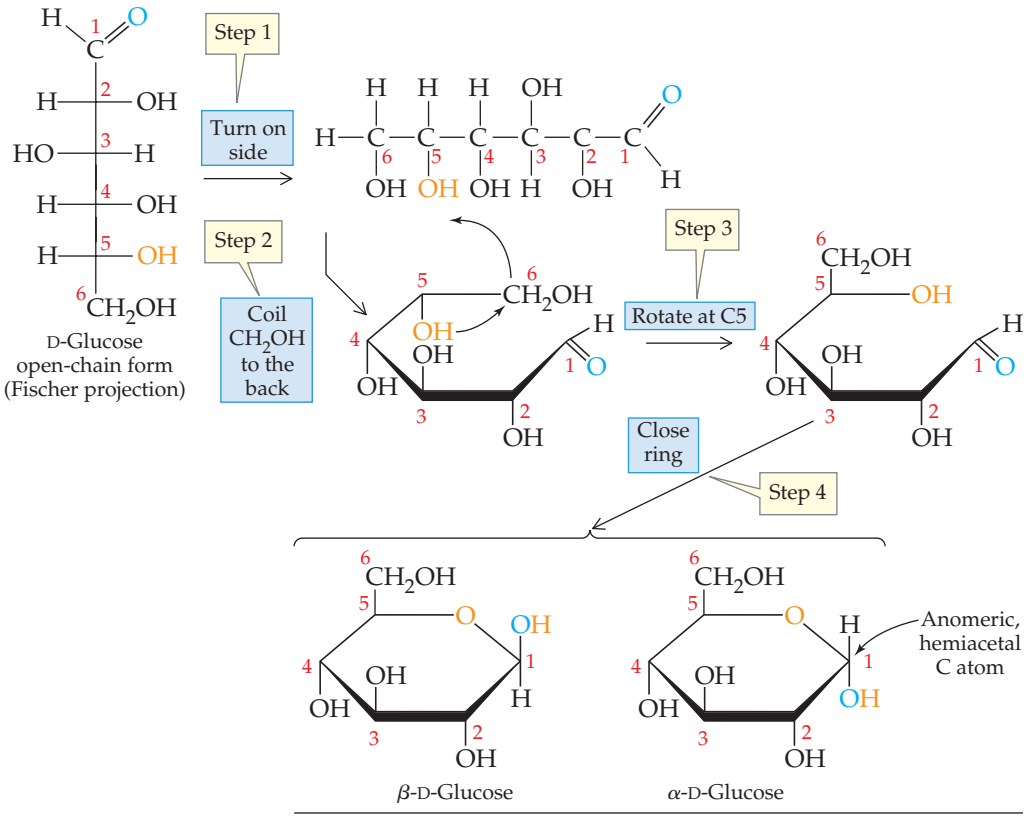
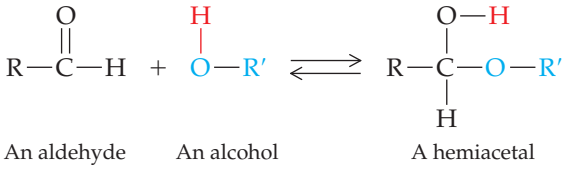


Figure 20.2
The structure of D-glucose.
D-Glucose can exist as an open-chain polyhydroxy aldehyde or as a pair of cyclic hemiacetals. The cyclic forms differ only at C1, where the —OH group is either on the opposite side of the six-membered ring from the CH_2OH (α) or on the same side (β). (Hs on carbons 2–5 are omitted here for clarity.)

Look at the Fischer projection of D-glucose at the top left-hand corner of Figure 20.2, and notice the locations of the aldehyde group and the hydroxyl groups. You learned that aldehydes and ketones react reversibly with alcohols to yield hemiacetals and hemiketals, respectively.

Since glucose has alcohol hydroxyl groups and an aldehyde carbonyl group in the same molecule, *internal* hemiacetal formation is possible. The aldehyde carbonyl group at carbon 1 (C1) and the hydroxyl group at carbon 5 (C5) in glucose react to form a six-membered ring that is a hemiacetal. Ketones undergo internal hemiketal formation as well; in ketones, the reacting carbonyl group is on C2. Monosaccharides with five or six carbon atoms form rings in this manner.



The four structures at the top in Figure 20.2 show how to picture the C5-hydroxyl and the C1-aldehyde group approaching each other for hemiacetal formation. When visualized in this manner, Fischer projections are converted to cyclic structures that (like the Fischer projections) can be interpreted consistently because the same relative arrangements of the groups on the chiral carbon atoms are maintained.

In the cyclic structures at the bottom of Figure 20.2, note how the —OH group on carbon 3, which is on the left in the Fischer projection, points *up* in the cyclic structure, and —OH groups that are on the right on carbons 2 and 4 point *down*. When Haworth projections are drawn as shown in Figure 20.2, such relationships are always maintained. Note also that the $-CH_2OH$ group in D sugars is always *above* the plane of the ring.

The hemiacetal carbon atom (C1) in the cyclic structures, like that in other hemiacetals, is bonded to two oxygen atoms (one in —OH and one in the ring). This carbon is chiral. As a result, there are two cyclic forms of glucose, known as the α and β forms. To see the difference, compare the locations of the hemiacetal —OH groups on C1 in the two bottom structures in Figure 20.2. In the β form, the hydroxyl at C1 points *up* and is on the same side of the ring as the $-CH_2OH$ group at C5. In the α form, the hydroxyl at C1 points *down* and is on the opposite side of the ring from the $-CH_2OH$ group.

Anomers Cyclic sugars that differ only in positions of substituents at the hemiacetal carbon (the anomeric carbon); the α form has the —OH on the opposite side from the $-CH_2OH$; the β form has the —OH on the same side as the $-CH_2OH$.

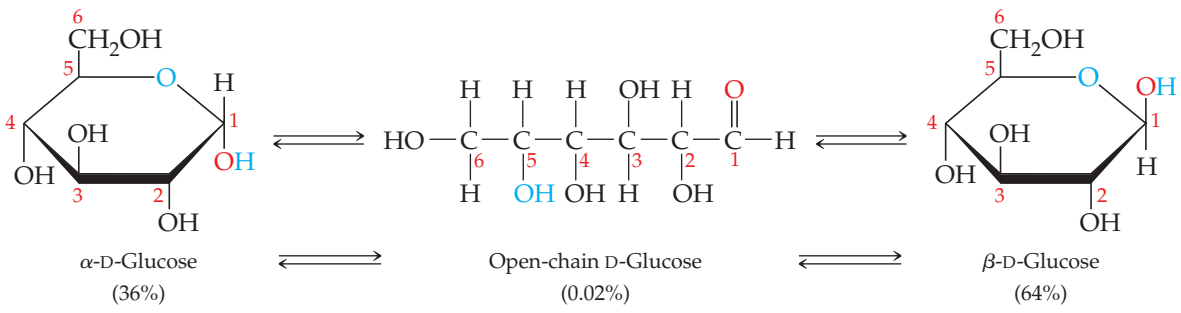
Anomeric carbon atom The hemiacetal C atom in a cyclic sugar; the C atom bonded to an —OH group and an O in the ring.

Mutarotation Change in rotation of plane-polarized light resulting from the equilibrium between cyclic anomers and the open-chain form of a sugar.

Cyclic monosaccharides that differ only in the positions of substituents at carbon 1 are known as **anomers,** and carbon 1 is said to be an **anomeric carbon atom.** It is the carbonyl carbon atom (C1 in an aldose and C2 in a ketose) that is now bonded to two O atoms. Note that the α and β anomers of a given sugar are not optical isomers because they are not mirror images.

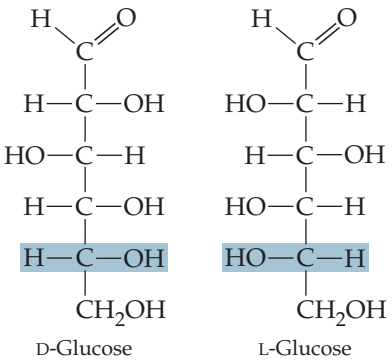
Although the structural difference between anomers appears small, it has enormous biological consequences. For example, this one small change in structure accounts for the vast difference between the digestibility of starch, which we can digest, and that of cellulose, which we cannot digest (Section 20.7).

Ordinary crystalline glucose is entirely in the cyclic α form. Once dissolved in water, however, equilibrium is established among the open-chain form and the two anomers. A solution of β-D-glucose or a mixture of the α and β forms undergoes a gradual change in rotation, known as **mutarotation,** until the ring opening and closing reactions come to the following equilibrium:

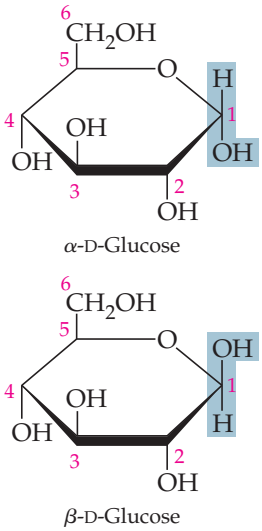


All monosaccharides with five or six carbon atoms establish similar equilibria but with different percentages of the different forms present.

Enantiomers



Anomers



HANDS-ON CHEMISTRY 20.1

Although monosaccharides can be written with the carbon atoms in an open-chain form (Fischer projection), monosaccharides with five or six carbon atoms exist primarily in their cyclic forms (Haworth projection) when in solution, as they are found in living organisms. Writing this conversion out on paper or doing it mentally can be confusing, but building a model and converting the model from one form to another helps to visualize the conversion.

You will use the same methods and techniques outlined in Hands-On Chemistry 13.1 (p. 444) and Hands-On Chemistry 15.1 (p. 526). For this exercise, you will build the straight chain Fischer model of glucose and then convert it to the Haworth model.

Building Blocks—for this exercise, you will need the following:

1 box of toothpicks—round are best but any will do.

12 carbon gumdrops—use either black or some other dark color, as long as they are different colors than those needed next.

4 ring oxygen gumdrops—use red or orange. Use these for the O atom on carbon numbers 1 and 5.

8 other oxygen gumdrops—use blue or green. You will use these to represent the OH groups that are attached to the ring and to carbon number 6

24 hydrogen gumdrops—use white or clear. You will use these to represent an H when it is attached to a ring carbon.

Build D-glucose in the open-chain, Fischer projection form as shown in Figure 20.2. Be certain that C2–C6 have tetrahedral angles. C1 and C5 should have red or orange O atoms. The OH on C5 must have an H attached to the O. The other H atoms may be omitted from OH groups. C1 is in the aldose form and the bonds angles are 120 degrees. Note that glucose is neither straight nor flat.

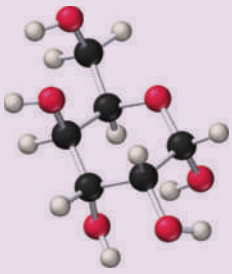
Follow the illustrations in Figure 20.2 while going through these steps.

Step 1: Converting the open-chain form to the cyclic form requires rotating the molecule so that it is horizontal with C6 on the left and C1 on the right.

Step 2: Keeping C1 in position, form an "almost" hexagon by coiling C6 to the back of the model.

Step 3: Rotate C6 around C5 so that it is above the plane of C1–C5.

Step 4: Form a hemiacetal bond between the O part of the —OH on C5 and C1. The H from the C5 —OH bonds with the O on C1 to form an OH. Depending on the orientation of the resulting C1 —OH group, you have either α-D-glucose or β-D-glucose.



Step 5: Build a second Fischer model of D-glucose and convert it to the cyclic form (Haworth) with the opposite orientation of the C1 —OH group.

Questions:

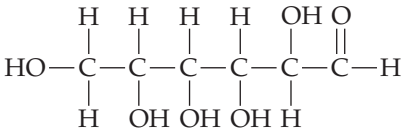
1. How many chiral carbon atoms are in glucose in the open-chain form?
2. How many chiral carbon atoms are in glucose in the cyclic form?
3. Are any of these different? Why?
4. What is the relationship between α-D-glucose or β-D-glucose? Are they mirror images?
5. What is an anomer? Are these two models anomers? Explain.

Monosaccharide Structures—Summary

- Monosaccharides are polyhydroxy aldehydes or ketones.
- Monosaccharides have three to seven carbon atoms.
- D and L enantiomers differ in the orientation of the —OH group on the chiral carbon atom farthest from the carbonyl. In Fischer projections, D sugars have this —OH on the right and L sugars have this —OH on the left.
- D-Glucose, and other 6-carbon aldoses, form cyclic hemiacetals conventionally represented (as in Figure 20.2) so that —OH groups on chiral carbons on the left in Fischer projections point up and those on the right in Fischer projections point down.
- In glucose, the hemiacetal carbon (*the anomeric carbon*) is chiral, and α and β anomers differ in the orientation of the —OH groups on this carbon. The α anomer has the —OH on the opposite side of the ring from the $-CH_2OH$, and the β anomer has the —OH on the same side of the ring as the $-CH_2OH$.

Worked Example 20.3 Converting Fischer Projections to Haworth Projections

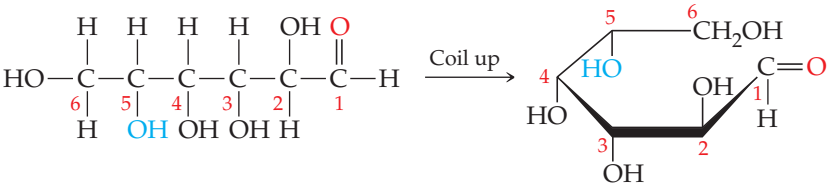
The open-chain form of D-altrose, an aldohexose isomer of glucose, has the following structure. Draw D-altrose in its cyclic hemiacetal form.



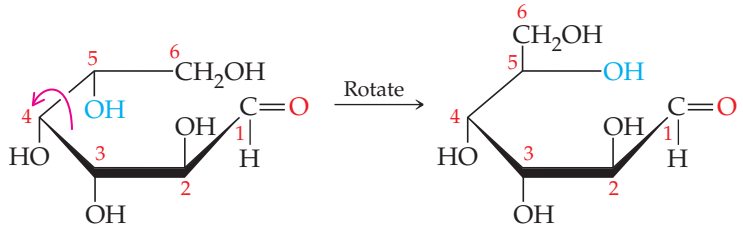
D-Altrose

SOLUTION

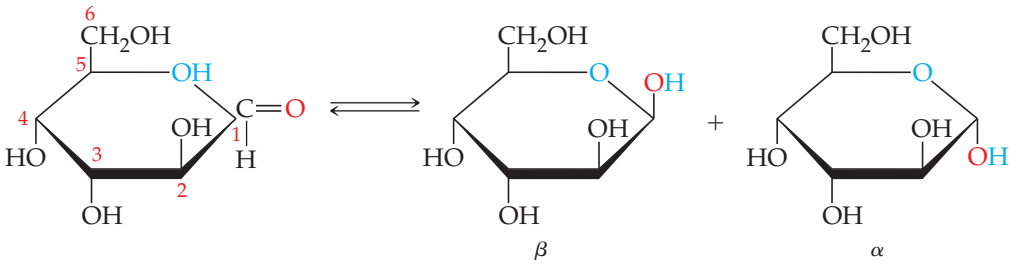
First, coil D-altrose into a circular shape by mentally grasping the end farthest from the carbonyl group and bending it backward into the plane of the paper.



Next, rotate the bottom of the structure around the single bond between C4 and C5 so that the $-CH_2OH$ group at the end of the chain points up and the —OH group on C5 points toward the aldehyde carbonyl group on the right.

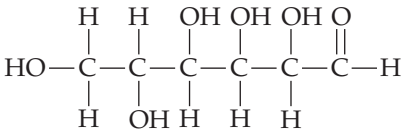


Finally, add the —OH group at C5 to the carbonyl C=O to form a hemiacetal ring. The new —OH group formed on C1 can be either up (β) or down (α).



PROBLEM 20.7

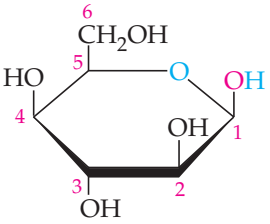
D-Talose, a constituent of certain antibiotics, has the open-chain structure shown next. Draw D-talose in its cyclic hemiacetal form.



D-Talose

PROBLEM 20.8

The cyclic structure of D-idose, an aldohexose, is shown in the margin. Convert this to the straight-chain Fischer projection structure.

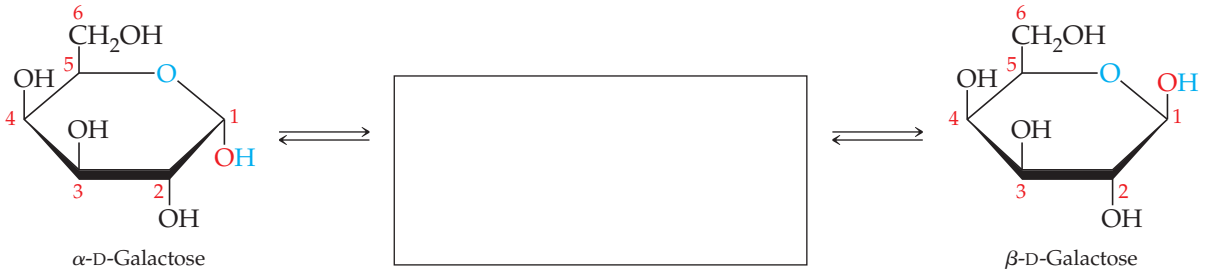


D-Idose

PROBLEM 20.9

Draw the structure that completes the mutarotation reaction between the two cyclic forms of (a) galactose and (b) fructose.

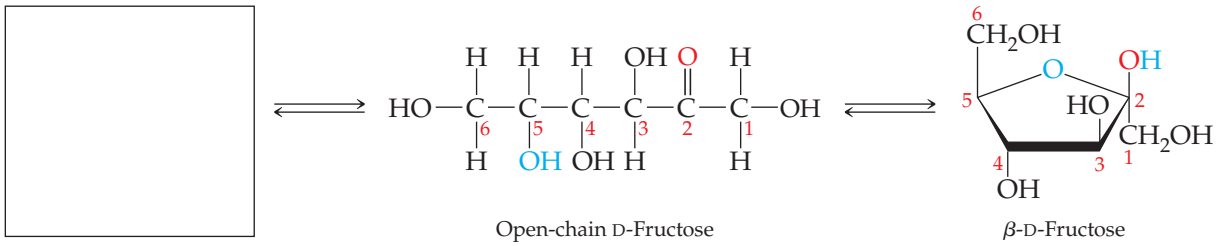
(a)



α-D-Galactose

β-D-Galactose

(b)



Open-chain D-Fructose

β-D-Fructose

20.4 Some Important Monosaccharides

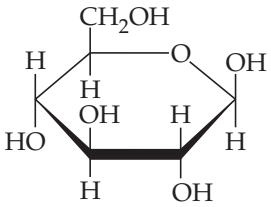
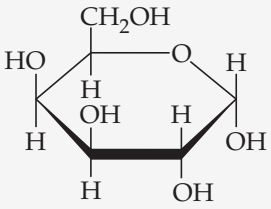
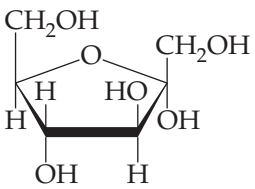
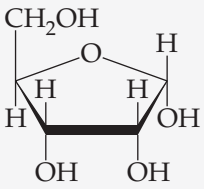
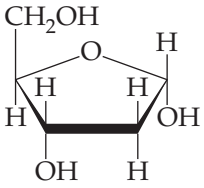
Learning Objective:

- Identify by name and structure the common monosaccharides, their sources and uses.

Monosaccharides can form multiple hydrogen bonds through their hydroxyl groups and are generally high-melting, white, crystalline solids that are soluble in water and insoluble in nonpolar solvents. Most monosaccharides and disaccharides are sweet-tasting (Table 20.2), digestible, and nontoxic (Figure 20.3). Except for glyceraldehyde (an aldotriose) and fructose (a ketohexose), the carbohydrates of interest in human biochemistry are all aldohexoses or aldopentoses. Most are in the D family. Of the five described in Table 20.1, glucose is the most important simple carbohydrate in human metabolism. It is the final product of complex carbohydrate digestion and provides acetyl groups for entry into the citric acid cycle as acetyl-CoA to be converted to energy.

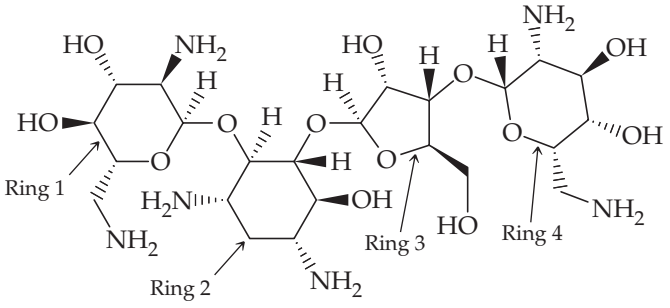
LOOKING AHEAD In Chapter 22, we will describe the metabolic pathway (glycolysis) by which glucose is converted to pyruvate and then to acetyl-CoA for entry into the citric acid cycle. The role of insulin in controlling blood glucose concentrations and the way in which those concentrations are affected by diabetes mellitus are also examined there.

Table 20.1 Common Monosaccharides

Monosaccharide Structure	Common Name and Class	Alternate Names	Source, Function, and Uses
	D-glucose aldohexose	Dextrose, Blood sugar	• Product of photosynthesis, made by plants and stored as starch • Found in fruits, vegetables, corn syrup, and honey • A building block for some disaccharides and polysaccharides • Source of acetyl groups for citric acid cycle to provide metabolic energy for mammals, especially for red blood cells, muscle tissue, kidney tissue, and brain tissue • Stored as glycogen in muscle for use as energy source • Glucose level in blood regulated by the hormones insulin and glucagon • Medical use to maintain blood glucose levels and supply energy source via intravenous drip
	D-galactose aldohexose	none	• Found in plant gums and pectins • Found in milk as half of the disaccharide lactose • Component of brain and nervous system tissues • Metabolized to glucose for energy-yielding pathways • Galactosemia results from an inherited deficiency of any of the enzymes needed to convert glucose to galactose, which may cause liver failure, mental retardation, and cataracts. Galactosemia is treated by a galactose-free diet
	D-fructose ketohexose	Levulose, Fruit sugar	• Found in fruits and honey • Produced by the hydrolysis of corn starch to make high-fructose corn syrup • One of the two units bonded to make sucrose • Phosphorylated fructose is an intermediate in glucose metabolism • Sweeter than sucrose, used to sweeten many beverages and prepared foods
	Ribose aldopentose	none	• Found as parts of larger molecules in organisms • Part of ribonucleic acid, involved in protein synthesis (Chapter 26) • Part of coenzyme A • Part of the second messenger cyclic AMP (Chapter 28)
	2-Deoxyribose	none	• Part of DNA, the genetic material of the cell (Chapter 26)

Worked Example 20.4 Identifying Sugars and Sugar Derivatives in Antibiotics

Framycetin, a topical antibiotic, is a four-ring molecule consisting of several aminoglycosides—sugars that have some of the —OH groups on the sugars replaced by $-NH_2$ groups—and another ring, with oxygen links between the rings. What sugar or other molecule is each ring derived from?

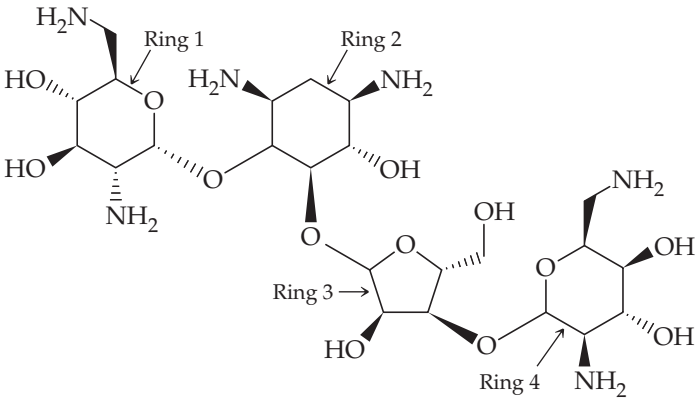


ANALYSIS Look at each ring carefully. Ring 2 does not include an O. It cannot be a sugar. Rings 1, 3, and 4 all contain O as a ring member. Imagine the rings as underivatized sugars, that is with —OH groups instead of —NH_2 groups; count the number of carbon atoms in each sugar and draw the sugar form to help identify the sugar.

SOLUTION
Ring 2 has six carbon atoms and no oxygen atoms as part of the ring; it is not a sugar, but is a cyclohexane derivative. Rings 1 and 4 are derived from the aldohexose, glucose, while ring 3 is derived from the aldopentose, ribose.

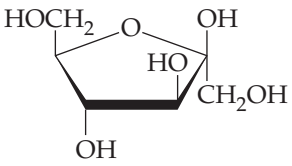
KEY CONCEPT PROBLEM 20.10

Neomycin is an antibiotic used in topical applications to inhibit the growth of bacteria. It is an aminoglycoside, that is, some of the —OH groups on the sugars have been replaced by —NH_2 or R groups. The four rings that constitute neomycin are joined by glycosidic bonds and two of the rings are amino sugars. In the structure shown, identify (a) the amino sugar rings by number, (b) the unmodified sugar ring structure, and (c) the non–sugar ring structure. List how many carbon atoms are in each ring.



PROBLEM 20.11

In the monosaccharide hemiacetal shown in the margin, number all the carbon atoms, identify the anomeric carbon atom, and identify it as the α or β anomer.

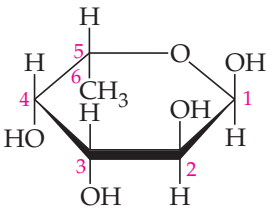


PROBLEM 20.12

Identify the chiral carbons in α-D-fructose, α-D-ribose, and β-D-2-deoxyribose.

PROBLEM 20.13

L-Fucose is one of the naturally occurring L monosaccharides. It is present in the short chains of monosaccharides by which blood groups are classified (see the Chemistry in Action "Cell-Surface Carbohydrates and Blood Type" on p. 674). Compare the structure of L-fucose shown in the margin with the structures of α- and β-D-galactose and answer the following questions.



L-Fucose

(a) Is L-fucose an α or β anomer?
(b) Compared with galactose, on which carbon is L-fucose missing an oxygen?
(c) How do the positions of the —OH groups above and below the plane of the ring on carbons 2, 3, and 4 compare in D-galactose and L-fucose?
(d) "Fucose" is a common name. Is 6-deoxy-L-galactose a correct name for fucose? Why or why not?

CHEMISTRY IN ACTION

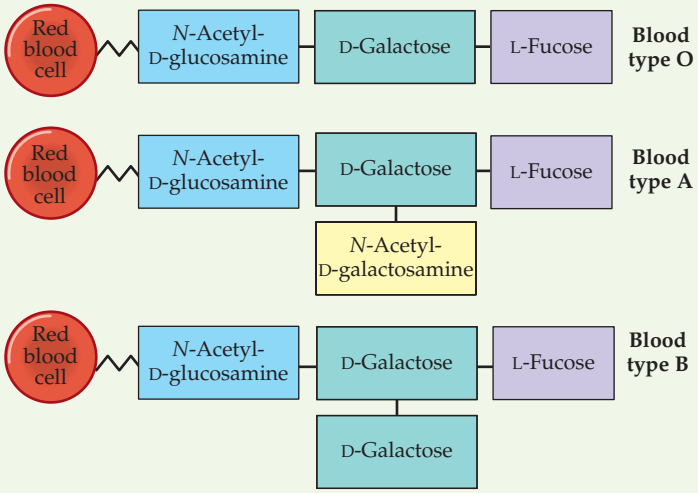
Cell-Surface Carbohydrates and Blood Type

A century ago, scientists discovered that human blood can be classified into four blood group types, called A, B, AB, and O. This classification indirectly results from the presence on red blood cell surfaces of three different oligosaccharides (sugar chains), designated A, B, and O (see the diagram). Individuals with type AB blood have both A and B oligosaccharides displayed on the same cells.

Selecting a matching blood type is vitally important in choosing blood for transfusions because a major component of the body's immune system (Chapter 29) is a collection of proteins called *antibodies* that recognize and attack foreign substances, such as viruses, bacteria, potentially harmful macromolecules, and foreign blood cells. Among the targets of these antibodies are cell-surface molecules that are not present on the individual's own cells and are thus "foreign blood cells." For example, if you have type A blood, your plasma (the liquid portion of the blood) contains antibodies to the type B oligosaccharide. Thus, if type B blood enters your body, its red blood cells will be recognized as foreign and your immune system will launch an attack on them. The result is clumping of the cells (agglutination), blockage of capillaries, and possibly death.

Because of the danger of such interactions, both the blood types that individuals can receive and the blood types of recipients to whom they can donate blood are limited, as indicated in the accompanying table. A few features of the table deserve special mention.

- People with blood types A, B, and AB all lack antibodies to type O cells. Individuals with type O blood are therefore known as "universal donors"—in an emergency, their blood can safely be given to individuals of all blood types.
- Type AB individuals are known as "universal recipients." Because people with type AB blood have both A and B molecules on their red cells, their blood contains no antibodies to A, B, or O, and they can, if necessary, receive blood cells of all types.



Individuals with blood type . . .	. . . have antibodies to type . . .	. . . can receive from type . . .	. . . and can donate to type
O	A and B	O	O, A, and B*
A	B	O and A	A and AB
B	A	O and B	B and AB
AB	None	O, A, and B*	AB

*Red blood cells only

CIA Problem 20.1 Look at the structures of the blood group determinants. What makes the blood types different?

CIA Problem 20.2 People with type O blood can donate blood to anyone, but they cannot receive blood from everyone. From whom can they not receive blood? People with type AB blood can receive blood from anyone, but they cannot give blood to everyone. To whom can they give blood? Why?

CIA Problem 20.3 All cells in your body contain glycoproteins (proteins with short oligosaccharide chains attached, Chapter 18) as part of the cell membrane. The carbohydrate part of a glycoprotein extends out of the membrane into the intercellular fluid and is the signaling part of the molecule. Red blood cells have specific glycoproteins that we use to specify the different blood types. Which sugars and sugar derivatives are found in all blood types? (Hint: Look closely at the sugar chains attached to each red blood cell in the diagram.)

20.5 Reactions of Monosaccharides

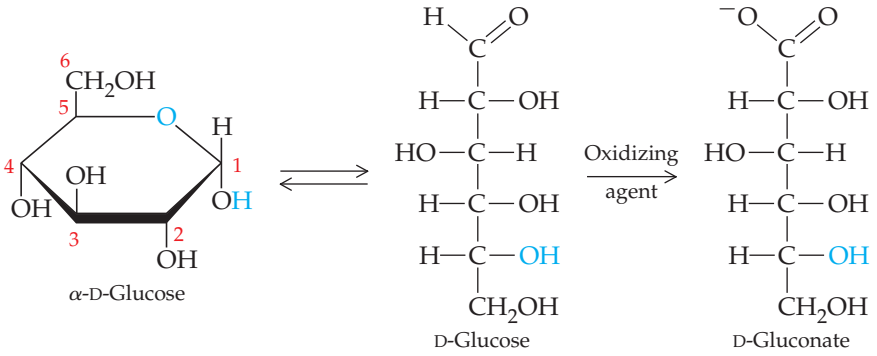
Learning Objectives:

- Predict the products of oxidation and reduction reactions on monosaccharides.
- Predict the products of reactions between monosaccharides and alcohols.
- Recognize and predict the products of hydrolysis reactions of polysaccharides and phosphorylation reactions of monosaccharides.

Reaction with Oxidizing Agents: Reducing Sugars

Aldehydes can be oxidized to carboxylic acids (RCHO ⟶ RCOOH) a reaction that applies only to the open-chain form of aldose monosaccharides (Section 15.5). As the open-chain aldehyde is oxidized, its equilibrium with the cyclic form is displaced, and, in accordance with Le Châtelier's principle, the open-chain form continues to be produced. As a result, the aldehyde group of the monosaccharide is ultimately oxidized to a carboxylic acid group. For glucose, the reaction is

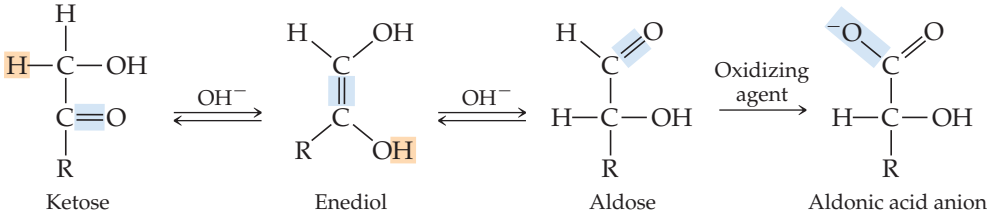
Le Châtelier's principle states that when a stress is applied to a system at equilibrium, the equilibrium shifts to relieve the stress (Section 7.9).



Carbohydrates that react with mild oxidizing agents are classified as **reducing sugars** (they reduce the oxidizing agent). The Benedict's test is a common test for the presence of reducing sugars. Benedict's test relies on the ability of Cu^{2+} in alkaline solution to be reduced by aldose and some ketose monosaccharides. The appearance of a green, brown, orange, or red precipitate upon heating the sample in Benedict's solution is a positive test for the presence of reducing sugar.

Reducing sugar A carbohydrate that reacts in basic solution with a mild oxidizing agent.

Recall from Section 15.5 that ketones do not generally undergo oxidation, because they lack the hydrogen attached to the carbonyl carbon that aldehydes have. In basic solution some ketoses are reducing sugars because a ketone that has an H atom on the carbon adjacent to the carbonyl carbon undergoes a rearrangement. This H atom moves over to the carbonyl oxygen. The product is an *enediol,* "ene" for the double bond and "diol" for the two hydroxyl groups. The enediol rearranges to give an aldose, which is susceptible to oxidation.

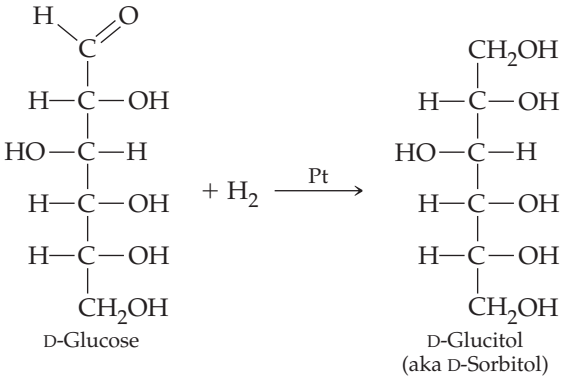


Here, also, oxidation of the aldehyde to an acid drives the equilibria toward the right, and complete oxidation of the ketose occurs. Thus, *in basic solution, all monosaccharides, whether aldoses or ketoses, are reducing sugars.* This ability to act as reducing agents is the basis for most laboratory tests for the presence of monosaccharides.

Reaction with Reducing Agents: Sugar Alcohols

Monosaccharides are easily converted to sugar alcohols, called alditols, by the reduction of the carbonyl group to an alcohol group. This is accomplished industrially by exposing the sugar to H_2 in the presence of the catalyst Pt. The sugar alcohols are named as derivatives of the sugars, with the suffix *-ose* replaced with *-itol*. Thus, D-glucose becomes D-glucitol, also known as D-sorbitol, D-xylose becomes D-xylitol, and D-mannose becomes D-mannitol. These three sugar alcohols are used as sweeteners in diet drinks and sugarless gums as well as in many diet foods designed for those who are on restricted sugar intake for health reasons. However, caution must be taken in the

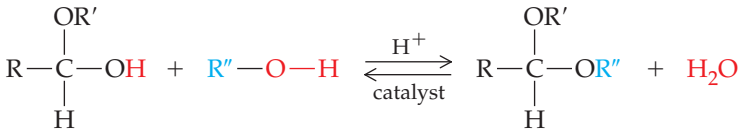
amount of sugar alcohols ingested at any time because too much may cause gas and diarrhea.



D-Glucose D-Glucitol (aka D-Sorbitol)

Reaction with Alcohols: Glycoside and Disaccharide Formation

Hemiacetals react with alcohols with the loss of water to yield acetals, compounds with two —OR groups bonded to the same carbon (Section 15.7).

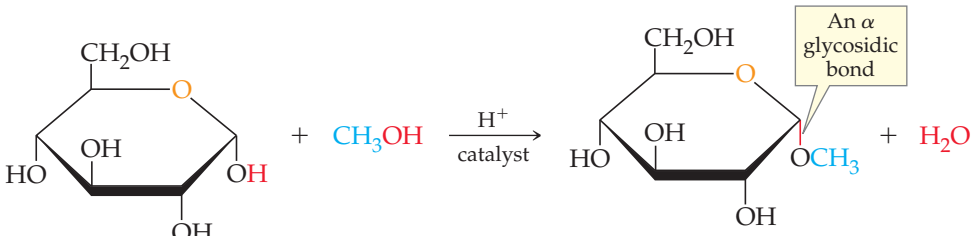


A hemiacetal An alcohol An acetal

Glycoside A cyclic acetal formed by reaction of a monosaccharide with an alcohol, accompanied by loss of H_2O.

Because glucose and other monosaccharides are cyclic hemiacetals, they also react with alcohols to form acetals, which are called **glycosides.** In a glycoside, the —OH group on the anomeric carbon atom is replaced by an —OR group. For example, glucose reacts with methanol to produce methyl glucoside. Note that a *gluc*oside is a cyclic acetal formed by glucose. A cyclic acetal derived from *any* sugar is a *glyc*oside.

Formation of a glycoside

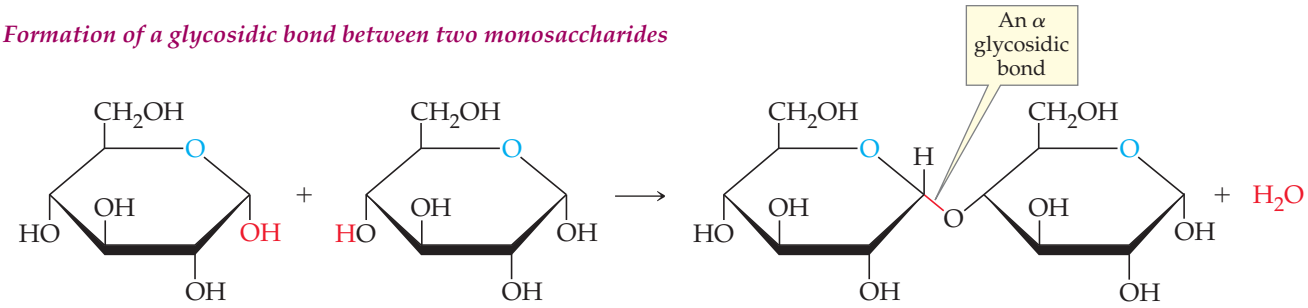


Glycosidic bond Bond between the anomeric carbon atom of a monosaccharide and an —OR group.

The bond between the anomeric carbon atom of the monosaccharide and the oxygen atom of the —OR group is called a **glycosidic bond.** Since glycosides like the one shown earlier do not contain hemiacetal groups that establish equilibria with open-chain forms, they are *not* reducing sugars.

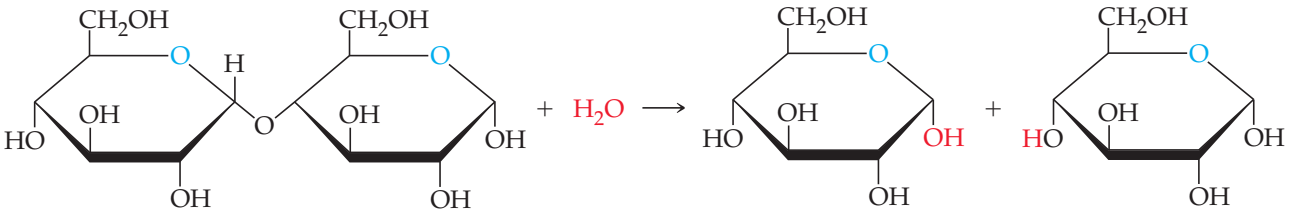
In larger molecules, including disaccharides and polysaccharides, monosaccharides are connected to each other by glycosidic bonds. For example, a disaccharide forms by reaction of the anomeric carbon of one monosaccharide with an —OH group of a second monosaccharide.

Formation of a glycosidic bond between two monosaccharides



The reverse of this reaction is a *hydrolysis* and is the reaction that takes place during digestion of all carbohydrates.

Hydrolysis of a disaccharide

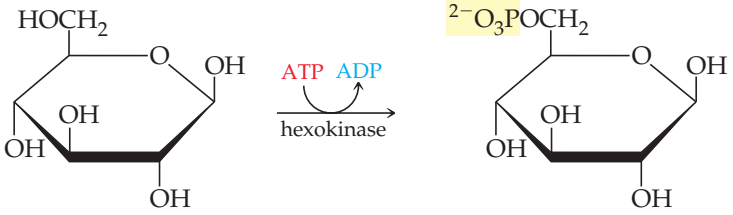


PROBLEM 20.14

Draw the structure of the α and β anomers that result from the reaction of methanol and ribose. Are these compounds acetals or hemiacetals?

Formation of Phosphate Esters of Alcohols

Phosphate esters of alcohols contain a $-PO_3^{2-}$ group bonded to the oxygen atom of an —OH group. The —OH groups of sugars can add $-PO_3^{2-}$ groups to form phosphate esters in the same manner. The resulting phosphate esters of monosaccharides appear as reactants and products throughout the metabolism of carbohydrates. Glucose phosphate is the first to be formed and sets the stage for subsequent reactions. It is produced by the transfer of a $-PO_3^{2-}$ group from ATP to glucose in the first step of glycolysis, the multistep metabolic pathway followed by glucose and other sugars, which is described in Chapter 22. Glycolysis converts glucose to the acetyl groups that are carried into the citric acid cycle.



20.6 Common Disaccharides

Learning Objective:

- Identify by name and structure the common disaccharides, the subunits and the bond between them, their sources and uses.

Every day, you eat a disaccharide—sucrose, common table sugar. Sucrose is made of two monosaccharides, one glucose and one fructose, covalently bonded to each other. Sucrose is present in modest amounts, along with other monosaccharides and disaccharides, in

(a)

(b)

(c)

▲ **Figure 20.3**
Common sugars.
(a) The disaccharide sucrose (glucose + fructose) is found in sugar cane and sugar beets. (b) Jam contains the monosaccharide galactose in the pectin that stiffens it. (c) Honey is high in the monosaccharide fructose.

1,4 Link A glycosidic link between the hemiacetal hydroxyl group at C1 of one sugar and the hydroxyl group at C4 of another sugar.

most fresh fruits and many fresh vegetables. But most sucrose in our diets has been added to something. Perhaps you add it to your coffee or tea. Or it is there in a ready-to-eat food product that you buy—maybe breakfast cereal, ice cream, or a "super-sized" soda, or even bread. Excessive consumption of high-sucrose foods has been blamed for everything from criminal behavior to heart disease to hyperactivity in children, but without any widely accepted scientific proof. A proven connection with heart disease does exist, of course, but by way of the contribution of excess sugar calories to obesity.

Sweetness of sugars and substitutes is determined on a relative scale with sucrose assigned a value of 100. Sweetness is assessed by taste panels and the results of many tests have been averaged to produce the relative values found in Table 20.2. Sugar alcohols and synthetic sweeteners are used in many foods advertised for those who for medical or personal reasons choose to reduce the amount of natural sugars in their diet. The sugar alcohols, found in products such as candy and desserts marketed to diabetics, are non-digestible and therefore do not influence blood sugar levels. However, the sugar alcohols can cause diarrhea if ingested in large amounts.

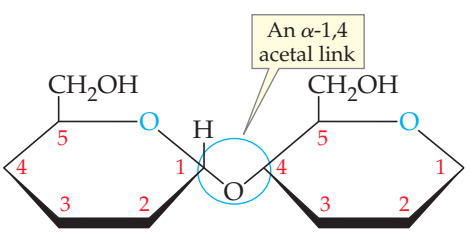
Table 20.2 Relative Sweetness of Some Sugars and Sugar Substitutes

Name/Type	Sweetness (relative to sucrose = 100)	Common Source
Monosaccharide		
Fructose	175	fruit
Galactose	30	fruit pectin
Glucose	75	sugar, starch
Disaccharide		
Lactose	16	milk
Maltose	33	germinating grain
Sucrose	100	sugar cane, sugar beets
Sugar Alcohol		
Maltitol	80	diet foods*
Sorbitol	60	diet foods*
Xylitol	100	diet foods*
Synthetic Sweetener		
Aspartame	18,000	sugar substitute
Cyclamate	3000	sugar substitute
Saccharin	45,000	sugar substitute
Sucralose	60,000	sugar substitute

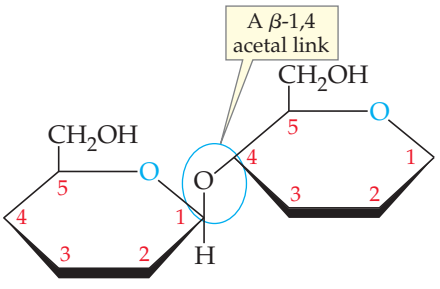
*Diet foods, especially for diabetics

Disaccharide Structure

The two monosaccharides in a disaccharide are connected by a glycosidic bond. The bond may be α or β, as in cyclic monosaccharides: α points below the ring and β points above the ring (see Figure 20.2). The structures include glycosidic bonds that create a **1,4 link,** that is, a link between C1 of one monosaccharide and C4 of the second monosaccharide.



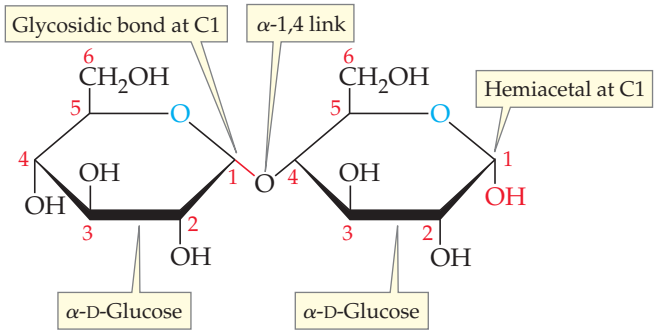
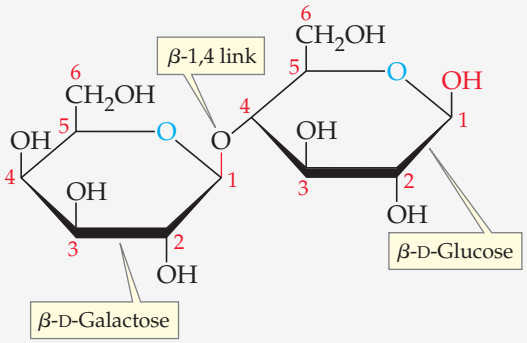
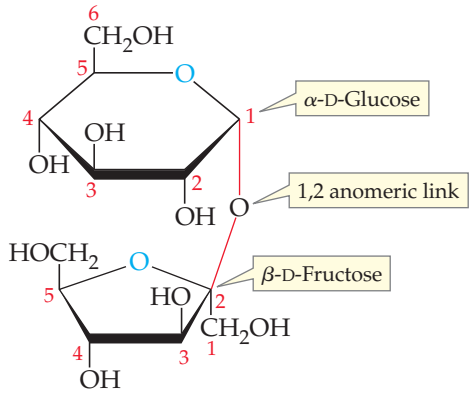
An α-1,4 disaccharide



A β-1,4 disaccharide

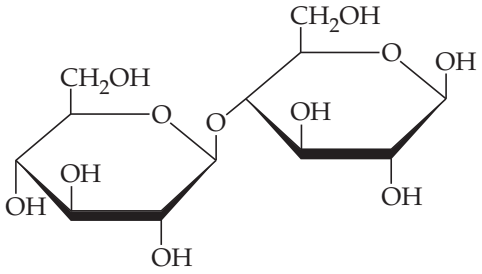
Table 20.3 outlines the three naturally occurring and most common disaccharides. These disaccharides illustrate the three different ways monosaccharides are linked: by a glycosidic bond in the α orientation (maltose), a glycosidic bond in the β orientation (lactose), or a bond that connects two anomeric carbon atoms (sucrose).

Table 20.3 Common Disaccharides

Disaccharide	Subunits and Linking Bonds	Facts
Maltose  Maltose	α-D-Glucose linked to α-D-glucose by an α-1,4 bond	• Hemiacetal bond on right glucose at C1 • Reducing sugar due to hemiacetal • Also known as malt sugar • Present in fermenting grains (beer production) • Used to sweeten prepared foods • Produced during digestion of starch by amylase in the small intestine • Hydrolyzed to glucose by maltase in the small intestine
Lactose  Lactose	β-D-Galactose linked to β-D-glucose by a β-1,4 bond	• Hemiacetal bond on β-D-glucose at C1 • Reducing sugar due to hemiacetal • Also known as milk sugar • Present at 7% in human milk • Hydrolyzed during digestion by lactase in the small intestine • In humans lacking lactase, lactose remains in the intestines, raising osmolarity and causing intestinal distress • Hydrolyzed by bacteria in the large intestine, also causing intestinal distress • These two conditions are called lactose intolerance
Sucrose  Sucrose	α-D-Glucose linked to β-D-fructose by a 1,2 anomeric bond	• Not a reducing sugar because glucose is now an acetal and fructose is a ketal • Also known as table sugar • Produced from sugar beets and sugar cane • Hydrolysis yields a 50:50 mixture of glucose and fructose called invert sugar • Invert sugar is used as a food additive • Invert sugar is sweeter than sucrose • Sucrose is hydrolyzed in the small intestine by sucrase

Worked Example 20.5 Identifying Reducing Sugars

The disaccharide cellobiose can be obtained by enzyme-catalyzed hydrolysis of cellulose. Do you expect cellobiose to be a reducing or a nonreducing sugar?



Cellobiose

ANALYSIS To be a reducing sugar, a disaccharide must contain a hemiacetal group, that is, a carbon bonded to one —OH group and one —OR group. The ring at the right in the structure above has such a group.

SOLUTION
Cellobiose is a reducing sugar.

▲ Milk for lactose-intolerant individuals. The lactose content of the milk has been decreased by treating it with lactase.

PROBLEM 20.15

Refer to the cellobiose structure in Worked Example 20.5. How would you classify the link between the monosaccharides in cellobiose?

PROBLEM 20.16

Refer to the cellobiose structure in Worked Example 20.5. Show the structures of the two monosaccharides that are formed on hydrolysis of cellobiose. What are their names?

KEY CONCEPT PROBLEM 20.17

Identify the following disaccharides. Give a natural source for each of these disaccharides. (a) The disaccharide that contains two glucose units joined by an α-glycosidic linkage. (b) The disaccharide that contains fructose and glucose. (c) The disaccharide that contains galactose and glucose.

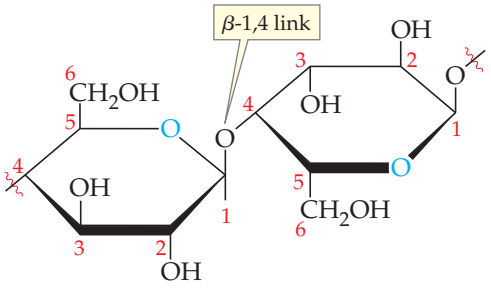
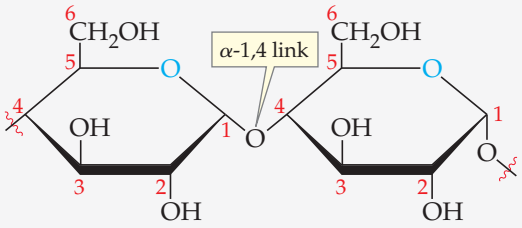
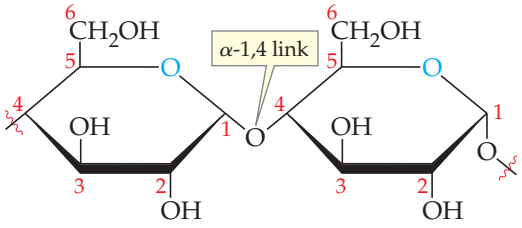
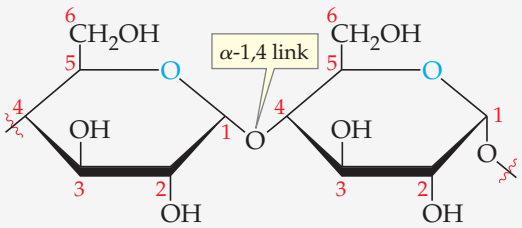
20.7 Some Important Polysaccharides Based on Glucose

Learning Objectives:

- Recognize common polysaccharides and identify where each polysaccharide is found in nature and its function.
- Identify the monomers and type of bond present in each polysaccharide.
- Identify the modified monosaccharides found in naturally occurring polysaccharides and identify the functions of these polysaccharides.

Polysaccharides are polymers of tens, hundreds, or even many thousands of monosaccharides linked together through glycosidic bonds of the same type as in maltose and lactose. Three of the most important polysaccharides are *cellulose, starch,* and *glycogen.* Compare the repeating units of cellulose and starch shown in Table 20.4. A slight change in the glycosidic bond has an enormous effect on the structure and function of a glucose polymer.

Table 20.4 Common Polysaccharides Containing Glucose

Molecule/Repeating Unit	Bond	Facts
Cellulose  Cellulose repeating unit	β-1,4 link	• Most abundant polysaccharide on earth • Fibrous polysaccharide found in plants • Forms part of cell walls • Provides rigid structure in plants • Each cellulose molecule consists of thousands of glucose units in an unbranched chain • β-1,4 Linkage confers a rigid, puckered conformation on the cellulose molecule • Microorganisms in the gut of some animals (cows and other grazing animals) and some insects (termites and moths) produce cellulase, which hydrolyzes cellulose to glucose • Humans do not digest cellulose • Provides "roughage" (fiber) in our diet • Cellulose is used to build houses, make cardboard, and other paper products • Cellulose derivatives are cellophane, rayon, and guncotton
Amylose (starch)  Starch and glycogen repeating unit	α-1,4 link	• Found in plants, especially in the seeds • Common sources are beans, grains like wheat and rice, and tubers like potatoes • Accounts for about 20% (m/m) of starch • Chains are several hundred to 1000 units long • α-1,4 linkage between units results in a flexible chain that coils into helices • Soluble in hot water • Hydrolyzed to glucose in animals by α-amylase in saliva and in small intestine to supply glucose for use in metabolism or for energy storage • Figure 20.4 shows the helical structure
Amylopectin (starch)  Starch and glycogen repeating unit	α-1,4 link with α-1,6 link branch points*	• Found in plants, especially in the seeds • Common sources are beans, grains like wheat and rice, and tubers like potatoes • Accounts for about 80% (m/m) of starch • Chains are several hundred to 1000 units long • α-1,4 Linkage between units results in a flexible chain • α-1,6 Linkage between units results in branching from a chain • Multiple branches occur in amylopectin • Insoluble in hot water • Molecular mass of amylopectin molecules is up to 200 million • Ideal glucose storage molecule; large, insoluble, and compact due to branching • Supplies energy for seed germination and early growth • Hydrolyzed to glucose in animals by amylase in small intestine to supply glucose for use in metabolism or for energy storage • Only α-1,4 bonds are hydrolyzed by α-amylase; α-1,6 bonds are not hydrolyzed by α-amylase
Glycogen  Starch and glycogen repeating unit	α-1,4 link with α-1,6 link branch points*	• Found in animals • Often referred to as animal starch • Used as glucose storage in liver and muscle cells • Stored in aggregates referred to as granules • Liver glycogen supplies glucose to maintain blood sugar levels and needs of other cell types • Muscle glycogen supplies glucose to muscle cells for conversion to ATP when these cells need energy during exercise (work) • α-1,4 Linkage between units results in a flexible chain • α-1,6 Linkage between units results in branching from a chain • Multiple branches occur in glycogen, but it is more highly branched than amylopectin • Glycogen has up to one million glucose units per molecule and is much larger than amylopectin

*The chain branching with α-1,6 linkages is shown in the drawings on page 683.

CHEMISTRY IN ACTION

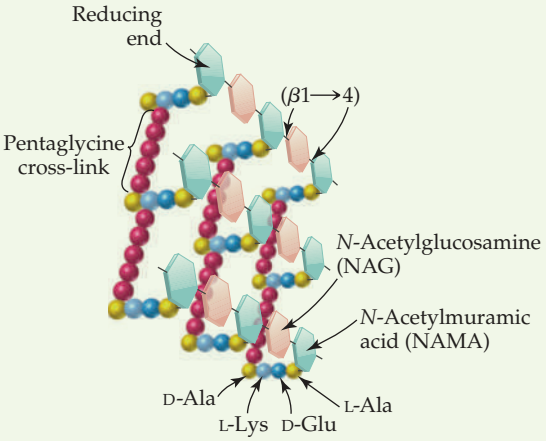
Bacterial Cell Walls: Rigid Defense Systems

All cells are defined by the presence of a plasma membrane, which confines the cell's contents inside a lipid bilayer studded with proteins (Section 21.3). Bacteria and higher plants surround the plasma membrane with a rigid cell wall, while cells of other organisms do not have walls, only a plasma membrane. Cell walls differ markedly in composition but not in function among organisms. The functions of a cell wall are to make the cell rigid, prevent the cell from bursting due to osmotic pressure, give shape to the cell, and protect it from pathogens.

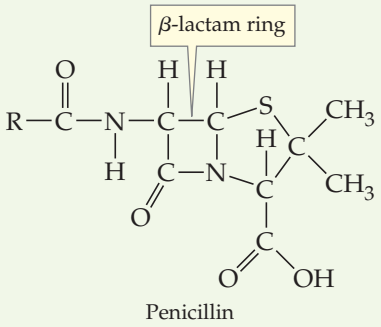
Bacterial cell walls provide strength, shape, and a rigid platform for the attachment of flagella and pilli. The composition of the cell wall also provides attachment sites for bacteriophages (viruses that infect bacteria). Cell-wall composition varies among bacterial species and is an important factor in distinguishing between some groups of bacteria. A majority of bacterial cell walls are composed of a polymer of *peptidoglycan,* an alternating sequence of the modified sugars *N*-acetylglucosamine (NAG) and *N*-acetylmuraminic acid (NAMA). Peptidoglycan strands are cross-linked to one another by short peptide bridges; these bridges are unique in that both D-alanine and L-alanine are present. The interlocked strands form a porous, multilayered grid over the bacterial plasma membrane.

Fortunately, animals have developed natural defenses that can control many bacteria. For example, lysozyme—an enzyme found naturally in tears, saliva, and egg white—hydrolyzes the peptidoglycan cell wall of pathogenic bacteria, thereby killing them. In the middle of the twentieth century the antibiotic penicillin was developed. The penicillin family members all contain a beta-lactam ring that allows these compounds to act as "suicide inhibitors" of the enzymes that synthesize the peptidoglycan cross-linking peptide chain. Penicillin and its relatives target only reproducing bacteria. Mammals do not contain the enzyme pathway that synthesizes peptidoglycans, and this is what allows us to kill the bacteria without harming ourselves.

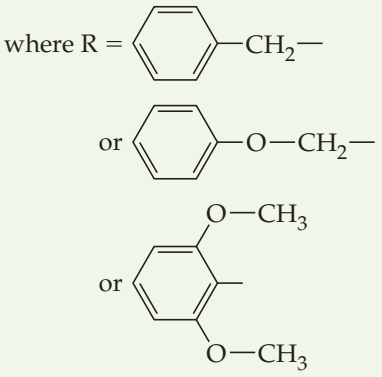
Today, we take the availability and effectiveness of antibiotics for granted. When penicillin was discovered, it was hailed as a "magic bullet" because it could cure bacterial infections that were often fatal. Unfortunately, many bacteria have developed resistance to penicillin and its relatives; resistant bacteria have developed enzymes that destroy the beta-lactam ring, thereby destroying the effectiveness of penicillin. Other antibiotics have since been developed, but the spread of antibiotic-resistant bacterial strains is a public health concern due to the "bullet-proof vest" nature of the bacterial cell wall in resistant strains.



▲ Peptidoglycan structure: Strands of alternating NAG and NAMA connected by peptides form a mesh covering the bacterial cell membrane.



Penicillin



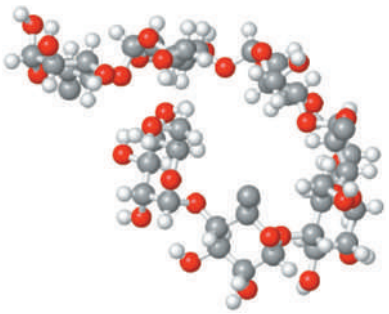
CIA Problem 20.4 List three functions of all cell walls.

CIA Problem 20.5 Name the individual units and the cross-link for the polymer that makes up most of a bacterial cell wall.

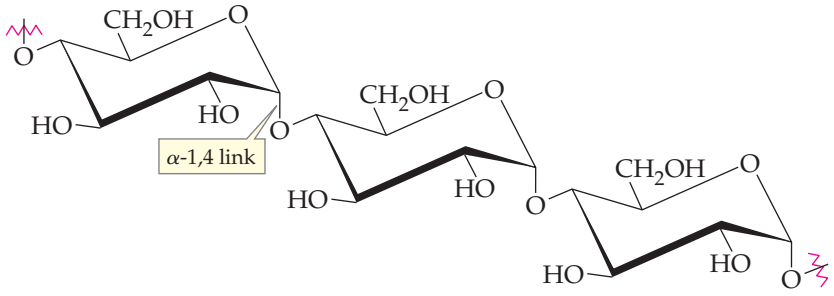
CIA Problem 20.6 How does penicillin inhibit the growth of certain bacteria?

CIA Problem 20.7 When you take the antibiotic penicillin when you are ill, why does the penicillin kill a bacterial cell but not your liver cells?

The following structures allow comparison of the structures of amylose, amylopectin, and cellulose. The small drawings compare the density of branch points in amylose versus glycogen.

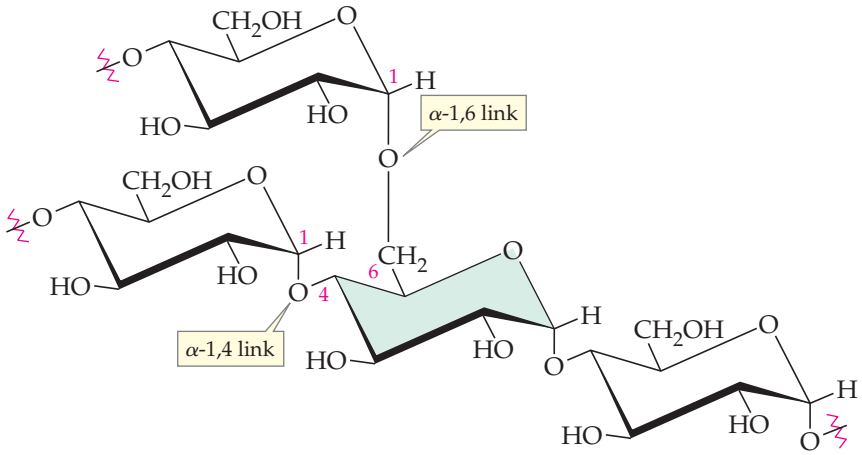


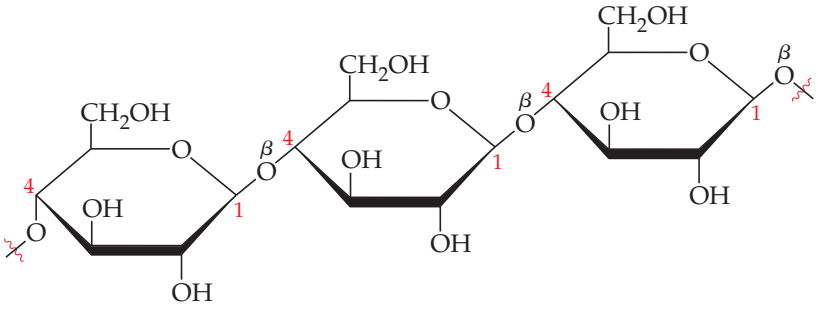
▲ **Figure 20.4**
Helical structure of amylose.



Amylose

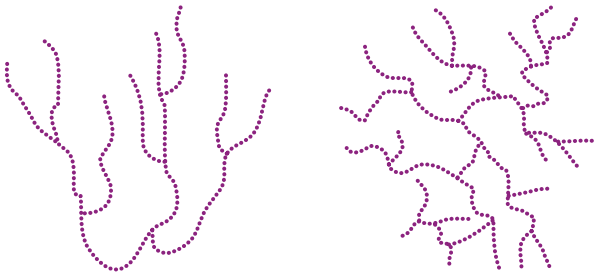
Branch point in amylopectin (also glycogen)





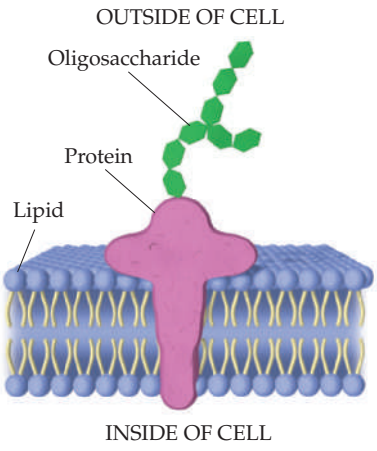
cellulose (1,4-β-D-polyglucose)

Comparison of branching in amylopectin and glycogen



Amylopectin
(in plants)

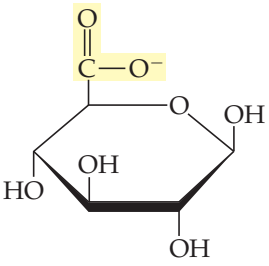
Glycogen
(in animals)



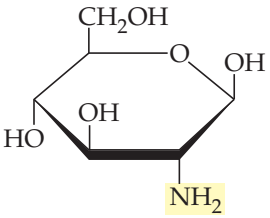
The basic components of cell membranes are lipid molecules. The wonderfully complex structure and function of the membrane are explored in Sections 23.5 and 23.6. Glycolipids—carbohydrates bonded to lipids—are, like glycoproteins, essential in cell membranes.

Some Polysaccharides Based on Modified Glucose

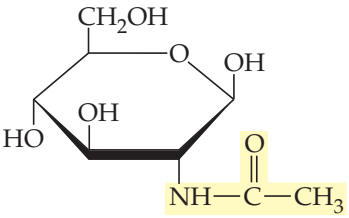
Monosaccharides with modified functional groups are components of a wide variety of biomolecules. Some of the modified monosaccharides form polymers with distinct functions. Additionally, short chains of monosaccharides bind to proteins forming glycoproteins and to lipids forming glycolipids; the addition of short chains of monosaccharides to some proteins and lipids enhance their functions. There are three common polymers of interest. Hyaluronate is formed from β-D-glucuronate and N-acetyl-β-D-glucosamine linked as a repeating pair and found in synovial fluid in joints and in the vitreous humor of the eye. Chondroitin-6-sulfate is a polymer of β-D-glucuronate and N-acetyl-β-D-glucosamine-6-sulfate; it is found in tendons and cartilage. Heparin is a polymer of β-D-glucuronate-2-sulfate and acetylsulfate -β-D-glucosamine-6-sulfate. Medically heparin is used as an anticoagulant (an agent that prevents blood clotting). The structures of the three modified glucose molecules found in these three polymers are shown next.



β-D-Glucuronate



β-D-Glucosamine



N-Acetyl-β-D-Glucosamine

PROBLEM 20.18

What is the structural difference between glucose and (a) β-D-glucuronate, (b) β-D-glucosamine, (c) N-acetyl-β-D-glucosamine?

PROBLEM 20.19

In *N*-linked glycoproteins, the sugar is usually attached to the protein by a bond to the N atom in a side-chain amide. Which amino acids can form such a bond?

HANDS-ON CHEMISTRY 20.2

Have you ever wondered what is in the packaged foods you buy in the grocery store? Do the food labels appear to be in a foreign language? You have learned enough chemistry to identify the sugars and complex carbohydrates among the ingredients listed on the food label.

For example, a box of multigrain crackers lists the following ingredients: enriched flour (wheat flour, niacin, folic acid), sunflower and/or canola oil (contains ascorbic acid), sugar, oats, inulin, rye flour, multigrain flour blend (wheat, rye, triticale, barley, corn, millet, soybean, sunflower seeds, rice, flax, durum, oats), wheat germ, modified corn starch, invert syrup, and some inorganic compounds used in baking. Any item in this list labeled flour is starch, a mixture of amylose and amylopectin; note the large number of starch sources used in this product. Sugars are represented by sugar, which in this context always means sucrose, and invert sugar.

a. There are three vitamins in this list. What are they?

b. Use the internet to look up the following: triticale, millet, flax, durum, inulin, and modified corn starch. What is each of these and why can each be used in food products?

c. List the ingredients on the label of your breakfast cereal, a granola bar, or some other food item in your home or local grocery store. Identify the sugars and complex carbohydrates present.

CHEMISTRY IN ACTION

Carbohydrates and Fiber in the Diet

As we learned from the chapter opener, carbohydrates are a large part of our diet and the major monosaccharides in our diets are fructose and glucose from fruits and honey. The major disaccharides are sucrose (table sugar) refined from both sugar cane and sugar beets and lactose from milk. In addition, our diets contain large amounts of the digestible polysaccharide starch, present in grains (wheat and rice), root vegetables (potatoes), and legumes (beans and peas). Nutritionists refer to these polysaccharides as *complex carbohydrates.* Some polysaccharides, such as cellulose, are not digested by humans. Cellulose and all other indigestible carbohydrates are collectively known as *dietary fiber.*

How easily and rapidly complex carbohydrates are digested and absorbed affects blood sugar levels. Consumption of rapidly digested carbohydrates, found in potatoes and refined foods (white bread and white rice), results in rapid elevation of blood glucose levels followed by lower-than-desired levels a few hours later. Carbohydrates that are digested and absorbed more slowly, such as those found in pasta, whole grain cereals and breads, and beans are associated with healthier blood sugar responses.

The body's major use of digestible carbohydrates is to provide energy, 16.7 kJ per gram of carbohydrate. A small amount of any excess carbohydrate is converted to glycogen for storage in the liver and muscles, but most dietary carbohydrate in excess of our immediate needs for energy is converted into fat.

The MyPlate meal-planning tool (p. 600) reflects the emphasis on decreasing the amounts of meat and increasing the amounts of other foods in our diet, especially complex carbohydrates and fiber through the consumption of whole grains, vegetables, and fruit.

In terms of *total* carbohydrate, which includes both digestible carbohydrates and fiber, the *Nutrition Facts* labels on packaged foods (p. 651) give percentages based on a recommended 300 g per day of total carbohydrate and 25 g per day of dietary fiber. This quantity of total carbohydrate represents 60% of the energy in an 8400 kJ/day diet. The *Nutrition Facts* label also gives the total grams of sugars in the food without a percentage because there is no recommended daily quantity of sugars. For purposes of the label, "sugars" are defined as all monosaccharides and disaccharides, whether naturally present or added.

As an option, the label may also include grams of *soluble fiber* and *insoluble fiber*. Taken together, these are the types of polysaccharides that are neither hydrolyzed to monosaccharides nor absorbed into the bloodstream. These polysaccharides include cellulose and all other indigestible polysaccharides in vegetables, both soluble and insoluble.

▲ Part of a healthy diet includes a variety of complex carbohydrates that can be supplied by whole grains, beans, and peas.

Foods high in insoluble fiber include wheat, bran cereals, and brown rice. Beans, peas, and other legumes contain both soluble and insoluble fiber. Fiber functions in the body to soften and add bulk to solid waste. Studies have shown that increased fiber in the diet may reduce the risk of colon and rectal cancer, hemorrhoids, diverticulosis, and cardiovascular disease. A reduction in the risk of developing colon and rectal cancer may also occur because potentially carcinogenic substances are absorbed on fiber surfaces and eliminated before doing any harm. Pectin, the soluble portion of dietary fiber, may also absorb and carry away bile acids, causing an increase in their synthesis from cholesterol in the liver and a resulting decrease in blood cholesterol levels.

The U.S. Food and Drug Administration is responsible for reviewing the scientific basis for health claims for foods. Two allowed claims relate to carbohydrates. The first states that a diet high in fiber may lower the risk of cancer and heart disease if the diet is also low in saturated fats and cholesterol. The second states that foods high in the soluble fiber from whole oats (oat bran) may also reduce the risk of heart disease, again when the diet is also low in saturated fats and cholesterol.

CIA Problem 20.8 Give an example of a complex carbohydrate in the diet and a simple carbohydrate in the diet. Are soluble fiber and insoluble fiber complex or simple carbohydrates?

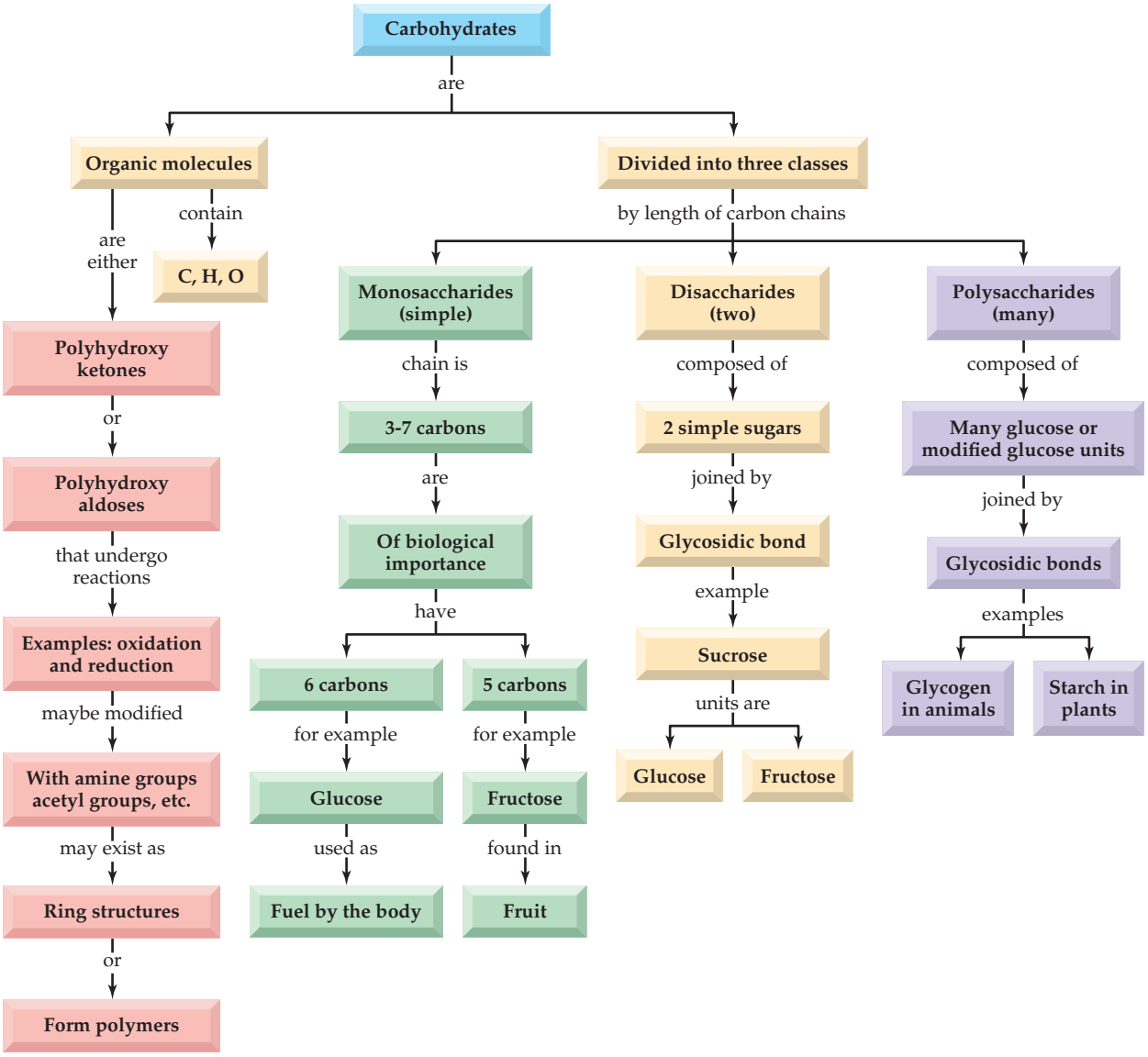
CIA Problem 20.9 Our bodies do not have the enzymes required to digest cellulose, yet it is a necessary addition to a healthy diet. Why?

CIA Problem 20.10 Name two types of soluble fiber and their sources.

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Classify carbohydrates by functional group and number of carbon atoms, and label them accordingly.** *Monosaccharides* are compounds with three to seven carbons, an aldehyde group on carbon 1 (an *aldose*) or a ketone group on carbon 2 (a *ketose*), and hydroxyl groups on all other carbons. *Disaccharides* consist of two monosaccharides; *polysaccharides* are polymers composed of up to thousands of monosaccharides *(see Problems 28–31 and 83)*.
- **Identify D and L enantiomers and any diastereomers of a monosaccharide from the Fischer projection.** Monosaccharides can contain several chiral carbon atoms, each bonded to one —H, one —OH and two other carbon atoms in the carbon chain. A monosaccharide with *n* chiral carbon atoms may have 2^n stereoisomers and half that number of pairs of enantiomers. The members of different enantiomeric pairs are *diastereomers*—they are *not* mirror images of each other *(see Problems 21, 23, 32, 33, and 38–43)*.
- **Draw the Fischer projection for a monosaccharide.** *Fischer projection formulas* represent the open-chain structures of monosaccharides. They have D and L enantiomers in a pair identified by having the —OH group on the chiral carbon farthest from the carbonyl group on the right (the D isomer) or the left (the L isomer). *(see Problems 34, 35, 74, 75, 78, and 79)*.
- **Convert five and six carbon monosaccharides from the Fischer projection to the Haworth projection.** The open-chain form of the monosaccharide (Fischer projection drawing) is coiled into the cyclic form of the monosaccharide (Haworth projection form) with the formation of the glycosidic bond closing the cyclic form *(see Problems 50, 51, 76, and 77)*.
- **Identify the anomeric carbon and the alpha (α) or beta (β) form of the monosaccharide and describe the role of mutarotation in cyclic structure.** In the cyclic form, the glycosidic bond contains the hemiacetal carbon (bonded to two O atoms), which is referred to as the *anomeric carbon,* and this carbon is chiral. Two isomers of the cyclic form of a D or L monosaccharide, known as *anomers,* are possible because the —OH on the anomeric carbon may lie above or below the plane of the ring *(see Problems 22, 46–49, 67, and 69)*.
- **Identify by name and structure the common monosaccharides, their sources and uses.** The five common monosaccharides are described in Table 20.2 *(see Problems 36, 37, and 84)*.
- **Predict the products of oxidation and reduction reactions on monosaccharides.** Oxidation of a monosaccharide can result in a carboxyl group on the first carbon atom (C1 in the Fischer projection). Ketoses, as well as aldoses, are *reducing sugars* because the ketose is in equilibrium with an aldose form that can be oxidized (*see Problems 24, 27, 44, 45, and 52–55*).
- **Predict the products of reactions between monosaccharides and alcohols.** Reaction of a hemiacetal with an alcohol produces an acetal. For a cyclic monosaccharide, reaction with an alcohol converts the —OH group on the anomeric carbon to an —OH group. The bond to the —OR group, known as a *glycosidic bond,* is α or β to the ring as was the —OH group. Disaccharides result from glycosidic bond formation between two monosaccharides *(see Problems 56–59)*.
- **Recognize and predict the products of hydrolysis reactions of polysaccharides and phosphorylation reactions of monosaccharides.** Hydrolysis reactions of polysaccharides produce the monomeric units that formed the polysaccharide. For example, hydrolysis of starch yields glucose. Phosphorylated monosaccharides become reactants in the metabolism of carbohydrates *(see Problems 20, 66, and 68)*.
- **Identify by name and structure the common disaccharides, the subunits and the bond between them, their sources and uses.** *Maltose* (D-glucose and D-glucose), *lactose* (D-galactose and D-glucose), and *sucrose* (D-fructose and D-glucose) are described in Table 20.3. Unlike maltose and lactose, sucrose is not a *reducing sugar* because it has no hemiacetal that can establish equilibrium with an aldehyde *(see Problems 25, 60, 61, 65, 81, 82, and 84–86)*.
- **Recognize common polysaccharides and identify where each polysaccharide is found in nature and its function.** *Cellulose* provides structure in plants. Starch is a storage form of glucose for plants and is digestible by humans. *Glycogen* is a storage form of glucose for animals *(see Problems 62–64 and 84)*.
- **Identify the monomers and type of bond present in each polysaccharide.** *Cellulose* is a straight-chain polymer of β-D-glucose with β-1,4 links. *Starch* is a polymer of α-D-glucose connected by α-1,4 links in straight-chain (*amylose*) and branched-chain (*amylopectin*) forms. Glycogen is also a polymer of α-D-glucose connected by α-1,4 links in straight-chain (*see Problems 26 and 70*).
- **Identify the modified monosaccharides found in naturally occurring polysaccharides and identify the functions of these polysaccharides.** Hyaluronate, chondroitin-6-sulfate, heparin, and glycoproteins have different modified glucose subunits paired (dimers) as repeating units in the polymer chains. Joints and intracellular spaces are lubricated by polysaccharides like *hyaluronate* and *chondroitin 6-sulfate*. *Heparin* binds to a clotting factor in the blood and thus acts as an anticoagulant. *Glycoproteins* function as receptors at cell surfaces *(see Problems 33, 72, and 73)*.

CONCEPT MAP: CARBOHYDRATES



▲ **Figure 20.5 Concept Map.** Carbohydrates are a diverse group of biologically important organic molecules unified by a common monomeric structural pattern. Monosaccharides are used for energy generation and are obtained primarily from dietary disaccharides and polysaccharides. Some energy reserves are maintained by the storage of glycogen by animals or starch by plants. This concept map shows the relationships and commonalities of these molecules.

KEY WORDS

1,4 Link, *p. 678*
Aldose, *p. 661*
Anomeric carbon atom, *p. 668*
Anomers, *p. 668*
Carbohydrate, *p. 661*
D Sugar, *p. 665*
Diastereomers, *p. 663*
Disaccharide, *p. 662*
Fischer projection, *p. 665*
Glycoside, *p. 676*
Glycosidic bond, *p. 676*
Ketose, *p. 661*
L Sugar, *p. 665*
Monosaccharide (simple sugar), *p. 661*
Mutarotation, *p. 668*
Polysaccharide (complex carbohydrate), *p. 662*
Reducing sugar, *p. 675*

UNDERSTANDING KEY CONCEPTS

20.20 During the digestion of starch from potatoes, the enzyme α-amylase catalyzes the hydrolysis of starch into maltose. Subsequently, the enzyme maltase catalyzes the hydrolysis of maltose into two glucose units. Write an equation (in words) for the enzymatic conversion of starch to glucose. Classify each of the carbohydrates in the equation as a disaccharide, monosaccharide, or polysaccharide.

20.21 Identify the following as diastereomers, enantiomers, and/or anomers. (a) α-D-fructose and β-D-fructose (b) D-galactose and L-galactose (c) L-allose and D-glucose (both aldohexoses)

20.22 Consider the trisaccharide A, B, C shown in Problem 20.23.

(a) Identify the hemiacetal and acetal linkages.

(b) Identify the anomeric carbon atoms, and indicate whether each is α or β.

(c) State the numbers of the carbon atoms that form glycosidic linkages between monosaccharide A and monosaccharide B.

(d) State the numbers of the carbon atoms that form glycosidic linkages between monosaccharide B and monosaccharide C.

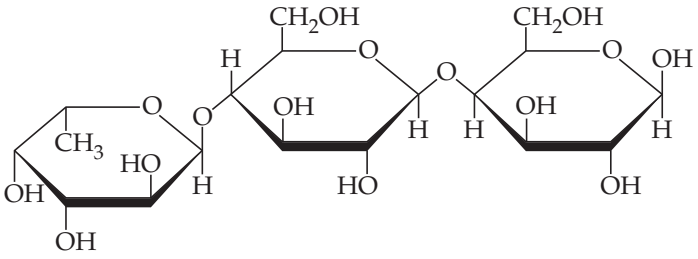
20.23 Hydrolysis of both glycosidic bonds in the following trisaccharide A, B, C yields three monosaccharides.

(a) Are any two of these monosaccharides the same?

(b) Are any two of these monosaccharides enantiomers?

(c) Draw the Fischer projections for the three monosaccharides.

(d) Assign a name to each monosaccharide.



20.24 The trisaccharide shown with Problem 20.23 has a specific sequence of monosaccharides. To determine this sequence, we could react the trisaccharide with an oxidizing agent. Since one of the monosaccharides in the trisaccharide is a reducing sugar, it would be oxidized from an aldehyde to a carboxylate. Which of the monosaccharides (A, B, or C) is oxidized? Write the structure of the oxidized monosaccharide that results after hydrolysis of the trisaccharide. How does this reaction assist in identifying the sequence of the trisaccharide?

20.25 Are one or more of the disaccharides maltose, lactose, cellobiose, and sucrose part of the trisaccharide in Problem 20.23? If so, identify which disaccharide and its location. (Hint: Look for an α-1,4 link, β-1,4 link, or 1,2 link, and then determine if the correct monosaccharides are present.)

20.26 Cellulose, amylose, amylopectin, and glycogen are the polysaccharides of glucose that we examined in this chapter. The major criteria that distinguish these four polysaccharides include α-glycosidic links or β-glycosidic links, 1,4 links or both 1,4 and 1,6 links, and the degree of branching. Create a table evaluating each polysaccharide using these five criteria.

20.27 In solution, glucose exists predominantly in the cyclic hemiacetal form, which does not contain an aldehyde group. How is it possible for mild oxidizing agents to oxidize glucose?

ADDITIONAL PROBLEMS

CLASSIFICATION AND STRUCTURE OF CARBOHYDRATES (SECTION 20.1)

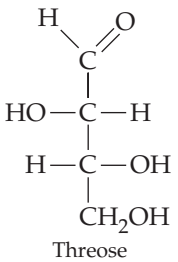
20.28 What is a carbohydrate?

20.29 What is the family-name ending for a sugar?

20.30 What is the structural difference between an aldose and a ketose?

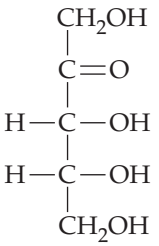
20.31 Classify the four carbohydrates (a)–(d) by indicating the nature of the carbonyl group and the number of carbon atoms present. For example, glucose is an aldohexose.

(a)



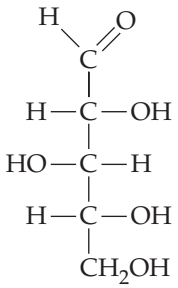
Threose

(b)



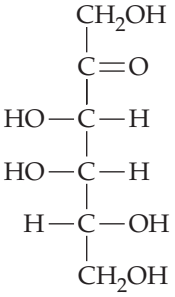
Ribulose

(c)



Xylose

(d)



Tagatose

20.32 How many chiral carbon atoms are present in each of the molecules shown in Problem 20.31?

20.33 How many chiral carbon atoms are there in each of the two parts of the repeating unit in heparin (p. 684)? What is the total number of chiral carbon atoms in the repeating unit?

20.34 Draw the open-chain structure of a ketoheptose.

20.35 Draw the open-chain structure of a 4-carbon deoxy sugar.

20.36 Name four important monosaccharides and tell where each occurs in nature.

20.37 Name a common use for each monosaccharide listed in Problem 20.36.

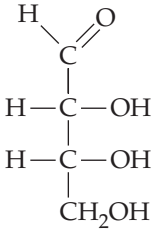
HANDEDNESS IN CARBOHYDRATES (SECTION 20.2)

20.38 How are enantiomers related to each other?

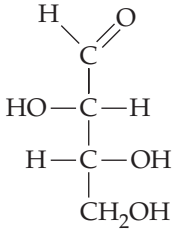
20.39 What is the structural relationship between L-glucose and D-glucose?

20.40 Only three stereoisomers are possible for 2,3-dibromo-2,3-dichlorobutane. Draw them, indicating which pair are enantiomers (optical isomers). Why does the other isomer not have an enantiomer?

20.41 In Section 15.6, you saw that aldehydes react with reducing agents to yield primary alcohols ($RCH{=}O \longrightarrow RCH_2OH$). The structures of two D-aldotetroses are shown. One of them can be reduced to yield a chiral product, but the other yields an achiral product. Explain.



D-Erythrose



D-Threose

20.42 Sucrose and D-glucose rotate plane-polarized light to the right; D-fructose rotates light to the left. When sucrose is hydrolyzed, the glucose–fructose mixture rotates light to the left.

(a) What does this indicate about the relative degrees of rotation of light of glucose and fructose?

(b) Why do you think the mixture is called "invert sugar"?

20.43 What generalization can you make about the direction and degree of rotation of light by enantiomers?

REACTIONS OF CARBOHYDRATES (SECTIONS 20.3, 20.4, AND 20.5)

20.44 What does the term *reducing sugar* mean?

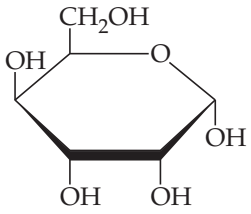
20.45 What structural property makes a sugar a reducing sugar?

20.46 What is mutarotation? Do all chiral molecules do this?

20.47 What are anomers, and how do the anomers of a given sugar differ from each other?

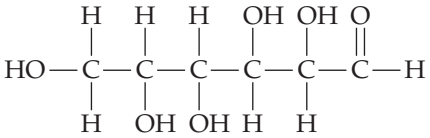
20.48 What is the structural difference between the α hemiacetal form of a carbohydrate and the β form?

20.49 D-Gulose, an aldohexose isomer of glucose, has the cyclic structure shown here. Which is shown, the α form or the β form?



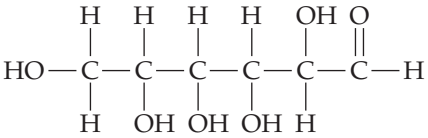
D-Gulose

20.50 In its open-chain form, D-mannose, an aldohexose found in orange peels, has the structure shown here. Coil mannose around and draw it in the cyclic hemiacetal α and β forms.



D-Mannose

20.51 In its open-chain form, D-altrose has the structure shown here. Coil altrose around and draw it in the cyclic hemiacetal α and β forms.



D-Altrose

20.52 Treatment of D-glucose with a reducing agent yields sorbitol, a substance used as a sugar substitute by people with diabetes. Draw the structure of sorbitol.

20.53 Reduction of D-fructose with a reducing agent yields a mixture of D-sorbitol along with a second, isomeric product. What is the structure of the second product?

20.54 Treatment of an aldose with an oxidizing agent such as Tollens' reagent (Section 15.5) yields a carboxylic acid. Gluconic acid, the product of glucose oxidation, is used as its magnesium salt for the treatment of magnesium deficiency. Draw the structure of gluconic acid.

20.55 Oxidation of the aldehyde group of ribose yields a carboxylic acid. Draw the structure of ribonic acid.

20.56 What is the structural difference between a hemiacetal and an acetal?

20.57 What are glycosides, and how can they be formed?

20.58 Look at the open-chain form of D-mannose (Problem 20.50) and draw the two glycosidic products that you expect to obtain by reacting D-mannose with methanol.

20.59 Draw a disaccharide of two cyclic mannose molecules attached by an α-1,4 glycosidic linkage. Explain why the glycosidic products in Problem 20.58 are *not* reducing sugars, but the product in this problem *is* a reducing sugar.

DISACCHARIDES AND POLYSACCHARIDES (SECTIONS 20.6 AND 20.7)

20.60 Give the names of three important disaccharides. Tell where each occurs in nature. From which two monosaccharides is each made?

20.61 Lactose and maltose are reducing disaccharides, but sucrose is a nonreducing disaccharide. Explain.

20.62 Amylose (a form of starch) and cellulose are both polymers of glucose. What is the main structural difference between them? What roles do these two polymers have in nature?

20.63 How are amylose and amylopectin similar to each other, and how are they different from each other?

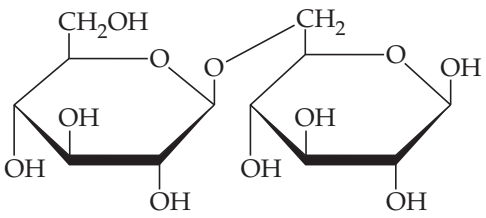
20.64 Which of the following is not a use for cellulose?

(a) lumber for building
(b) fodder for cattle
(c) raw material for computer chips
(d) fabric for t-shirts

20.65 Which of the following foods can someone who has lactose intolerance eat?

(a) ice cream
(b) french fries
(c) a chocolate milkshake

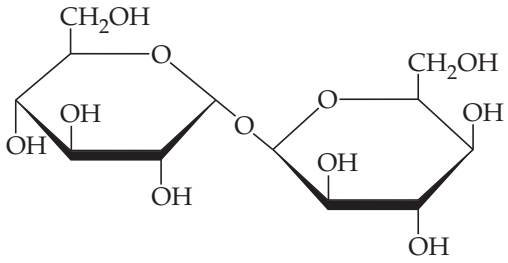
20.66 *Gentiobiose,* a rare disaccharide found in saffron, has the following structure. What simple sugars do you obtain on hydrolysis of gentiobiose?



Gentiobiose

20.67 Does gentiobiose (Problem 20.66) have an acetal grouping? A hemiacetal grouping? Do you expect gentiobiose to be a reducing or nonreducing sugar? How would you classify the linkage (α or β and carbon numbers) between the two monosaccharides?

20.68 *Trehalose,* a disaccharide found in the blood of insects, has the following structure. What simple sugars would you obtain on hydrolysis of trehalose? (Hint: Rotate one of the rings in your head or redraw it rotated.)



Trehalose

20.69 Does trehalose (Problem 20.68) have an acetal grouping? A hemiacetal grouping? Do you expect trehalose to be a reducing or nonreducing sugar? Classify the linkage between the two monosaccharides.

20.70 Amylopectin (a form of starch) and glycogen are both α-linked polymers of glucose. What is the structural difference between them?

20.71 What is the physiological purpose of starch in a seed or other plant tissue? What is the physiological purpose of glycogen in a mammal?

20.72 What modified sugars makeup heparin, hyaluronate, and chondroitin-6-sulfate?

20.73 What is the function of heparin, hyaluronate, and chondroitin-6-sulfate?

CONCEPTUAL PROBLEMS

20.74 Are the α and β forms of monosaccharides enantiomers of each other? Why or why not?

20.75 Are the α and β forms of the disaccharide lactose enantiomers of each other? Why or why not?

20.76 D-Fructose can form a six-membered cyclic hemiacetal as well as the more prevalent five-membered cyclic form. Draw the α isomer of D-fructose in the six-membered ring.

20.77 *Raffinose,* found in sugar beets, is the most prevalent trisaccharide. It is formed by an α-1,6 linkage of D-galactose to the glucose portion of sucrose. Draw the structure of raffinose.

20.78 Write the open-chain structure of the only ketotriose. Name this compound and explain why it has no optical isomers.

20.79 Write the open-chain structure of the only ketotetrose. Name this compound. Does it have an optical isomer?

20.80 What is lactose intolerance, and what are its symptoms?

20.81 What is the group of disorders that result when the body lacks an enzyme necessary to digest galactose? What are the symptoms?

20.82 When a person cannot digest galactose, its reduced form, called dulcitol, often accumulates in the blood and tissues. Write the structure of the open-chain form of dulcitol. Does dulcitol have an enantiomer? Why or why not?

20.83 Describe the differences between mono-, di-, and polysaccharides.

20.84 Name a naturally occurring carbohydrate and its source for each type of carbohydrate listed in Problem 20.83.

20.85 Compare and contrast lactose intolerance with galactosemia. (Hint: Make a table.)

GROUP PROBLEMS

20.86 Many people who are lactose intolerant can eat yogurt, which is prepared from milk curdled by bacteria, without any digestive problems. Give a reason why this is possible. (Hint: Read the label on each of several yogurt containers. Do the ingredients make a difference?)

20.87 Carbohydrates provide 16.7 kJ per gram. If a person eats 200 g per day of digestible carbohydrates, what percentage of an 8350 kJ daily diet would be digestible carbohydrate?

20.88 A 33 cL can of cherry-flavored cola contains 42 grams of sugar. If sugar provides 16.7 kJ per gram, how many kilojoules are in one can of cola?

20.89 Explain why cotton fibers, which are nearly pure cellulose, are insoluble in water, while glycogen, another polymer of glucose, will dissolve in water.

21

The Generation of Biochemical Energy

CONTENTS

CONCEPTS TO REVIEW

A. Oxidation-Reduction Reactions (Sections 5.5 and 5.6)

B. Energy in Chemical Reactions (Sections 7.2 and 7.4)

C. Enzymes (Sections 19.1 and 19.4)

▲ Exercise routines like this require the constant generation of large amounts of biological energy, the topic of this chapter.

Jasmine, 22, was enthusiastic about bodybuilding and how it improved her self-confidence. After a year of training and following advice on dietary supplements from older bodybuilders, Jasmine prepared for competition by sculpting. Sculpting involves losing fat to emphasize muscles and requires dieting. After several weeks of dieting, Jasmine turned to diet pills recommended by others at the training gym to try to speed up her results. Unsatisfied with her slow fat loss, Jasmine doubled the daily dose of the diet pills.

Several hours later she collapsed and was unresponsive. When she arrived at the emergency room (ER), Jasmine's body temperature was 41 °C (314 K) and rising. In her possession were diet pills containing dinitrophenol, a known toxic substance with dangerous side effects. We'll learn more about dinitrophenol (or DNP) later in the chapter in the Chemistry in Action "Metabolic Poisons" on page 717.

All organisms obtain energy from their surroundings to stay alive. In animals, the energy comes from food and is released through the exquisitely interconnected reaction pathways of metabolism. We are powered by the oxidation of biomolecules made mainly of carbon, hydrogen, and oxygen. The end products are carbon dioxide, water, and energy.

$$\text{C, H, O (food molecules)} + O_2 \longrightarrow CO_2 + H_2O + \text{Energy}$$

The principal food molecules—lipids, proteins, and carbohydrates—differ in structure and are broken down by individual pathways that are examined in later chapters. The product of these individual pathways, usually acetyl coenzyme A, enters the central final pathways that yield usable energy. In this chapter, we are going to concentrate on these final common pathways that release energy from all types of food molecules.

21.1 Energy, Life, and Biochemical Reactions

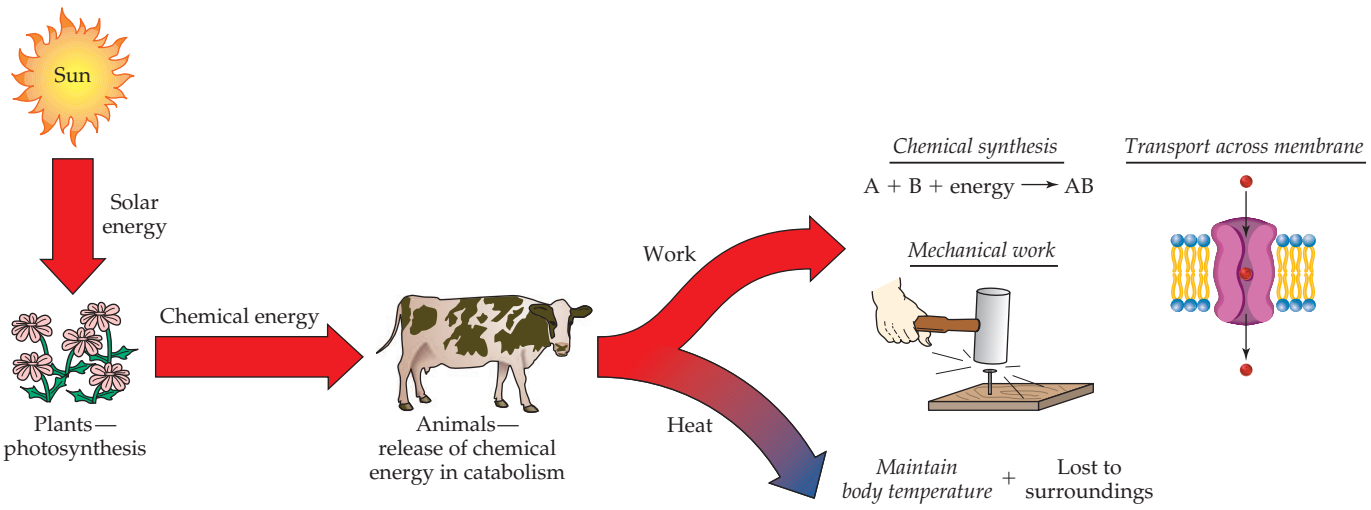
Learning Objectives:

- Identify energy sources and our specific requirements for energy regulation.
- Explain the significance of exergonic and endergonic reactions in metabolism.

Living things must do mechanical work—microorganisms engulf food, plants bend toward the sun, and humans walk about. Organisms must do the chemical work of synthesizing the biomolecules needed for energy storage, growth, repair, and replacement. In addition, cells need energy for the work of moving molecules and ions across cell membranes. In humans, it is the energy released from food that allows this work to be done.

Energy can be converted from one form to another but can be neither created nor destroyed (see Section 7.2). Ultimately, the energy used by all but a few living things comes from the sun (Figure 21.1). Plants convert sunlight to potential energy stored mainly in the chemical bonds of carbohydrates.

Plant-eating animals utilize this energy, some of it for immediate needs and the rest to be stored for future needs, mainly in the chemical bonds of fats. Other animals, including humans, are able to eat plants or animals and use the chemical energy these organisms have stored.



▲ **Figure 21.1**
The flow of energy through the biosphere.
Energy from the sun is ultimately stored in chemical bonds, used for cellular or mechanical work, used to maintain body temperature, or lost as heat.

Our bodies do not produce energy by burning up a meal all at once because the release of a large quantity of energy (primarily as heat) would be harmful to us. Furthermore, it is difficult to capture energy for storage once it has been converted to heat. We need energy that can be stored and then released in the right amounts when and where it is needed, whether we are jogging, studying, or sleeping. We, therefore, have some specific requirements for energy.

- Energy must be released from food gradually.
- Energy must be stored in readily accessible forms as glycogen and fat (triacylglycerides).
- Release of energy from storage must be finely controlled so that it is available exactly when and where it is needed.
- Just enough energy must be released as heat to maintain constant body temperature.
- Energy in a form other than heat must be available to drive chemical reactions that are not favorable at body temperatures.

This chapter looks at some of the ways these requirements for energy regulation are met. We begin by reviewing basic concepts about energy and then learn about *metabolism*. Next, we look at the *citric acid cycle* and *oxidative phosphorylation,* which together form the common pathway for the production of energy.

Biochemical Reactions

CONCEPTS TO REVIEW Review entropy, enthalpy, endergonic, exergonic, and free-energy change in Sections 7.2–7.4.

Chemical reactions either release or absorb energy. Whether a reaction is favorable or not depends on either the release or absorption of energy as heat (the change in enthalpy, ΔH), together with the increase or decrease in disorder (ΔS, the entropy change) caused by the reaction. The net effect of these changes is given by the free-energy change of a reaction: $\Delta G = \Delta H - T\Delta S$.

Reactions in living organisms are no different from reactions in a chemistry laboratory. Both follow the same laws, and both have the same energy requirements. Spontaneous reactions—that is, those that are *favorable* in the forward direction—release free energy, and the energy released is available to do work. Such reactions, described as *exergonic,* are the source of our biochemical energy.

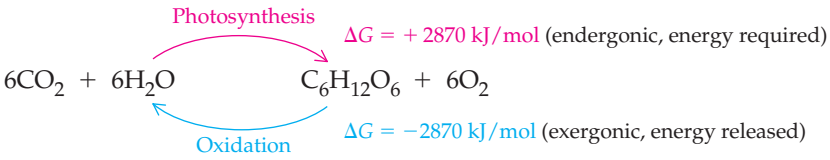
As shown by the energy diagram in Figure 7.3 the products of a favorable, exergonic reaction are farther *downhill* on the energy scale than the reactants. That is, the products are more stable than the reactants, and as a result the free-energy change (ΔG) has a negative value. Oxidation reactions, for example, are usually downhill reactions that release energy. Oxidation of glucose, the principal source of energy for animals, produces 2870 kJ of free energy per mole of glucose.

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O \qquad \Delta G = -2870\ \text{kJ/mol}$$

The greater the amount of free energy released, the farther a reaction proceeds toward product formation before reaching equilibrium.

Reactions in which the products are higher in energy than the reactants can also take place, but such *unfavorable* reactions cannot occur without the input of energy from an external source; such reactions are *endergonic.*

The free-energy change switches sign for the reverse of a reaction, but the value does not change. Photosynthesis, the process whereby plants convert CO_2 and H_2O to glucose and O_2, is the reverse of the oxidation of glucose. Its ΔG is therefore positive and equal to the value for the oxidation of glucose (see the Chemistry in Action "Plants and Photosynthesis" on p. 696). The sun provides the necessary external energy for photosynthesis (2870 kJ/mol of glucose formed).



Living systems make constant use of this principle in the series of chemical reactions we know as the biochemical ***pathways.*** Energy is stored in the products of an overall endergonic reaction pathway. This stored energy is released as needed in an overall exergonic reaction pathway that regenerates the original reactants. It is not necessary that every reaction in the pathways between the reactants and products be the same, so long as the pathways connect the same reactants and products.

Pathway A series of enzyme-catalyzed chemical reactions that are connected by their intermediates, that is, the product of the first reaction is the reactant for the second reaction, and so on.

Worked Example 21.1 Determining Reaction Energy

Are the following reactions exergonic or endergonic?

(a) Glucose 6-phosphate $\longrightarrow$ Fructose 6-phosphate

$\Delta G = +2.09$ kJ/mol

(b) Fructose 6-phosphate + ATP $\longrightarrow$ Fructose 1,6-bisphosphate + ADP

$\Delta G = -14.2$ kJ/mol

ANALYSIS Exergonic reactions release free energy, and ΔG is negative. Endergonic reactions gain free energy, and so ΔG is positive.

SOLUTION

Reaction (a), the conversion of glucose 6-phosphate to fructose 6-phosphate has a positive ΔG; therefore, it is endergonic. Reaction (b), the conversion of fructose 6-phosphate to fructose 1,6-bisphosphate has a negative ΔG; therefore it is exergonic.

KEY CONCEPT PROBLEM 21.1

In a cell, glucose can be oxidized via metabolic pathways. Alternatively, you could burn glucose in the laboratory. Which of these methods consumes or produces more energy? (Hint: All of the energy comes from converting the energy stored in the reduced bonds in glucose into the most oxidized form, carbon dioxide.)

KEY CONCEPT PROBLEM 21.2

The overall equation in this section,

$$6CO_2 + 6H_2O \underset{\text{oxidation}}{\overset{\text{photosynthesis}}{\rightleftharpoons}} C_6H_{12}O_6 + 6O_2,$$

shows the cycle between photosynthesis and oxidation. Pathways operating in opposite directions cannot be exergonic in both directions.

(a) Which of the two pathways in this cycle is exergonic and which is endergonic?
(b) Where does the energy for the endergonic pathway come from?

CHEMISTRY IN ACTION

Plants and Photosynthesis

The principal biochemical difference between humans and plants is that plants derive energy directly from sunlight and we cannot. In the process of *photosynthesis,* plants use solar energy to synthesize oxygen and energy-rich carbohydrates from energy-poor reactants: CO_2 and water. Our metabolism breaks down energy-rich reactants to extract the useful energy and produce energy-poor products: CO_2 and water. Is it surprising to discover that despite this difference in the direction of their reactions, plants rely on biochemical pathways very much like our own?

The energy-capturing phase of photosynthesis takes place mainly in green leaves. Plant cells contain *chloroplasts,* which, though larger and more complex in structure, resemble mitochondria. Embedded in membranes within the chloroplasts are large groups of *chlorophyll* molecules and the enzymes of an electron-transport chain. Chlorophyll is similar in structure to heme but contains magnesium ions (Mg^{2+}) instead of iron ions (Fe^{2+}).

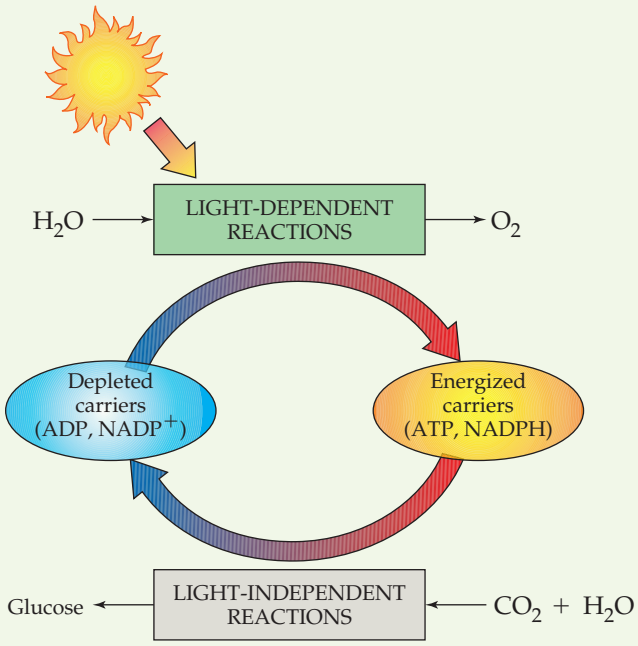
As solar energy is absorbed, chlorophyll molecules pass it along to specialized reaction centers, where it is used to boost the energy of electrons. The excited electrons then give up their extra energy as they pass down a pair of electron-transport chains.

Some of this energy is used to oxidize water, splitting it into oxygen, hydrogen ions, and electrons (which replace those entering the electron-transport chain). At the end of the chain, the hydrogen ions, together with the electrons, are used to reduce $NADP^+$ to NADPH. Along the way, part of the energy of the electrons is used to pump hydrogen ions across a membrane to create a concentration gradient. As in mitochondria, the hydrogen ions can only return across the membrane at enzyme complexes that convert ADP to ATP. Water needed for these *light-dependent reactions* enters the plant through the roots and leaves, and the oxygen that is formed is released through openings in the leaves.

The energy-carrying ATP and NADPH enter the fluid interior of the chloroplasts. Here their energy is used to drive the synthesis of carbohydrate molecules. So long as ATP and NADPH are available, this part of photosynthesis is *light-independent*—it can proceed in the absence of sunlight.

Plants have mitochondria as well as chloroplasts, so they can also carry out the release of energy from stored carbohydrates. Because the breakdown of carbohydrates continues in many harvested fruits and vegetables, the goal in storage is to slow it down. Refrigeration is one measure that is taken, since (like most chemical reactions) the rate of respiration decreases at lower temperatures. Another is replacement of air over stored fruits and vegetables with carbon dioxide or nitrogen.

▲ These flowers are converting the potential energy of the sun into chemical potential energy stored in the bonds of carbohydrates.



▲ The coupled reactions of photosynthesis.

CIA Problem 21.1 Chlorophyll is similar in structure to heme in red blood cells but does not have an iron atom. What metal ion is present in chlorophyll?

CIA Problem 21.2 Photosynthesis consists of both light-dependent and light-independent reactions. What is the purpose of each type of reaction?

CIA Problem 21.3 One step of the cycle that incorporates CO_2 into glyceraldehyde in plants is the production of two 3-phosphoglycerates. $\Delta G = -3.5$ kJ/mol for this reaction. Is this process endergonic or exergonic?

CIA Problem 21.4 What general process does refrigeration of harvested fruits and vegetables slow? What cellular processes are slowed by refrigeration?

21.2 Cells and Their Structure

Learning Objective:

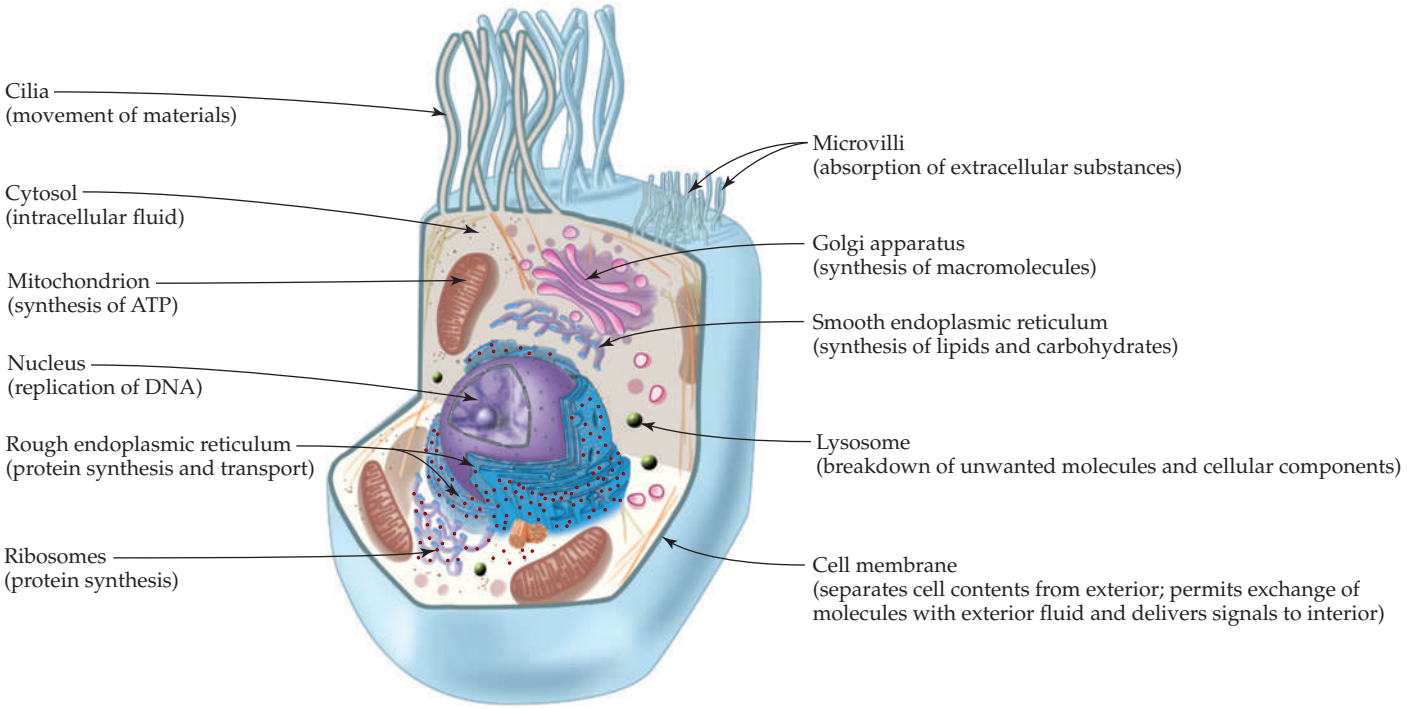
- Describe the eukaryotic cell and explain the function of each structure.

Before learning about metabolism, it is important to see where the energy-generating reactions take place within the cells of living organisms. There are two main categories of cells: *prokaryotic cells,* found in single-celled organisms (e.g., bacteria and blue-green algae), and *eukaryotic cells,* found in some single-celled organisms, such as yeast, and all plants and animals.

Eukaryotic cells are about 1000 times larger than bacterial cells, have a membrane-enclosed nucleus that contains their deoxyribonucleic acid (DNA), and include several other kinds of internal structures known as *organelles*—small, functional units that perform specialized tasks. A generalized eukaryotic cell is shown in Figure 21.2 with short descriptions of the functions of some of its major parts. Everything between the cell membrane and the nuclear membrane in a eukaryotic cell, including the various organelles, is the **cytoplasm.** The organelles are surrounded by the fluid part of the cytoplasm, the **cytosol,** which contains electrolytes, nutrients, and many enzymes, all in aqueous solution.

Cytoplasm The region between the cell membrane and the nuclear membrane in a eukaryotic cell.

Cytosol The fluid part of the cytoplasm surrounding the organelles within a cell, contains dissolved proteins and nutrients.



▲ **Figure 21.2**
A generalized eukaryotic cell.
Major cell components are labeled with a description of their primary function.

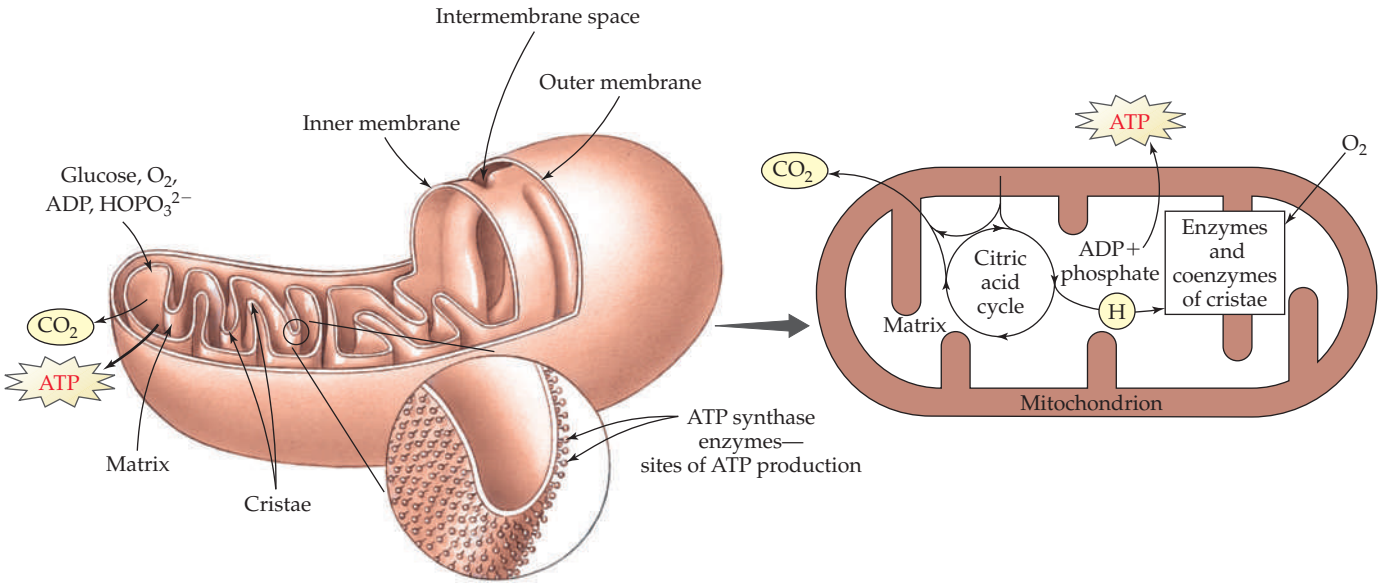
The **mitochondria** (singular, **mitochondrion**), often called the cell's "power plants," are the most important of the organelles for energy production and produce about 90% of the body's energy-carrying molecule, ATP.

A mitochondrion is a roughly egg-shaped structure composed of a smooth outer membrane and a folded inner membrane (Figure 21.3). The space enclosed by the inner membrane is the **mitochondrial matrix.** Within the matrix, the citric acid cycle (Section 21.7) and production of most of the body's **adenosine triphosphate (ATP)** take place. The coenzymes and proteins that manage the transfer of energy to the chemical bonds of ATP (Section 21.8) are embedded in the inner membrane of the mitochondrion.

Mitochondrion (plural, mitochondria) An egg-shaped organelle where small molecules are broken down to provide the energy for an organism.

Mitochondrial matrix The space surrounded by the inner membrane of a mitochondrion.

Adenosine triphosphate (ATP) The principal energy-carrying molecule, removal of a phosphoryl group to give ADP releases free energy.



▲ **Figure 21.3**
The mitochondrion.
Cells have many mitochondria. The citric acid cycle takes place in the matrix. Electron transport and ATP production, the final stage in biochemical energy generation (described in Section 21.8), take place at the inner surface of the inner membrane. The numerous folds in the inner membrane—known as *cristae*—increase the surface area over which these pathways can take place.

Mitochondria contain their own DNA, synthesize some of their own proteins, and multiply using chemicals moved from the cell cytosol into the mitochondrial matrix. The number of mitochondria is greatest in eye, brain, heart, and muscle cells, where the need for energy is greatest. The ability of mitochondria to reproduce is seen in athletes who put heavy energy demands on their bodies—they develop an increased number of mitochondria to aid in energy production.

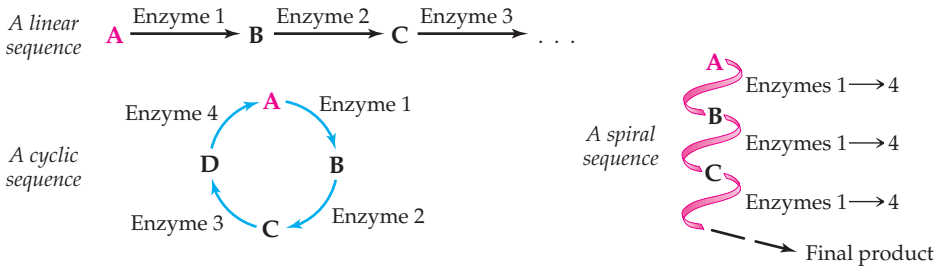
21.3 An Overview of Metabolism and Energy Production

Learning Objective:

- List the stages in catabolism of food and describe the role of each stage.

Metabolism The sum of all of the chemical reactions that take place in an organism.

Together, all of the chemical reactions that take place in an organism constitute its **metabolism.** Most of these reactions occur in the reaction sequences of *metabolic pathways,* a sequence of reactions where the product of one reaction serves as the starting material for the next. Such pathways may be linear (a series of reactions that convert a reactant into a specific product through a series of intermediate molecules and reactions), cyclic (a series of reactions that regenerates one of the first reactants), or spiral (the same set of enzymes progressively builds up or breaks down a molecule).

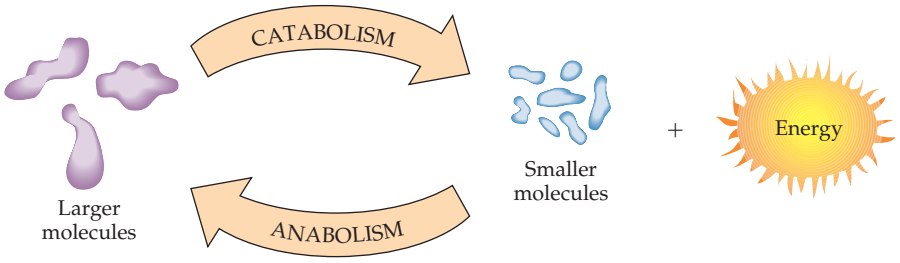


Catabolism Metabolic reaction pathways that break down food molecules and release biochemical energy.

As we study metabolism we will encounter each of these types of pathways. Those pathways that break molecules apart are known collectively as **catabolism,** whereas those that put building blocks back together to assemble larger molecules are known

collectively as **anabolism.** The purpose of catabolism is to release energy from food, and the purpose of anabolism is to synthesize new biomolecules, including those that store energy.

Anabolism Metabolic reactions that build larger biological molecules from smaller pieces.

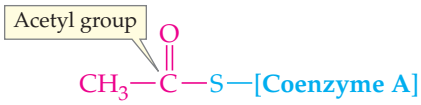


The overall picture of digestion, catabolism, and energy production is simple: eating provides fuel, breathing provides oxygen, and our bodies oxidize the fuel to extract energy. The process can be roughly divided into the four stages described here and shown in Figure 21.4.

STAGE 1: Digestion Enzymes in saliva, the stomach, and the small intestine convert the large molecules of carbohydrates, proteins, and lipids to smaller molecules. Carbohydrates are broken down to glucose and other sugars; proteins are broken down to amino acids; and triacylglycerols, the lipids commonly known as fats and oils, are broken down to glycerol plus long-chain carboxylic acids, termed fatty acids. These smaller molecules are transferred into the blood for transport to cells throughout the body.

STAGE 2: Acetyl-coenzyme A production The small molecules from digestion follow separate pathways that separate their carbon atoms into two-carbon acetyl groups. The acetyl groups are attached to coenzyme A by a high-energy bond between the sulfur atom of the thiol (—SH) group at the end of the coenzyme A molecule and the carbonyl carbon atom of the acetyl group.

Attachment of acetyl group to coenzyme A



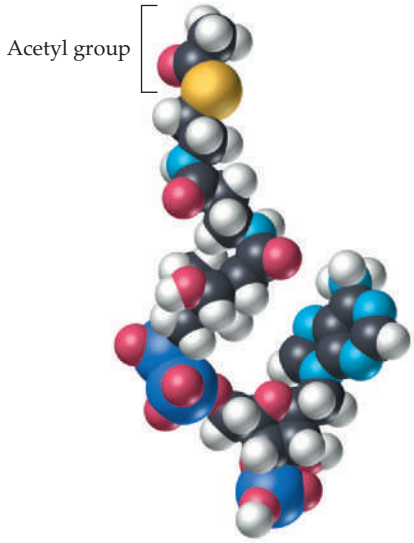
The resultant compound, **acetyl-coenzyme A,** which is abbreviated **acetyl-CoA,** is an intermediate in the breakdown of *all* classes of food molecules. It carries the acetyl groups into the common pathways of catabolism—Stage 3, the citric acid cycle and Stage 4, electron transport and ATP production.

STAGE 3: Citric acid cycle Within mitochondria, the acetyl-group carbon atoms are oxidized to the carbon dioxide that we exhale. Most of the energy released in the oxidation leaves the citric acid cycle in the chemical bonds of reduced coenzymes (NADH, $FADH_2$). Some energy also leaves the cycle stored in the chemical bonds of ATP or a related triphosphate.

STAGE 4: ATP production Electrons from the reduced coenzymes are passed from molecule to molecule down an electron-transport chain. Along the way, their energy is harnessed to produce more ATP. At the end of the process, these electrons—along with hydrogen ions from the reduced coenzymes—combine with oxygen we breathe in to produce water. Thus, the reduced coenzymes are in effect oxidized by atmospheric oxygen, and the energy that they carried is stored in the chemical bonds of ATP molecules.

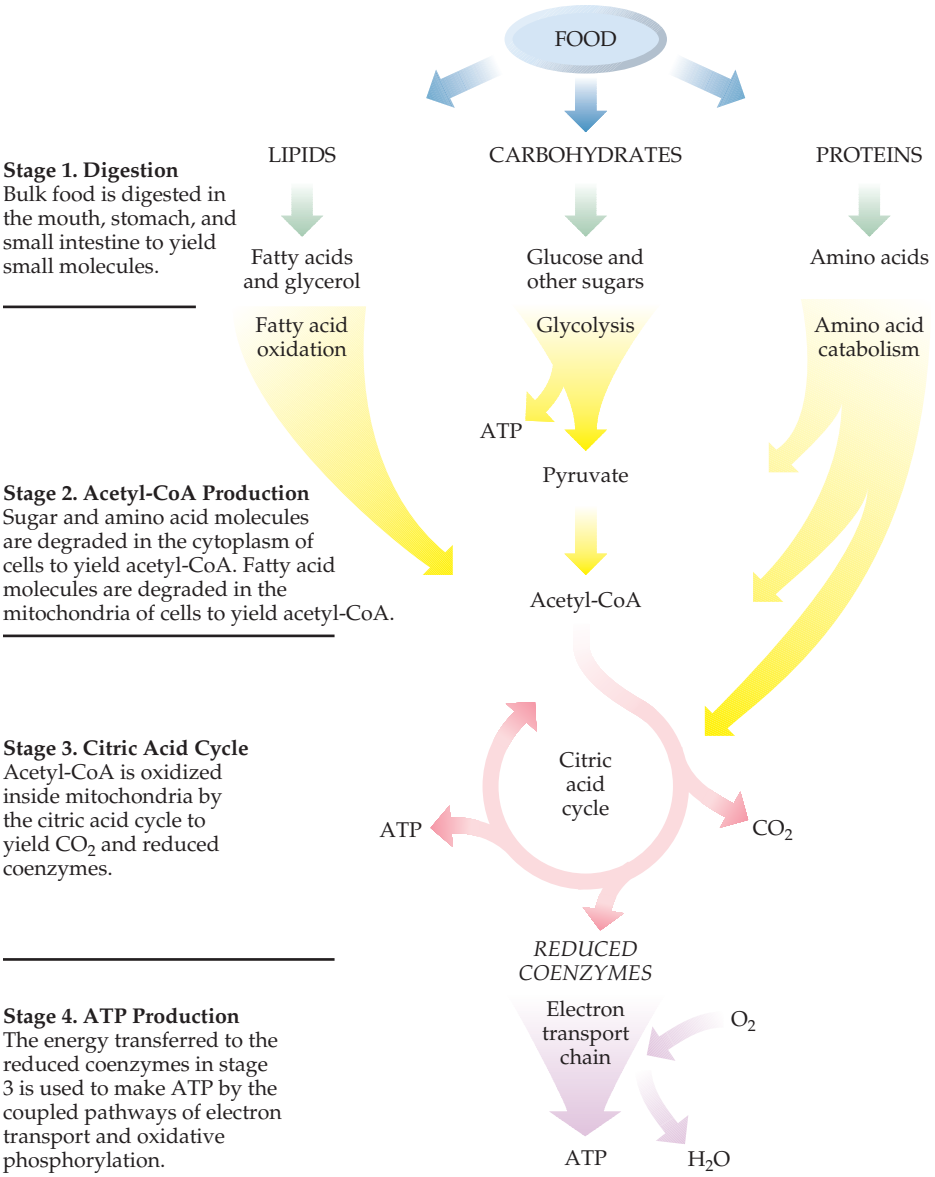
See the chemical structure of coenzyme A in Figure 19.10.

Acetyl-coenzyme A (acetyl-CoA) Acetyl-substituted coenzyme A—the common intermediate that carries acetyl groups into the citric acid cycle.



Acetyl-coenzyme A

LOOKING AHEAD Digestion and conversion of food molecules to acetyl-CoA, Stages 1 and 2 in Figure 21.4, occur by different metabolic pathways for carbohydrates, lipids, and proteins. Each of these pathways is discussed separately in later chapters: carbohydrate metabolism in Chapter 22, lipid metabolism in Chapter 24, and protein metabolism in Chapter 25.



▶ Figure 21.4
Pathways for the digestion of food and the production of biochemical energy. This diagram summarizes pathways covered in this chapter (the citric acid cycle and electron transport) and also the pathways discussed in Chapter 22 for carbohydrate metabolism, in Chapter 24 for lipid metabolism, and in Chapter 25 for protein metabolism.

Worked Example 21.2 Identifying Metabolic Pathways That Convert Basic Molecules to Energy

(a) In Figure 21.4, identify the stages in the catabolic pathway in which lipids ultimately yield ATP.
(b) In Figure 21.4, identify the place at which the products of lipid catabolism can join the common metabolism pathway.

ANALYSIS Look at Figure 21.4 and find the pathway for lipids. Follow the arrows to trace the flow of energy. Note that Stage 3 is the point at which the products of lipid, carbohydrate, and protein catabolism all feed into a central, common metabolic pathway, the citric acid cycle. The lipid molecules that feed into Stage 3 do so via acetyl-CoA (Stage 2). Note also that most products of Stage 3 catabolism feed into Stage 4 catabolism to produce ATP.

SOLUTION
The lipids in food are broken down in Stage 1 (digestion) to fatty acids and glycerol. Stage 2 (acetyl-CoA production) results in fatty acid oxidation to acetyl-CoA. In Stage 3 (citric acid cycle), acetyl-CoA enters the citric acid cycle (the common metabolism pathway), which produces ATP, reduced coenzymes, and CO_2. In Stage 4 (ATP production), the energy stored in the reduced coenzymes (from the citric acid cycle) is converted to ATP energy.

PROBLEM 21.3

(a) In Figure 21.4, identify the stages in the pathway for the conversion of the energy from carbohydrates to energy stored in ATP molecules.

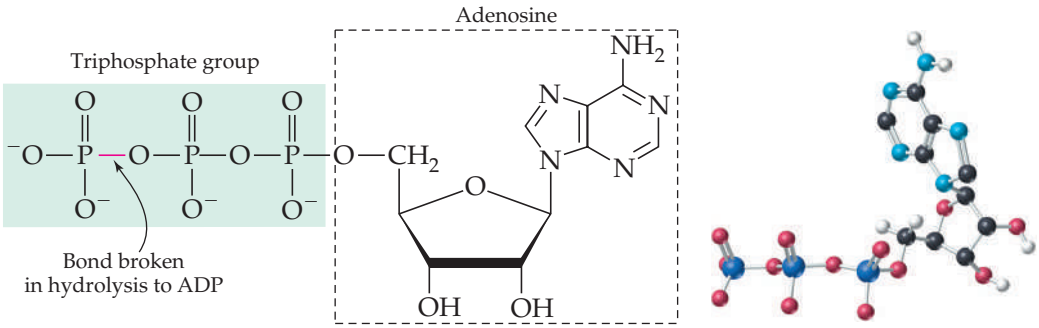
(b) In Figure 21.4, identify the three places at which the products of amino acid catabolism can join the central metabolism pathway.

21.4 Strategies of Metabolism: ATP and Energy Transfer

Learning Objective:

- Describe the role of ATP in energy transfer.

ATP is the body's energy-transporting molecule. What exactly does that mean? Consider that the molecule has three $-PO_3^-$ groups.



Removal of the terminal $-PO_3^{-2}$ group from ATP by hydrolysis gives adenosine diphosphate (ADP). The ATP → ADP reaction is exergonic; it releases chemical energy that was held in the bond to the $-PO_3^{2-}$ group.

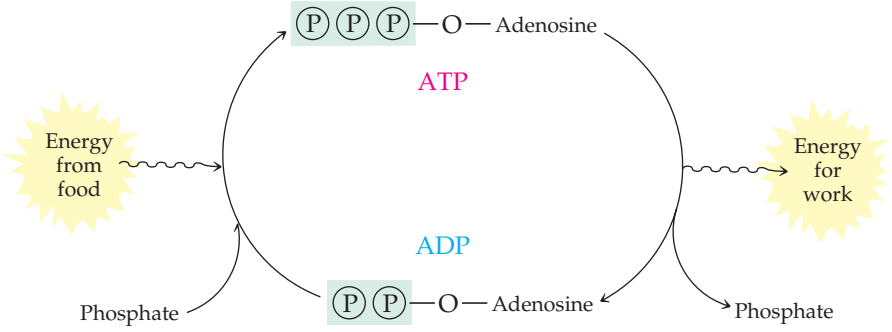
$$\text{ATP} + H_2O \longrightarrow \text{ADP} + HOPO_3^{2-} + H^+ \quad \Delta G = -30.5 \text{ kJ/mol}$$

The reverse of ATP hydrolysis—a phosphorylation reaction—is endergonic.

$$\text{ADP} + HOPO_3^{2-} + H^+ \longrightarrow \text{ATP} + H_2O \quad \Delta G = +30.5 \text{ kJ/mol}$$

(In equations for biochemical reactions, we represent ATP and other energy-carrying molecules in red and their lower-energy equivalent molecules in blue.)

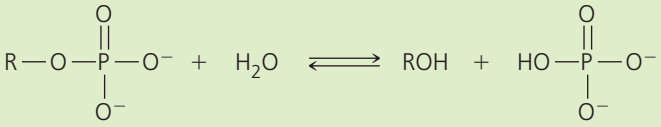
ATP is an energy transporter because its production from ADP requires an input of energy that is released when the reverse reaction occurs. Biochemical energy is gathered from exergonic reactions and stored in the bonds of the ATP molecule. ATP hydrolysis releases energy for energy-requiring work. *Biochemical energy production, transport, and use, all depend upon the ATP ⇌ ADP interconversion.*



The hydrolysis of ATP to give ADP and its reverse, the phosphorylation of ADP, are reactions perfectly suited to their role in metabolism for two major reasons. Firstly, ATP hydrolysis occurs slowly in the absence of a catalyst, so the stored energy is released only in the presence of the appropriate enzymes.

Secondly, the free energy of hydrolysis of ATP is an intermediate value for energy carriers (Table 21.1). Since the primary metabolic function of ATP is to transport energy, it is often referred to as a "high-energy" molecule or as containing "high-energy" phosphorus–oxygen bonds. These terms are misleading because they promote the idea that ATP is somehow different from other compounds. The terms mean only that ATP is reactive and that a useful amount of energy is released when a phosphoryl group is removed from it by hydrolysis.

Table 21.1 Free Energies of Hydrolysis of Some Phosphates

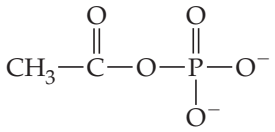


Compound Name	Function	ΔG (kJ/mol)
Phosphoenol pyruvate	Final intermediate in conversion of glucose to pyruvate (glycolysis)—Stage 2, Figure 21.5	−61.9
1, 3-Bisphosphoglycerate	Another intermediate in glycolysis	−49.4
Creatine phosphate	Energy storage in muscle cells	−43.1
ATP (⟶ ADP)	Principal energy carrier	−30.5
Glucose 1-phosphate	First intermediate in breakdown of carbohydrates stored as starch or glycogen	−20.9
Glucose 6-phosphate	First intermediate in glycolysis	−13.8
Fructose 6-phosphate	Second intermediate in glycolysis	−13.8

In fact, if removal of a phosphoryl group from ATP released *unusually* large amounts of energy, other reactions would not be able to provide enough energy to convert ADP back to ATP. ATP is a convenient energy carrier in metabolism because its free energy of hydrolysis has an *intermediate value* among high energy carriers. For this reason, the phosphorylation of ADP can be driven by coupling this reaction with a more exergonic reaction.

PROBLEM 21.4

Acetyl phosphate, whose structure is given here, is another compound with a relatively high free energy of hydrolysis.



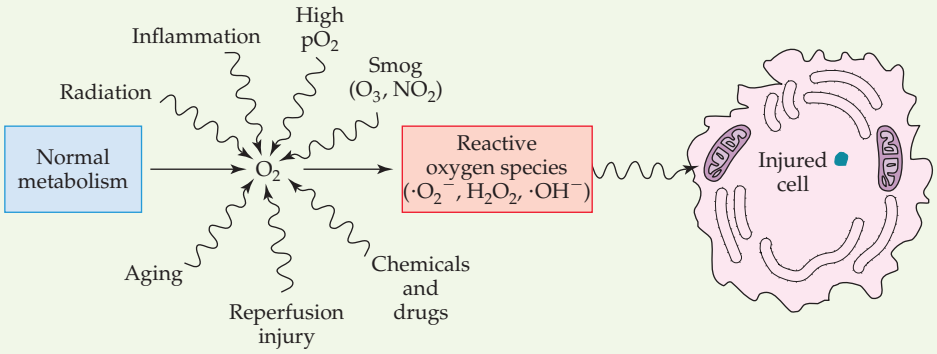
Using structural formulas, write the equation for the hydrolysis of this phosphate.

PROBLEM 21.5

A common metabolic strategy is the lack of reactivity—that is, the slowness to react—of compounds whose breakdown is exergonic. For example, hydrolysis of ATP to ADP or adenosine monophosphate (AMP) is exergonic but does not take place without an appropriate enzyme present. Why would the cell use this metabolic strategy?

CHEMISTRY IN ACTION

Harmful Oxygen Species and Antioxidant Vitamins



More than 90% of the oxygen we breathe is used in electron-transport–ATP synthesis reactions. In these and other O_2 consuming reactions, the product can be water or one of these oxygen-containing free radicals: the superoxide ion ($\cdot O_2^-$), the hydroxyl free radical ($\cdot OH^-$), and hydrogen peroxide, H_2O_2, a relatively strong oxidizer. These three species are dangerous to cells; the superoxide ion is beneficial in destroying infectious microorganisms. In what is known as a "respiratory burst," *phagocytes* (cells that engulf bacteria) produce superoxide ions that react destructively with bacteria.

$$2\,O_2 + \text{NADPH} \longrightarrow 2 \cdot O_2^- + \text{NADP}^+ + H^+$$

Reactive oxygen species (ROS) are dangerous to our own cells, especially since most ROS are produced in mitochondria where they can disrupt energy production. ROS can break covalent bonds in enzymes and other proteins, DNA, and the lipids in cell membranes causing cell injury or death. Among the possible outcomes of such destruction are cancer, liver damage, rheumatoid arthritis, heart disease, immune system damage, and possibly the changes regarded as normal aging. Internal processes such as inflammation and drug ingestion and external influences like radiation and smog, including second-hand cigarette smoke, all produce these ROS in our bodies.

Our protection against ROS is provided by superoxide dismutase (converts the superoxide ion to hydrogen peroxide) and catalase (converts hydrogen peroxide to water), which are among the fastest-acting enzymes (see Section 19.1). Other enzymes in cells also provide some protection; however, certain vitamins, such as vitamins E, C, and A (or its precursor β-carotene), function as antioxidants as well. These molecules disarm free radicals by bonding with them (see Section 19.9). Vitamin E is fat-soluble, and its major function is to protect cell membranes from potential damage initiated when a cell membrane lipid (RH) is converted to an oxygen-containing free radical ROO $\cdot$. Because Vitamin C is water-soluble, it is a free-radical scavenger in the blood. There are also many other natural antioxidants among the chemical compounds distributed in fruits and vegetables.

CIA Problem 21.5 Which of the following are ROS?
(a) H_2O **(b)** H_2O_2 **(c)** ROO $\cdot$ **(d)** $\cdot OH^-$

CIA Problem 21.6 How does a cell disarm each of the ROS in CIA Problem 21.5? What enzymes and vitamins are involved?

21.5 Strategies of Metabolism: Metabolic Pathways and Coupled Reactions

Learning Objective:

- Explain why some reactions are coupled and give an example of a coupled reaction.

How is stored chemical energy gradually released and how is it used to drive endergonic (uphill) reactions? Remember that your body cannot burn up the energy obtained from consuming a meal all at once. As shown in Figure 7.3, however, the energy difference between a reactant (the meal) and the ultimate products of its catabolism (mainly carbon dioxide and water) is a fixed quantity. The same amount of energy is released no matter what pathway is taken between reactants and products. The metabolic pathways of catabolism take advantage of this fact by releasing energy bit by bit in a series of reactions, somewhat like the stepwise release of potential energy as water flows down an elaborate waterfall.

The overall reaction and the overall free-energy change for any series of reactions can be found by summing up the equations and the free-energy changes for the individual steps. For example, glucose is converted to pyruvate via the 10 reactions of the glycolysis pathway (part of Stage 2, Figure 21.4, and Section 22.3). The overall free-energy change for glycolysis is about −33.5 kJ/mol, showing

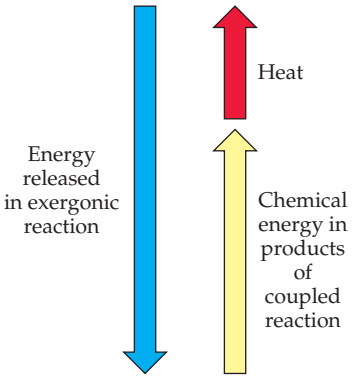
▲ This waterfall illustrates a stepwise release of potential energy. No matter what the pathway from the top to the bottom, the amount of potential energy released as the water falls from the top to the very bottom is the same.

that the pathway is exergonic—that is, downhill and favorable. The reactions of all metabolic pathways *sum* to favorable processes with negative free-energy changes.

Unlike the waterfall, however, not every individual step in every metabolic pathway is downhill. The metabolic strategy for dealing with what would be an energetically unfavorable reaction is to *couple* it with an energetically favorable reaction so that the overall energy change for the two reactions is favorable. For example, consider the reaction of glucose with hydrogen phosphate ion ($HOPO_3^{2-}$) to yield glucose 6-phosphate plus water, for which $\Delta G = +13.8$ kJ/mol. This reaction is unfavorable because the two products are 13.8 kJ/mol higher in energy than the starting materials. This phosphorylation of glucose is, however, the essential first step toward all metabolic use of glucose. To accomplish this reaction, it is coupled with the exergonic hydrolysis of ATP to give ADP.

(*Unfavorable*)	Glucose + $HOPO_3^{2-}$ ⟶ Glucose 6-phosphate + H_2O	$\Delta G = +13.8$ kJ/mol
(*Favorable*)	ATP + H_2O ⟶ ADP + $HOPO_3^{2-}$ + H^+	$\Delta G = -30.5$ kJ/mol
(*Favorable*)	Glucose + ATP ⟶ Glucose 6-phosphate + ADP	$\Delta G = -16.7$ kJ/mol

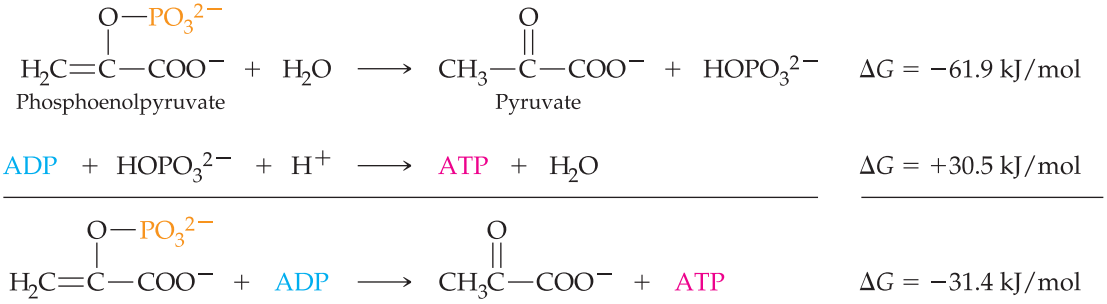
The net energy change for this pair of coupled reactions is favorable: 16.7 kJ of free energy is released for each mole of glucose that is phosphorylated. Only by such coupling can the energy stored in one chemical compound be transferred to other compounds. Any excess energy is released as heat and contributes to maintaining body temperature (Figure 21.5).



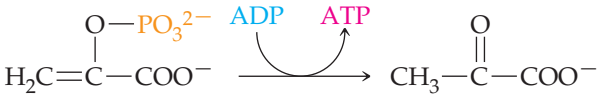
▲ Figure 21.5
Energy exchange in coupled reactions.
The energy provided by an exergonic reaction is either released as heat or stored as chemical potential energy in the bonds of products of the coupled endergonic reaction.

Although these reactions are written separately to show how their energies combine, coupled reactions do not take place separately. The net change occurs all at once as represented by the overall equation. The phosphoryl group is transferred directly from ATP to glucose without the intermediate formation of $HOPO_3^{2-}$.

The same principle of coupling is used for the endergonic synthesis of ATP from ADP, $\Delta G = +30.5$ kJ/mol. For this endergonic reaction to occur, it must be coupled with a reaction that releases *more* than 30.5 kJ/mol. In a different step of glycolysis, for example, the formation of ATP is coupled with the hydrolysis of phosphoenolpyruvate, a phosphate of higher energy than ATP (Table 21.1). Here, the overall reaction is transfer of a phosphoryl group from phosphoenolpyruvate to ADP.



Remember that in equations representing coupled reactions, a *curved arrow* often connects the reactants and products in one of the two chemical changes. For example, the reaction of phosphoenolpyruvate illustrated earlier can be written as



PROBLEM 21.6

One of the steps in lipid metabolism is the reaction of glycerol (1,2,3-propanetriol, $HOCH_2CH(OH)CH_2OH$), with ATP to yield glycerol 1-phosphate. Write the equation for this reaction using the curved arrow symbolism.

PROBLEM 21.7

Why must a metabolic pathway that synthesizes a given molecule occur by a different series of reactions than a pathway that breaks down the same molecule?

CHEMISTRY IN ACTION

Basal Metabolism

The minimum amount of energy expenditure required per unit of time to stay alive—to breathe, maintain body temperature, circulate blood, and keep all body systems functioning—is referred to as the *basal metabolic rate.* Ideally, it is measured in a person who is awake, is lying down at a comfortable temperature, has fasted and avoided strenuous exercise for 12 hours, and is not under the influence of any medications. The basal metabolic rate is measured by monitoring respiration and finding the rate of oxygen consumption, which is proportional to the energy used.

An *average* basal metabolic rate is 293 kJ/hr or about 7100 kJ/day. The rate varies with many factors, including sex, age, mass, and physical condition. A rule of thumb used by nutritionists to estimate basal energy needs per day is the requirement for 4.2 kJ/hr per kilogram of body mass by a male and 4 kJ/hr per kilogram of body mass by a female. For example, a 50 kg female has an estimated basal metabolic rate of $(50\,kg)(4\,kJ/kg\,hr) = 200\,kJ/hr$, resulting in a daily requirement of 4800 kJ.

The total energy a person needs each day is determined by his or her basal requirements plus the energy used in additional physical activities. The energy consumption rates associated with some activities are listed in the accompanying table. A relatively inactive person requires about 30% above basal requirements per day, a lightly active person requires about 50% above basal, and a very active person such as an athlete or construction worker can use 100% above basal requirements in a day. Each day that you consume food with more energy than you use, the excess energy is stored as potential energy in the chemical bonds of fats in your body and your body mass rises. Each day that you consume food with less energy than you burn, some chemical energy in your body is taken out of storage to make up the deficit. Fat is metabolized to CO_2 and H_2O, which the body gets rid of, and your mass drops.

▲ The cola drink contains 680 kJ and the hamburger contains 2100 kJ. How long would you have to jog at 8 km/h to burn off this energy?

Energy Used in Various Activities

Activity	Kilojoules Used per Minute
Sleeping	5 kJ
Reading	5.4 kJ
Listening to lecture	7.1 kJ
Weeding garden	23 kJ
Walking, 5.6 km/h	23 kJ
Pick-and-shovel work	25 kJ
Recreational tennis	29 kJ
Soccer, basketball	38 kJ
Walking up stairs	42–75 kJ
Running, 7.5 min/km (8 km/h)	42 kJ
Running, 3 min/km (20 km/h)	105 kJ

CIA Problem 21.7 How is basal metabolic rate defined?

CIA Problem 21.8 An average 33 cL. can of soda pop contains 680 kJ and a typical hamburger contains 2100 kJ. Using the table, calculate how long would you need to jog at 8 kilometers per hour to burn off this energy.

CIA Problem 21.9 Calculate the total energy in joules needed in a day for an 80 kg lightly active male. Use the "Kilojoules Used per Minute" values given in the table in the application.

CIA Problem 21.10 Why do activities such as walking raise a body's needs above the basal metabolic rate?

HANDS-ON CHEMISTRY 21.1

How much energy (in J) do you need in a day to maintain your current mass? The best way is to estimate joules by using this formula:

$$\text{Basal joules} + \text{activity joules} = \text{total joules}$$

Calculate your basal metabolism energy need as described in the Chemistry in Action "Basal Metabolism" (p. 705).

Next, estimate your other energy needs based on your activities. Are you inactive, lightly active, or highly active? Use that as a guide and add the energy of activity to the basal energy. Is this an accurate estimate?

As a check, list your daily activities and search the Web for a chart of activities and joules expended. Estimate time spent on these activities, especially if you exercise regularly, have a strenuous job or similar activity, and add this energy to your basal metabolism energy requirement. Is there a difference from your first estimate? If so, why do you suppose there is a difference?

Worked Example 21.3 Determining If a Coupled Reaction Is Favorable

The hydrolysis of succinyl-CoA is coupled with the production of GTP (guanosine triphosphate—closely related to ATP). The equations for the reactions are given below. Combine the equations appropriately and determine if the coupled reaction is favorable.

$$\text{Succinyl-CoA} \longrightarrow \text{Succinate} + \text{CoA} \qquad \Delta G = -39.3\ \text{kJ/mol}$$
$$\text{GDP} + \text{HOPO}_3^{2-} + \text{H}^+ \longrightarrow \text{GTP} + \text{H}_2\text{O} \qquad \Delta G = +30.5\ \text{kJ/mol}$$

ANALYSIS Add the two equations together to produce the equation for the coupled reaction. Also add the ΔG values together, paying close attention to the signs. If the ΔG is positive, the reaction is not favorable and will not occur; if the ΔG is negative, the reaction is favorable and will occur.

SOLUTION

$$\text{Succinyl-CoA} + \text{GDP} + \text{HOPO}_3^{2-} + \text{H}^+ \longrightarrow \text{Succinate} + \text{GTP} + \text{H}_2\text{O} + \text{CoA}$$
$$\Delta G = -8.8\ \text{kJ/mol}$$

Since ΔG is negative, the coupled reaction will occur as written.

PROBLEM 21.8

The hydrolysis of acetyl phosphate to give acetate and hydrogen phosphate ion has $\Delta G = -43.1$ kJ/mol. Combine the equations and ΔG values to determine whether coupling of this reaction with phosphorylation of ADP to produce ATP is favorable. (You need give only compound names or abbreviations in the equations.)

21.6 Strategies of Metabolism: Oxidized and Reduced Coenzymes

Learning Objective:

- Give an example of a coenzyme changing from oxidized to reduced form in a reaction and explain the purpose of the change.

The net result of catabolism is the oxidation of food molecules to release energy. Many metabolic reactions are therefore oxidation–reduction reactions, which means that a steady supply of oxidizing and reducing agents must be available. To meet this requirement, a few coenzymes cycle continuously between their oxidized and reduced forms, just as adenosine cycles continuously between its triphosphate and diphosphate forms.

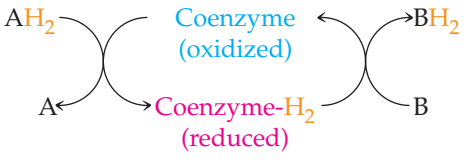


Table 21.2 lists some important cycling coenzymes in their oxidized and reduced forms. The oxidized form acts as an oxidizing agent for a reaction while the reduced form acts as a reducing agent for the reverse reaction. For example, lactate is oxidized by lactate dehydrogenase in the presence of NAD^+ (oxidizing agent) to pyruvate; in the reverse reaction pyruvate is reduced in the presence of NADH (reducing agent) to lactate.

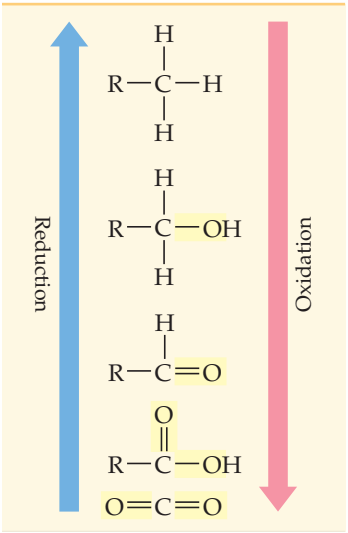
Table 21.2 Oxidized and Reduced Forms of Important Coenzymes

Coenzyme	Oxidized Form	Reduced Form
Nicotinamide adenine dinucleotide	NAD^+	$NADH/H^+$
Nicotinamide adenine dinucleotide phosphate	$NADP^+$	$NADPH/H^+$
Flavin adenine dinucleotide	FAD	$FADH_2$
Flavin mononucleotide	FMN	$FMNH_2$

To review briefly, keep in mind these important points about oxidation and reduction:

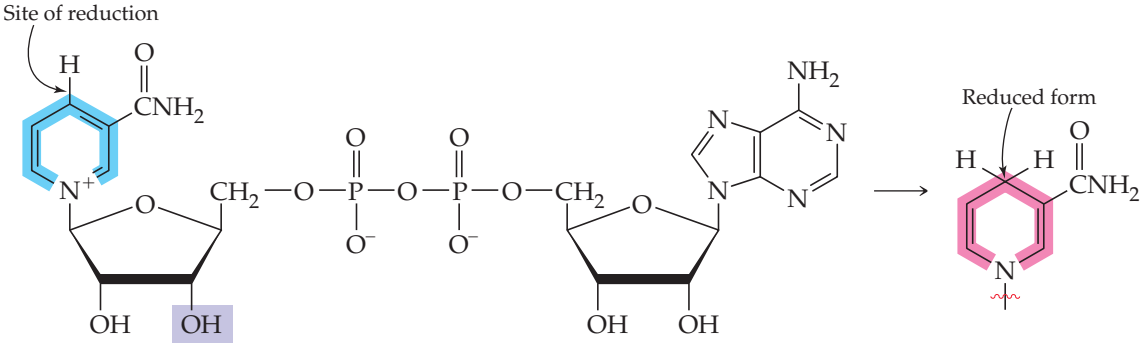
- Oxidation can be loss of electrons, loss of hydrogen, or addition of oxygen.
- Reduction can be gain of electrons, gain of hydrogen, or loss of oxygen.
- Oxidation and reduction always occur together.

Each increase in the number of carbon–oxygen bonds is an oxidation, and each increase in the number of carbon–hydrogen bonds is a reduction, as shown in Figure 21.6. Oxidation of carbon increases by increased bonding to oxygen.

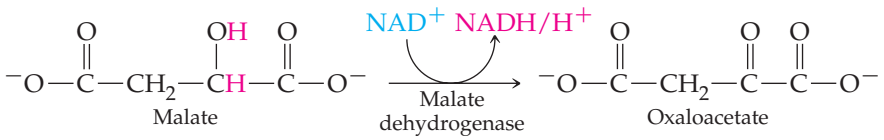


▲ **Figure 21.6**
Oxidation of carbon by increased bonding to oxygen

The coenzymes nicotinamide adenine dinucleotide (NAD^+/NADH) and nicotinamide adenine dinucleotide phosphate ($NADP^+$/NADPH) are ubiquitous in cells and organelles, where they participate in oxidation/reduction reactions in conjunction with oxidoreductases. As oxidizing agents, NAD^+ and $NADP^+$ remove hydrogen from a substrate, and as reducing agents, NADH and NADPH provide hydrogen that adds to a substrate. Some enzymes, such as lactate dehydrogenase, require the cofactor NAD^+/NADH, while enzymes involved in fatty acid synthesis require $NADP^+$/NADPH as the cofactor. The complete structure of NAD^+ is shown with the change that converts it to NADH. The only difference between the structures of NAD^+/NADH and $NADP^+$/NADPH is that the color-shaded —OH group in NAD^+/NADH is instead a $—OPO_3^{2-}$ group in $NADP^+$ and NADPH.



As an example, consider a reaction in the citric acid cycle (step 8 in Figure 21.8, Section 21.7) from the oxidation–reduction, or redox, point of view.



Oxidation of malate to oxaloacetate requires the removal of two hydrogen atoms to convert a secondary alcohol to a ketone. The oxidizing agent, which will be reduced

Recall from Section 15.1 that a ketone is $R_2C=O$.

during the reaction, is NAD^+, functioning as a *coenzyme* for the enzyme malate dehydrogenase. Sometimes NAD^+ is written as a reactant or product to emphasize its role in a reaction. Keep in mind that although it is free to enter and leave the active site, it always functions as a coenzyme with the appropriate enzyme for the reaction.

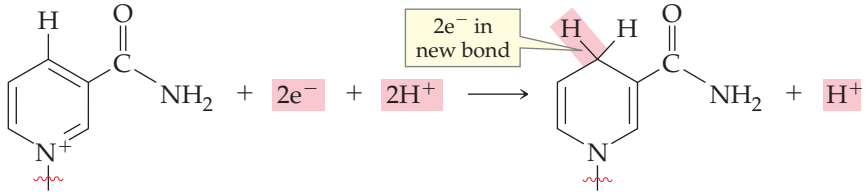
When considering enzyme-catalyzed redox reactions, it is important to recognize that a hydrogen atom is equivalent to a hydrogen *ion,* H^+, plus an electron, e^-. Thus, for the two hydrogen atoms removed in the oxidation of malate,

$$2H \text{ atoms} = 2H^+ + 2e^-$$

When NAD^+ is reduced, both electrons accompany one of the hydrogen atoms to give a hydride ion,

$$H^+ + 2e^- = :H^-$$

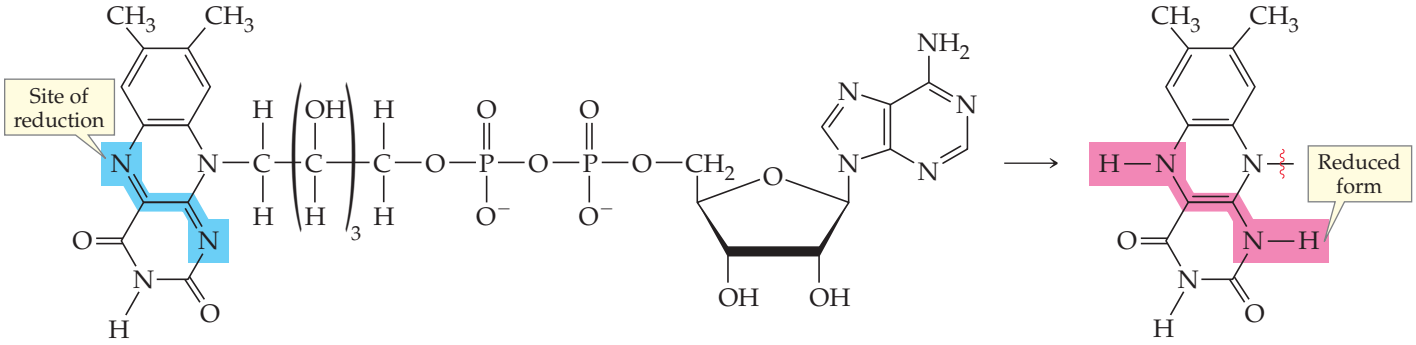
The reduction of NAD^+ occurs by addition of H^- to the ring in the nicotinamide part of the structure, where the two electrons of H^- form a covalent bond.



NAD^+ $\qquad$ $NADH/H^+$

The second hydrogen removed from the oxidized substrate enters the surrounding aqueous solution as a hydrogen ion, H^+. The product of NAD^+ reduction is therefore often represented as $NADH/H^+$ to show that two hydrogen atoms have been removed from the reactant, one of which has bonded to NAD^+ and the other of which is a hydrogen ion in solution. ($NADP^+$ is reduced in the same way to form $NADPH/H^+$.)

Flavin adenine dinucleotide (FAD), another common oxidizing agent in catabolic reactions, is reduced by the formation of covalent bonds to two hydrogen atoms to give $FADH_2$. It participates in several reactions of the citric acid cycle, which is described in the next section.



FAD $\qquad$ $FADH_2$

Because the reduced coenzymes, NADH and $FADH_2$, have picked up electrons (in their bonds to hydrogen) that are passed along in subsequent reactions, they are often referred to as *electron carriers.* As these coenzymes cycle through their oxidized and reduced forms, they also carry energy along from reaction to reaction. Ultimately, this energy is passed on to the bonds in ATP, as described in Section 21.8.

PROBLEM 21.9

Which of the following is found in the coenzyme FAD?

(a) Two heterocyclic rings
(b) ADP
(c) A substituted benzene ring
(d) A phosphate anhydride bond

PROBLEM 21.10

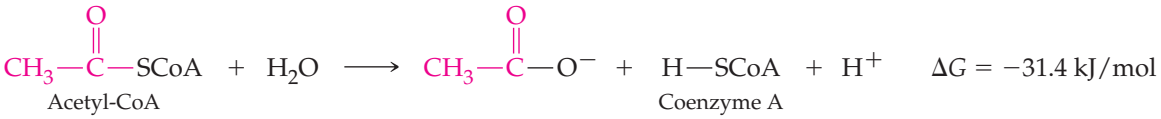
Look ahead to Figure 21.8 for the citric acid cycle. (a) Draw the structures of the reactants in steps 3, 6, and 8, and indicate which hydrogen atoms are removed in these reactions. (b) What class of enzymes carry out these reactions?

21.7 The Citric Acid Cycle

Learning Objective:

- Describe the reactions in the citric acid cycle and explain its role in energy production.

The carbon atoms from the first two stages of catabolism are carried into the third stage as acetyl groups bonded to coenzyme A. Like the phosphoryl groups in ATP molecules, the acetyl groups in acetyl-SCoA molecules are readily removed in an energy-releasing hydrolysis reaction.

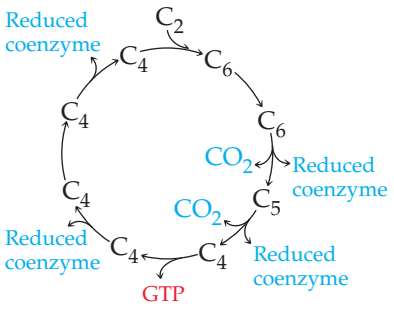


Oxidation of two carbons to give two CO_2 and transfer of energy to reduced coenzymes occur in the **citric acid cycle,** also known as the *tricarboxylic acid cycle (TCA)* or *Krebs cycle* (after Sir Hans Krebs, who unraveled its complexities in 1937). As its name implies, the citric acid *cycle* is a closed loop of reactions in which the product of the final step, oxaloacetate, a 4-carbon molecule, is the reactant in the first step. The pathway of carbon atoms through the cycle and the significant products formed are summarized in Figure 21.7 and shown in greater detail in Figure 21.8. The two carbon atoms of the acetyl group add to the four carbon atoms of oxaloacetate in step 1, and two carbon atoms are set free as carbon dioxide in steps 3 and 4. The cycle continues as 4-carbon intermediates progress toward regeneration of oxaloacetate and production of additional reduced coenzymes.

A brief description of the eight steps of the citric acid cycle is given in Figure 21.8. The enzymes involved in each step are listed in the accompanying table. The cycle takes place in mitochondria, where seven of the enzymes are dissolved in the matrix and one (for step 6) is embedded in the inner mitochondrial membrane. The citric acid cycle is not reversible in an organism, although some enzymes of the cycle can carry out the reverse reaction in a test tube.

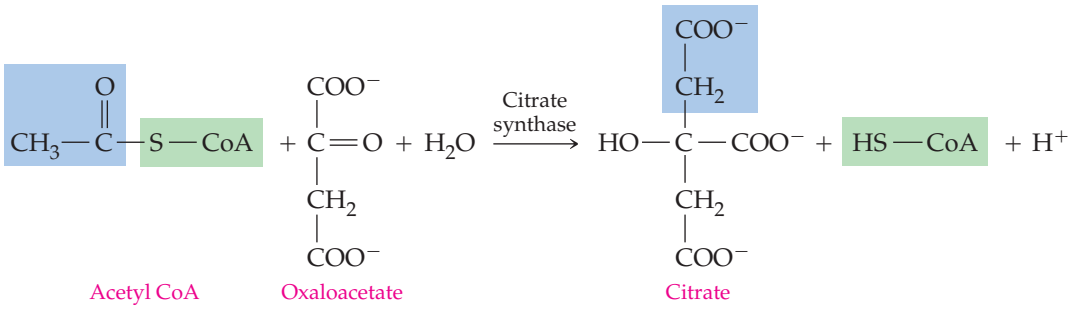
The cycle operates as long as acetyl groups are available from acetyl-CoA and the oxidizing agent coenzymes NAD^+ and FAD are available. Since these compounds are not stored, the reduced coenzymes NADH and $FADH_2$ must be reoxidized via the electron-transport chain in Stage 4 of catabolism (described in Section 21.8). Because Stage 4 relies on oxygen as the final electron acceptor, the cycle is also dependent upon the availability of oxygen. The steps of the citric acid cycle are summarized next.

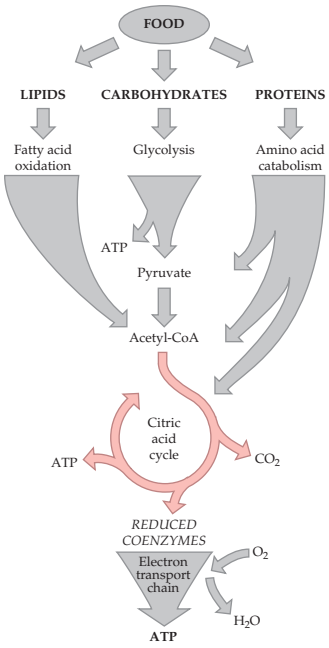
Citric acid cycle The series of biochemical reactions that breaks down acetyl groups to produce energy carried by reduced coenzymes and carbon dioxide.



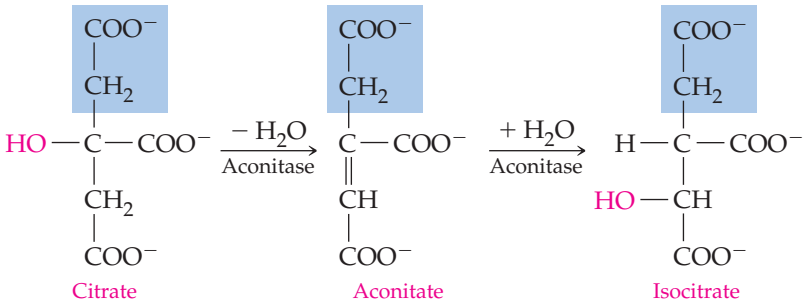
▲ Figure 21.7
Significant outcomes of the citric acid cycle.
For every acetyl-CoA the eight steps of the cycle produce two molecules of carbon dioxide, four molecules of reduced coenzymes, and one energy-rich phosphate (GTP). The final step regenerates the reactant for step 1 of the next turn of the cycle. (step 1 occurs where C_2 enters the cycle to form C_6 by adding to C_4.)

STEP 1: Addition of acetate from acetyl-CoA by citrate synthase to 4-carbon oxaloacetate yields citrate, a 6-carbon intermediate in the cycle. Citrate is a tertiary alcohol and cannot be oxidized. $\Delta G = -32.2$ kJ/mol.

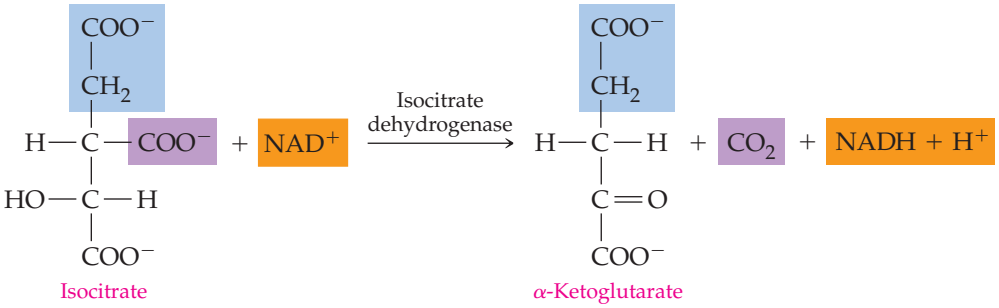




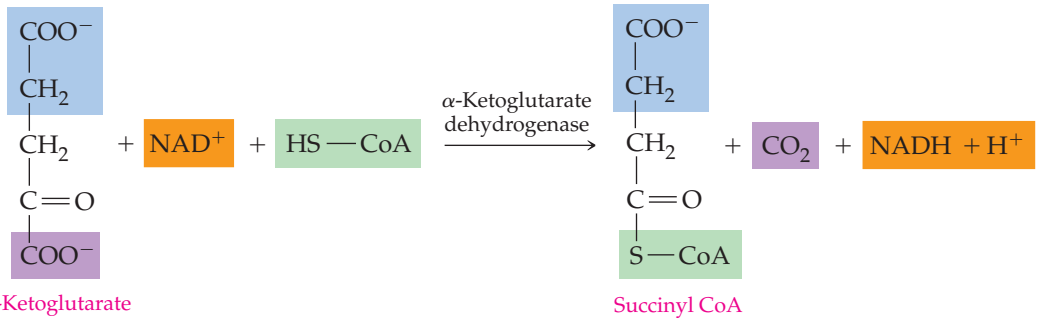
STEP 2: Conversion of citrate to its isomer isocitrate, a secondary alcohol that can be oxidized, is done in a two-step reaction with both steps catalyzed by aconitase. Water is removed, creating a temporary double bond, and then added back to the intermediate, which remains in the active site, so that the −OH is on a different carbon atom. $\Delta G = +13.3$ kJ/mol



STEP 3: Isocitrate is oxidized to α-ketoglutarate by isocitrate dehydrogenase with the simultaneous reduction of NAD^+ to NADH and the release of CO_2. α-Ketoglutarate is a 5-carbon molecule with a ketone group. $\Delta G = -8.4$ kJ/mol



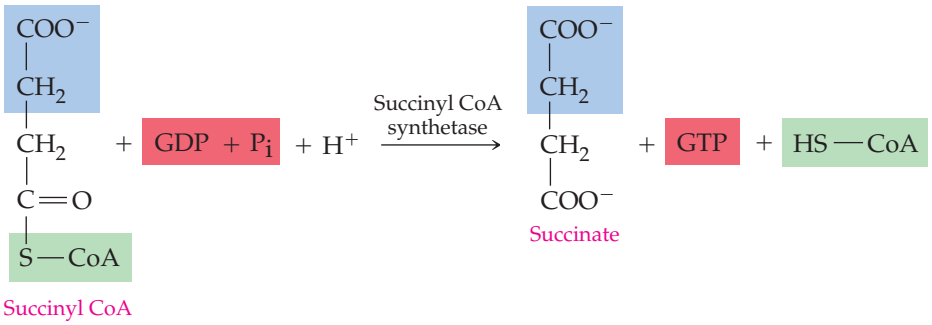
STEP 4: α-Ketoglutarate dehydrogenase converts α-ketoglutarate to succinate in a reaction requiring CoA and NAD^+. The products of the reaction are succinyl-CoA, $NADH/H^+$, and CO_2. Succinyl-CoA carries four carbon atoms along to the next step. $\Delta G = -33.5$ kJ/mol



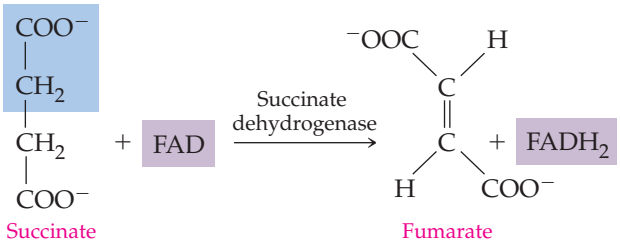
Guanosine diphosphate (GDP)
An energy-carrying molecule that can gain or lose a phosphoryl group to transfer energy.

Guanosine triphosphate (GTP)
An energy-carrying molecule similar to ATP; removal of a phosphoryl group to give GDP releases free energy.

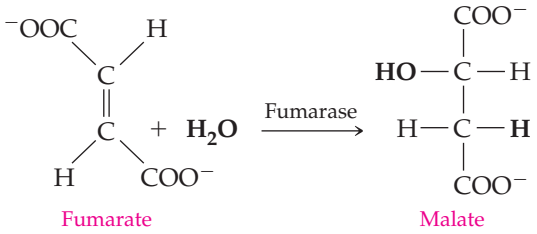
STEP 5: This step begins rebuilding oxaloacetate for the next turn of the cycle. Conversion of succinyl-CoA to succinate by succinyl-CoA synthetase is coupled with phosphorylation of **guanosine diphosphate (GDP)** to give **guanosine triphosphate (GTP).** GTP is immediately converted to ATP by coupling the GTP to GDP reaction with the ADP to ATP reaction. This is the only step in the cycle that generates an energy-rich triphosphate. $\Delta G = -2.9$ kJ/mol



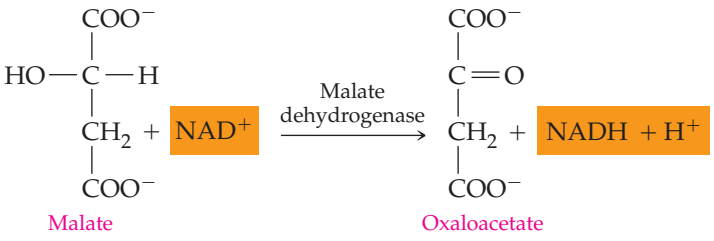
STEP 6: Succinate is oxidized by succinate dehydrogenase to yield fumarate, a 4-carbon molecule containing a carbon–carbon double bond. FAD is reduced to $FADH_2$ in this reaction. FAD is covalently bonded to succinate dehydrogenase, which is embedded in the inner mitochondrial membrane. Succinate dehydrogenase and FAD participate in Stage 4 of catabolism by passing electrons directly into electron transport. $\Delta G = 0\ \text{kJ/mol}$



STEP 7: Fumarase adds water across the double bond of fumarate to give malate, which contains a secondary alcohol group. $\Delta G = -3.8\ \text{kJ/mol}$



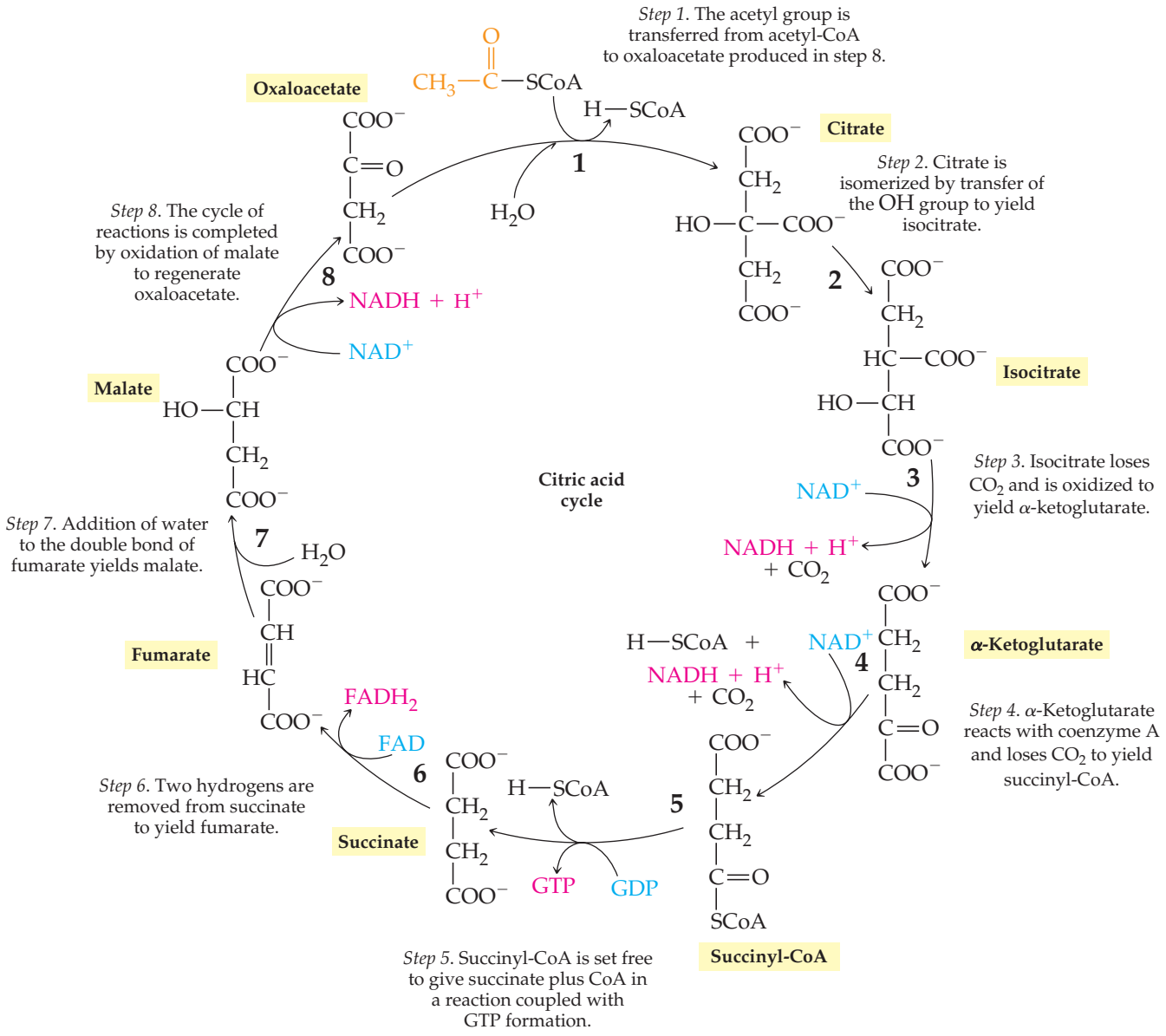
STEP 8: Malate dehydrogenase oxidizes malate to oxaloacetate, changing the secondary alcohol to a ketone group. At the same time NAD^+ is reduced to $NADH/H^+$. Oxaloacetate has been regenerated for the next turn of the cycle. $\Delta G = +29.7\ \text{kJ/mol}$



Net result of citric acid cycle

$$\text{Acetyl-CoA} + 3\text{NAD}^+ + \text{FAD} + \text{GDP} + \text{HOPO}_3^{2-} + \text{H}_2\text{O} \longrightarrow \text{HSCoA} + 3\text{NADH} + 3\text{H}^+ + \text{FADH}_2 + \text{GTP} + 2\text{CO}_2$$

- Production of four reduced coenzyme molecules (3NADH, $1FADH_2$)
- Conversion of an acetyl group to two CO_2 molecules
- Production of one energy-rich molecule (GTP, *converted immediately to ATP*)



Enzymes of the Citric Acid Cycle

Step	Enzyme Name	Enzyme Class/Subclass	Reaction Product
1	Citrate synthase	Lyase/synthase	Citrate
2	Aconitase	Lyase/dehydrase	Isocitrate
3	Isocitrate dehydrogenase complex	Oxidoreductase/oxidase	α-Ketoglutarate
4	α-Ketoglutarate dehydrogenase complex	Oxidoreductase/oxidase	Succinyl-CoA
5	Succinyl-CoA synthetase	Ligase/synthetase	Succinate
6	Succinate dehydrogenase	Oxidoreductase/oxidase	Fumarate
7	Fumarase	Lyase/dehydrase	Malate
8	Malate dehydrogenase	Oxidoreductase/oxidase	Oxaloacetate

▲ **Figure 21.8**

The citric acid cycle.

The net effect of this eight-step cycle of reactions is the metabolic breakdown of acetyl groups (from acetyl-CoA) into two molecules of carbon dioxide and energy carried by reduced coenzymes. Here and throughout this and the following chapters, energy-rich reactants or products (ATP, reduced coenzymes) are shown in red and their lower-energy counterparts (ADP, oxidized coenzymes) are shown in blue.

The rate of the citric acid cycle is controlled by the body's cellular need for ATP and reduced coenzymes and for the energy derived from them. For example, when energy is being used at a high rate, ADP accumulates and acts as an allosteric activator (positive regulator, see Section 19.7) for isocitrate dehydrogenase, the enzyme for step 3 and for α-ketoglutarate dehydrogenase, the enzyme for step 4. When the body's supply of energy is abundant, ATP and NADH are present in excess and act as inhibitors of both of those enzymes. By such feedback mechanisms, as well as by variations in the concentrations of necessary reactants, the cycle is activated when energy is needed and inhibited when energy is in good supply.

Worked Example 21.4 Identifying Reactants and Products in the Citric Acid Cycle

What substance(s) are the substrate(s) for the citric acid cycle? What are the products of the citric acid cycle?

ANALYSIS Study Figure 21.8. Note that acetyl-CoA feeds into the cycle but does not come out anywhere. Can you see that all of the other reaction substrates are integral to the cycle and are always present, being continuously synthesized and degraded? Note also that the coenzymes NAD^+ and FAD are reduced and the reduced versions are considered energy-carrying products of the cycle. Also, CO_2 is produced at two different steps in the cycle. Finally, GDP is converted to GTP in step 5 of the cycle.

SOLUTION

Acetyl-CoA is the substrate for the cycle. Along with GDP and CoA, the oxidized coenzymes NAD^+ and FAD might also be considered substrates, despite their status as coenzymes, because these substances cycle between the reduced and oxidized states. The products of the cycle are CO_2 and the energy-rich reduced coenzymes $NADH/H^+$ and $FADH_2$ as well as GTP.

PROBLEM 21.11

Which substances in the citric acid cycle are tricarboxylic acids (thus giving the cycle its alternative name)?

PROBLEM 21.12

In Figure 21.11, identify the steps at which reduced coenzymes are produced.

PROBLEM 21.13

Why, do you suppose, the coenzyme for the reaction in the citric acid cycle that is catalyzed by succinate dehydrogenase is FAD and not NAD^+?

PROBLEM 21.14

Identify the participants in the citric acid cycle that contain alcohol groups. Identify these groups as primary, secondary, or tertiary alcohols.

PROBLEM 21.15

Which of the reactants in the citric acid cycle have two chiral carbon atoms?

KEY CONCEPT PROBLEM 21.16

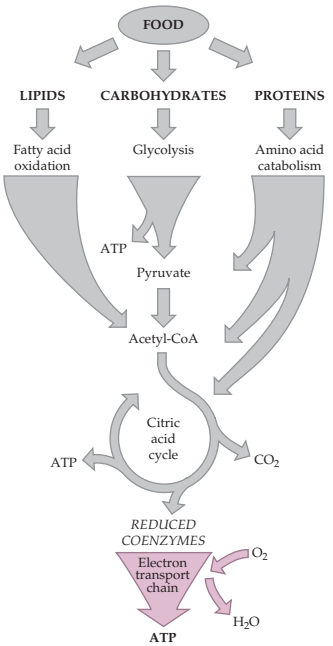
The citric acid cycle can be divided into two stages. In one stage, carbon atoms are added and removed, and in the second stage, oxaloacetate is regenerated. Which steps of the citric acid cycle correspond to each stage?

21.8 The Electron-Transport Chain and ATP Production

Learning Objective:

- Describe the electron-transport chain, oxidative phosphorylation, and how the two processes are coupled.

Keep in mind that in some ways catabolism is just like burning fuel oil. In both cases, the goal is to produce useful energy and the reaction products are water and carbon



dioxide. The difference is that in catabolism the products are not released all at once and not all of the energy is released as heat.

For each turn of the citric acid cycle, the reduced coenzymes formed during the turn donate their energy to making additional ATP. The energy is released in a series of oxidation–reduction reactions that move electrons from one electron carrier to the next as each carrier is reduced (gains an electron from the preceding carrier) and then oxidized (loses an electron by passing it along to the next carrier). Each reaction in the series is favorable; that is, it is exergonic. You can think of each reaction as a step along the way down a waterfall. The sequence of reactions that move the electrons along is known as the **electron-transport chain or system (ETS)** and is also called the *respiratory chain*. The enzymes and coenzymes of the chain and ATP synthesis are embedded in the inner membrane of the mitochondrion (Figure 21.9).

Electron-transport chain The series of biochemical reactions that passes electrons from reduced coenzymes to oxygen and is coupled to ATP formation. Also called the respiratory chain.

In the last step of the chain, the electrons combine with the oxygen that we breathe and with hydrogen ions from their surroundings to produce water.

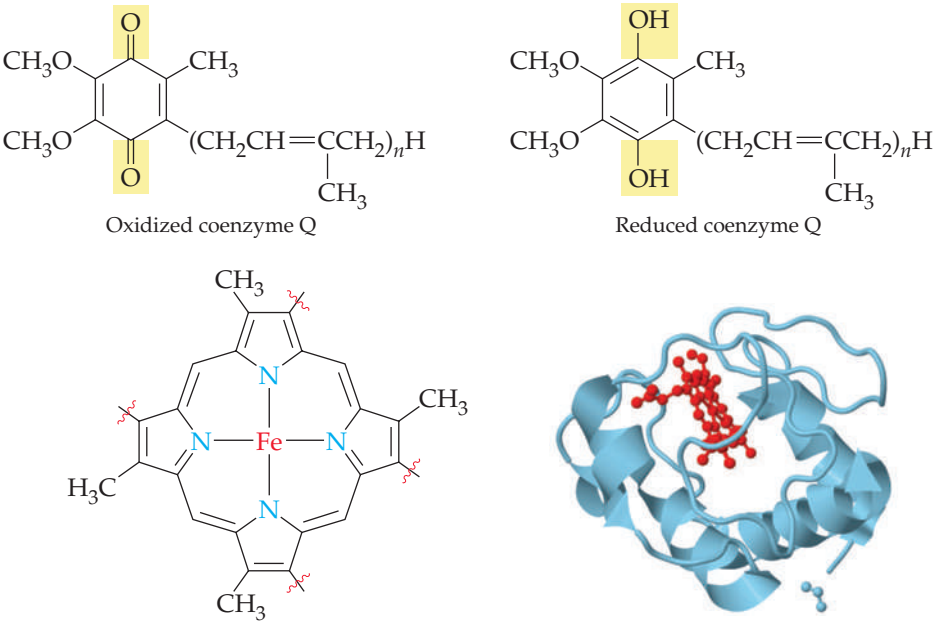
$$O_2 + 4e^- + 4H^+ \longrightarrow 2H_2O$$

This reaction is fundamentally the combination of hydrogen and oxygen gases. Carried out all at once with the gases themselves, the reaction is explosive. What happens to all that energy during electron transport?

As electrons move down the electron-transport pathway, the energy released is used to move hydrogen ions out of the mitochondrial matrix by crossing the inner membrane and into the intermembrane space. Because the inner membrane is otherwise impermeable to the H^+ ion, the result is a higher H^+ concentration in the intermembrane space than in the mitochondrial matrix. Moving ions from a region of lower concentration to one of higher concentration opposes the natural tendency for random motion to equalize concentrations throughout a mixture and therefore requires energy to make it happen. This energy is recaptured for use in ATP synthesis.

Electron Transport

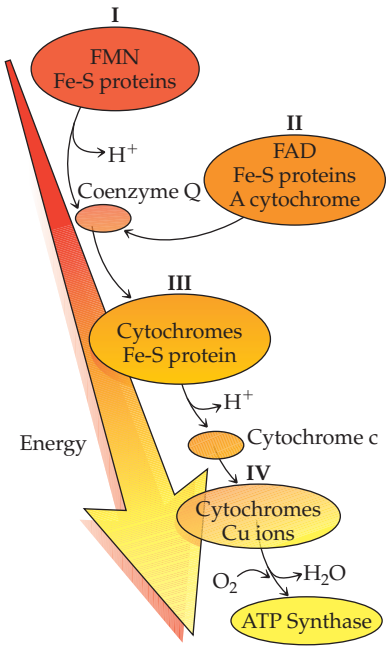
Electron transport proceeds via four enzyme complexes held in fixed positions within the inner membrane of mitochondria, along with two electron carriers that move through the membrane from one complex to another. The complexes and mobile electron carriers are organized in the sequence of their ability to pick up electrons, as illustrated in Figure 21.9. The four fixed complexes are very large assemblages of polypeptides and electron acceptors. The most important electron acceptors are of three types: (1) various cytochromes that are proteins that contain heme groups (Figure 21.9a) in which the



▸ **Figure 21.9**
A heme group and a cytochrome. (a) Heme groups, in which the substituents at the bonds marked in red vary, are iron-containing coenzymes in the cytochromes of the electron-transport chain. They are also the oxygen carriers in hemoglobin in red blood cells. (b) In the cytochrome shown here, the coiled blue ribbon is the amino acid chain and the heme group is in red.

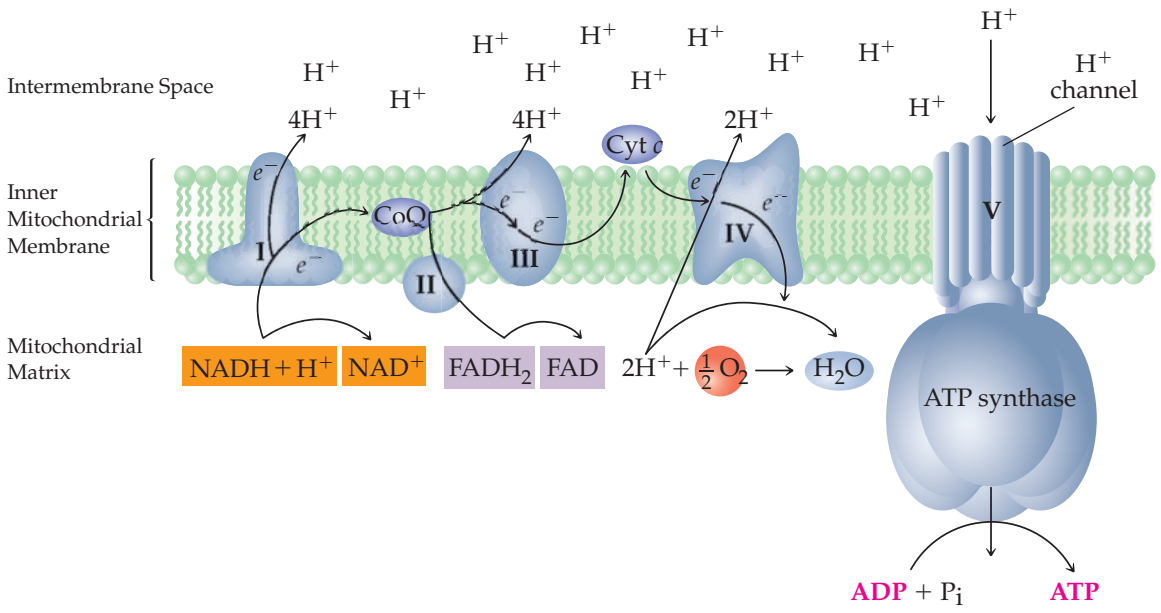
iron cycles between Fe^{2+} and Fe^{3+}; (2) proteins containing iron–sulfur groups in which the iron also cycles between Fe^{2+} and Fe^{3+}; and (3) coenzyme Q (CoQ), often known as *ubiquinone* because of its ubiquitous (widespread) occurrence and because its ring structure with the two ketone groups is a *quinone*.

The details of the reactions that move electrons in the electron-transport chain are not important here. Focus only on the following essential features of the pathway (Figure 21.10; refer also to Figure 21.11).



◂ Figure 21.10
Pathway of electrons in electron transport.
Each of the enzyme complexes I–IV contains several electron carriers. FMN in complex I is similar in structure to FAD. Hydrogen ions and electrons move through the components of the electron-transport pathway in the direction of the arrow. Energy is transferred, with some loss, at each complex; each succeeding complex is at a lower energy level than the preceding, as indicated by the color change.

- Hydrogen ions and electrons from NADH and $FADH_2$ enter the electron-transport chain at enzyme complexes I and II, respectively. These complexes function independently and not necessarily in numerical order. The enzyme for step 6 of the citric acid cycle is part of complex II, where $FADH_2$ is produced when that step of the cycle occurs. $FADH_2$ does not leave complex II. It is immediately oxidized there by reaction with mobile coenzyme Q, forming QH_2. After formation of reduced mobile coenzyme QH_2, hydrogen ions no longer participate directly in the reductions of electron carriers. Instead, electrons are transferred directly, one by one from carrier to carrier.
- Electrons are passed from weaker to increasingly stronger oxidizing agents, with energy released at each transfer. Much of this energy is conserved during the transfer; however, some energy is used to pump protons across the inner mitochondrial membrane, and some is lost as heat at each electron transfer.
- Hydrogen ions are released for transport through the inner mitochondrial membrane to the intermembrane space at complexes I, III, and IV, creating an H^+ gradient, with the intermembrane space becoming acidic and the matrix alkaline due to changes in H^+ concentration. Some of these ions come from the reduced coenzymes and some from the matrix—exactly how the hydrogen ions are transported to the intermembrane space is not yet fully understood, although the process appears to be via an energy-requiring pump.
- The H^+ concentration difference creates a potential energy difference across the two sides of the inner membrane (like the energy difference between water at the top and bottom of a waterfall). The maintenance of this concentration gradient across the membrane is *crucial*—it is the mechanism by which energy for ATP formation is made available.



▲ **Figure 21.11**
The mitochondrial electron-transport chain and ATP synthase.
The arrows show the path of electrons and the hydrogen ions. The movement of hydrogen ions across the inner membrane at complexes I, III, and IV creates a higher concentration of hydrogen ions on the intermembrane side of the inner membrane than on the matrix side. The energy released by hydrogen ions returning to the matrix through ATP synthase provides the energy needed for ATP synthesis.

Plant cells, like animal cells, contain mitochondria and carry out oxidative phosphorylation. In addition, plant cells also contain chloroplasts, organelles that are similar to mitochondria but instead carry out photosynthesis, a series of reactions that also involve electron and hydrogen ion transfer through a series of enzyme complexes arranged in an electron transport chain. See the Chemistry in Action "Plants and Photosynthesis" on page 696 for more information.

ATP Synthesis

Oxidative phosphorylation The synthesis of ATP from ADP using energy released in the electron-transport chain.

ATP synthase The enzyme complex in the inner mitochondrial membrane where hydrogen ions cross the membrane and ATP is synthesized from ADP.

The reactions of the electron-transport chain are tightly coupled to **oxidative phosphorylation,** the conversion of ADP to ATP, by a reaction that is both an oxidation and a phosphorylation. Hydrogen ions can return to the matrix only by passing through a channel that is part of the **ATP synthase** enzyme complex. In doing so, they release the potential energy gained as they were moved against the concentration gradient at the enzyme complexes of the electron-transport chain. This energy release drives the phosphorylation of ADP by reaction with hydrogen phosphate ion $(HOPO_3^{2-})$.

$$ADP + HOPO_3^{2-} \longrightarrow ATP + H_2O$$

ATP synthase has knob-tipped stalks that protrude into the matrix and are clearly visible in electron micrographs. ADP and $(HOPO_3^{2-})$ are attracted into the knob portion. As hydrogen ions flow through the complex, ATP is produced and released back into the matrix. The reaction is facilitated by changes in the shape of the enzyme complex that are induced by the flow of hydrogen ions.

How much ATP energy is produced from a molecule of NADH or a molecule of $FADH_2$ by oxidative phosphorylation? The electrons from molecules of NADH enter

the electron-transport chain at complex I, while those from $FADH_2$ enter at complex II. These different entry points into the electron-transport chain result in different yields of ATP molecules. In this book, we use the yields of three ATP molecules generated for every NADH molecule and two ATP molecules generated from every $FADH_2$ molecule during oxidative phosphorylation.

PROBLEM 21.17

Within the mitochondrion, is the pH higher in the intermembrane space or in the mitochondrial matrix? Why?

PROBLEM 21.18

Plants carry out both photosynthesis and oxidative phosphorylation (see the Chemistry in Action "Plants and Photosynthesis" on p. 696). Photosynthesis occurs in chloroplasts, while oxidative phosphorylation occurs in mitochondria. Name some similarities and some differences between photosynthesis and oxidative phosphorylation.

KEY CONCEPT PROBLEM 21.19

The reduced coenzymes NADH and $FADH_2$ are oxidized in the ETS. What is the final electron acceptor of the ETS? What is the function of the H^+ ion in ATP synthesis?

CHEMISTRY IN ACTION

Metabolic Poisons

Cyanide and barbiturates such as sodium amytal have long been known to be so dangerous—even fatal—that mystery writers often use these substances in their books as murder weapons. What makes them so dangerous? They are among a group of substances that block respiration (oxidative phosphorylation) at one of the electron transfer stages, resulting in blockage of electron flow through the ETS and cessation of ATP production. Blockers interfere with electron transfer in several ways. Barbiturates act as reversible inhibitors while inorganic ions like CN^- (cyanide) and HS^- bind tightly to Fe^{2+} and Cu^{2+} in cytochromes acting as irreversible inhibitors and preventing electron transfer. CO and CN^- bind to the heme groups present in cytochromes preventing electron transfer in mitochondria. Blocking of electron transport is an emergency for the organism. Because ATP is not stored, continuous production of ATP at tightly regulated levels is crucial to an organism's survival. ATP is the energy link between the oxidation of fuels and energy-requiring processes. Without continuous ATP production, the organism will die.

A second category of molecules act as uncouplers of electron transport. These molecules allow electron transport to occur but prevent the conversion of ADP to ATP by ATP synthase. If this happens, the rate of oxygen use increases as the proton gradient between the mitochondrial matrix and the intermembrane space dissipates, with the simultaneous formation of water but no ATP.

When ATP production is severed from energy use, we say ATP production is *uncoupled* from the energy of the proton gradient. One chemical that has this effect, once used as a weight-reducing drug is 2,4-dinitrophenol (DNP). Occupational exposure in a munitions factory during World War I led to the first deaths from DNP.

However, during the 1930's DNP, available as an over-the-counter drug, was used as a weight-loss aid. Yes, indeed, taking DNP resulted in rapid weight loss without dieting. It seemed to be the ideal weight-loss aid. But, DNP ingestion also results in an increase in body temperature to fever levels, sweating, shortness of breath, and rapid heart rate. Some users of DNP develop cataracts or skin lesions and animal studies suggest DNP is a carcinogen. Aside from these side effects, a major difficulty with DNP is that the toxic dose is very close to the therapeutic dose. Ingesting a toxic dose often results in death.

As a supplement and not a drug, DNP is not regulated by any government agency and is available for use. DNP is particularly popular with bodybuilders and athletes with a recent increase in use and accidental abuse. Jasmine, the bodybuilder discussed at the beginning of the chapter, was sculpting her body for competition, using diet pills containing DNP in addition to exercise. When she increased the dosage for faster results, she ingested a lethal dose and the ER staff was unable to save her life.

CIA Problem 21.11 Why is DNP no longer recommended as a weight-loss aid?

CIA Problem 21.12 How does a blocker of respiration work?

CIA Problem 21.13 How does an uncoupler of respiration work?

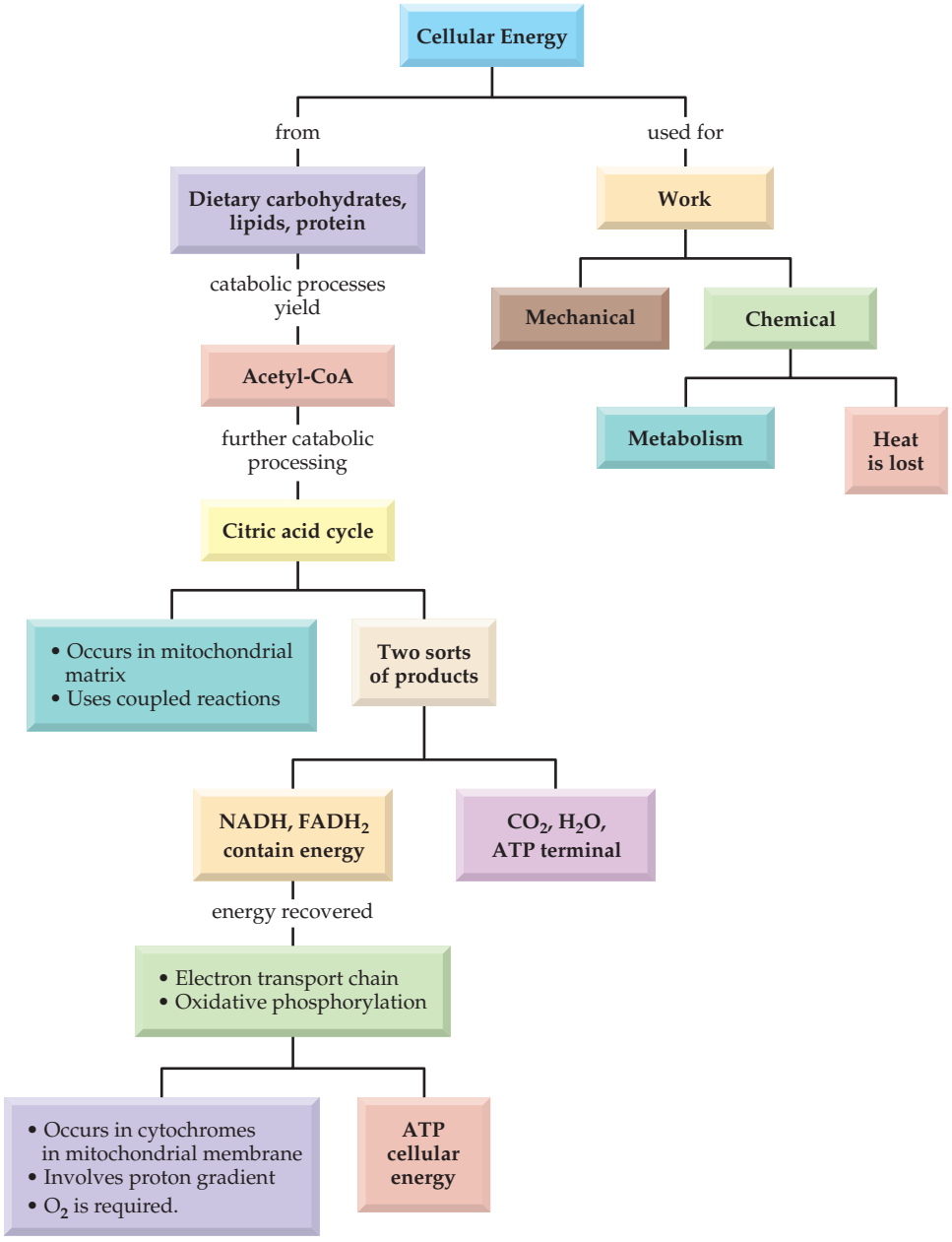
SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Identify energy sources and our specific requirements for energy regulation.** We derive energy by oxidation of food molecules that contain energy captured by plants from sunlight. The energy is released gradually in exergonic reactions and is available to do work, to drive endergonic reactions, to provide heat, or to be stored until needed. Energy generation in eukaryotic cells takes place in *mitochondria (see Problems 20, 27–32, and 76).*
- **Explain the significance of exergonic and endergonic reactions in metabolism.** *Exergonic* reactions are favorable, proceed spontaneously, and release free energy. *Endergonic* reactions are unfavorable and require an external source of free energy to occur *(see Problems 20 and 27–29).*
- **Describe the eukaryotic cell and explain the function of each structure.** The eukaryotic cell is a membrane-bound entity containing a number of specialized organelles in a nutrient- and protein-rich fluid called the cytosol. See Figure 21.2 *(see Problems 33–38).*
- **List the stages in catabolism of food and describe the role of each stage.** Food molecules undergo *catabolism* (are broken down) to provide energy in four stages (Figure 21.4): (1) digestion to form smaller molecules that can be absorbed into cells; (2) decomposition (by separate pathways for lipids, carbohydrates, and proteins) into two-carbon acetyl groups that are bonded to coenzyme A in *acetyl coenzyme A*; (3) reaction of the acetyl groups via the *citric acid cycle* to generate energy-rich reduced coenzymes and liberate carbon dioxide; and (4) *electron transport* and transfer of the energy of the reduced coenzymes from the citric acid cycle to our principal energy transporter, ATP *(see Problems 21 and 39–42).*
- **Describe the role of ATP in energy transfer.** Using the energy from exergonic reactions, ADP is *phosphorylated* to give ATP. Where energy must be expended, it is released by removal of a phosphoryl group from ATP to give back ADP *(see Problems 22, 43, and 44).*
- **Explain why some reactions are coupled and give an example of a coupled reaction.** An otherwise "uphill" reaction in a metabolic pathway is driven by coupling with an exergonic, "downhill" reaction that provides enough energy that their combined outcome is exergonic and favorable *(see Problems 45–48).*
- **Give an example of a coenzyme changing from oxidized to reduced form in a reaction and explain the purpose.** The oxidizing and reducing agents needed by the many redox reactions of metabolism are coenzymes that constantly cycle between their oxidized and reduced forms *(see Problems 23, 49, 50, 79, and 81).*
- **Describe the reactions in the citric acid cycle and explain its role in energy production.** The *citric acid cycle* (Figure 21.8) is a cyclic pathway of eight reactions, in which the product of the final reaction is the substrate for the first reaction. The reactions of the citric acid cycle (1) set the stage for oxidation of the acetyl group (steps 1 and 2); (2) remove two carboxyl groups as CO_2 molecules (oxidative decarboxylation) from the tricarboxylic acid isocitrate (steps 3 and 4); and (3) oxidize the 4-carbon dicarboxylic acid succinate and regenerate oxaloacetate so that the cycle can start again (steps 5–8). Along the way, four reduced coenzyme molecules and one molecule of GTP (converted immediately to ATP) are produced for each acetyl group oxidized. The reduced coenzymes carry energy for the subsequent production of additional ATP. The cycle is activated when energy is in short supply and inhibited when energy is in good supply *(see Problems 24, 25, 51–58, 77, and 78).*
- **Describe the electron-transport chain, oxidative phosphorylation, and how the two processes are coupled.** ATP generation is accomplished by a series of enzyme complexes in the inner membranes of mitochondria (Figure 21.9). Electrons and hydrogen ions enter the first two complexes of the electron-transport chain from succinate (in the citric acid cycle), NADH, and $FADH_2$, where they are transferred to *coenzyme Q*. Then, the electrons and hydrogen ions proceed independently; the electrons gradually give up their energy to the transport of hydrogen ions across the inner mitochondrial membrane to maintain different concentrations on opposite sides of the membrane. The hydrogen ions return to the matrix by passing through *ATP synthase,* where the energy they release is used to convert ADP to ATP *(see Problems 26, 59–75, and 80).*

KEY WORDS

Acetyl-coenzyme A (acetyl-CoA), *p. 699*
Adenosine triphosphate (ATP), *p. 697*
Anabolism, *p. 699*
ATP synthase, *p. 716*
Catabolism, *p. 698*
Citric acid cycle, *p. 709*
Cytoplasm, *p. 697*
Cytosol, *p. 697*
Electron-transport chain, *p. 714*
Guanosine diphosphate (GDP), *p. 710*
Guanosine triphosphate (GTP), *p. 710*
Metabolism, *p. 698*
Mitochondrial matrix, *p. 697*
Mitochondrion, *p. 697*
Oxidative phosphorylation, *p. 716*
Pathway, *p. 695*

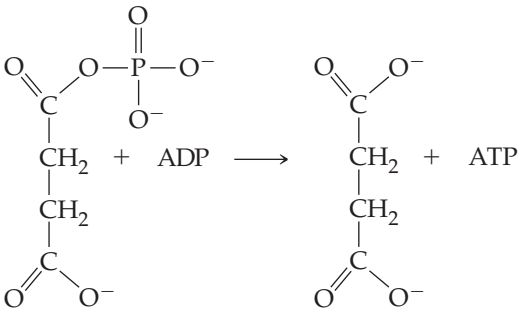
CONCEPT MAP: THE GENERATION OF BIOCHEMICAL ENERGY



▲ **Figure 21.12** **Concept Map.** This concept map shows both the uses and the sources of cellular energy by focusing on the generation of ATP from the total oxidation of acetyl-CoA through the citric acid cycle and recovery of the energy stored in the NADH and $FADH_2$ produced in the cycle. This energy is recovered by the ETS coupled with oxidative phosphorylation to yield ATP. All of these processes follow the principles of thermodynamics, which are connected to these concepts. The concept map above summarizes the ideas in this chapter and shows their connection to Figure 7.7 through thermodynamics.

UNDERSTANDING KEY CONCEPTS

21.20 The following coupled reaction is the result of an exergonic reaction and an endergonic reaction:



Succinyl phosphate Succinate

(a) Write the exergonic portion of the reaction.

(b) Write the endergonic portion of the reaction.

21.21 Each of these reactions is involved in one of the four stages of metabolism shown in Figure 21.4. Identify the stage in which each reaction occurs.

(a) Hydrolysis of starch to produce glucose

(b) Oxidation of NADH coupled with synthesis of ATP

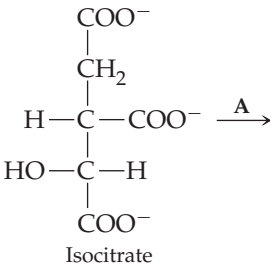
(c) Conversion of glucose to acetyl-CoA

(d) Oxidation of acetyl-CoA in a series of reactions where NAD^+ is reduced and CO_2 is produced

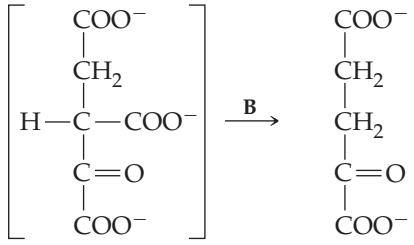
21.22 For the first step in fatty acid catabolism, we say that ATP is used to "drive" the reaction that links the fatty acid with coenzyme-A. Without ATP hydrolysis, would you predict that the linking of fatty acid to coenzyme-A would be exergonic or endergonic? In fatty acid CoA synthesis, the hydrolysis of the ATP portion is based on what major strategy of metabolism?

21.23 Since no molecular oxygen participates in the citric acid cycle, the steps in which acetyl groups are oxidized to CO_2 involve removal of hydride ions and hydrogen ions. What is the acceptor of hydride ions? What is the acceptor of hydrogen ions?

21.24 The reaction that follows is catalyzed by isocitrate dehydrogenase and occurs in two steps, the first of which (step A) is formation of an unstable intermediate (shown in brackets).



Isocitrate



α-Ketoglutarate

(a) In which step is a coenzyme needed? Identify the coenzyme.

(b) In which step is CO_2 evolved and a hydrogen ion added?

(c) Which of the structures shown can be described as a β-keto acid?

(d) To what class of enzymes does isocitrate dehydrogenase, the enzyme that catalyzes this reaction, belong?

21.25 For each of the eight reactions in the citric acid cycle, give the type of reaction occurring, name the enzyme involved, and indicate which of the six classes of enzymes it belongs to. Some may have more than one kind of enzyme activity.

21.26 The electron-transport chain uses several different metal ions, especially iron, copper, zinc, and manganese. Why are metals used frequently in these two pathways? What can metals do better than organic biomolecules?

ADDITIONAL PROBLEMS

FREE ENERGY AND BIOCHEMICAL REACTIONS (SECTION 21.1)

21.27 What energy requirements must be met in order for a reaction to be favorable?

21.28 What is the difference between an endergonic process and an exergonic process?

21.29 Why is ΔG a useful quantity for predicting the favorability of biochemical reactions?

21.30 Many biochemical reactions are catalyzed by enzymes. Do enzymes have an influence on the magnitude or sign of ΔG? Why or why not?

21.31 The following reactions occur during the catabolism of acetyl-CoA. Which are exergonic? Which is endergonic? Which reaction produces a phosphate that later yields energy by giving up a phosphate group?

(a) Succinyl-CoA + GDP + Phosphate $(P_i) \rightarrow$ Succinate + CoA-SH + GTP + H_2O
$\Delta G = -1.67$ kJ/mol

(b) Acetyl-CoA + Oxaloacetate $\rightarrow$ Citrate + CoA-SH
$\Delta G = -33.5$ kJ/mol

(c) L-Malate + $NAD^+ \rightarrow$ Oxaloacetate + NADH + H^+
$\Delta G = +29.7$ kJ/mol

21.32 The following reactions occur during the catabolism of glucose. Which are exergonic? Which is endergonic? Which proceeds farthest toward products at equilibrium?

(a) 1,3-Biphosphoglycerate + $H_2O \rightarrow$ 3-Phosphoglycerate + P_i
$\Delta G = -49.4$ kJ/mol

(b) Phosphoenol pyruvate + $H_2O \rightarrow$ Pyruvate + Phosphate (P_i)
$\Delta G = -61.9$ kJ/mol

(c) Glucose + $P_i \rightarrow$ Glucose 6-phosphate + H_2O
$\Delta G = +13.8$ kJ/mol

CELLS AND THEIR STRUCTURE (SECTION 21.2)

21.33 Which of the following organisms are prokaryotes, and which are eukaryotes?

(a) Humans

(b) The bacteria responsible for "strep throat"

(c) Carrots

(d) Brewer's yeast

21.34 Label each of the following as a characteristic of a prokaryote or a eukaryote.

(a) DNA is surrounded by a membrane

(b) Has a cell wall as well as a cell membrane

(c) Contains chloroplasts

(d) Lives in specialized groups termed organs

(e) Single-celled organisms

21.35 What is the difference between the cytoplasm and the cytosol?

21.36 What is an organelle?

21.37 Describe in general terms the structural makeup of a mitochondrion.

21.38 What is the function of cristae in the mitochondrion?

METABOLISM (SECTION 21.3)

21.39 What is the difference between catabolism and anabolism?

21.40 What is the difference between digestion and metabolism?

21.41 Arrange the following events in the order in which they occur in a catabolic process: electron transport, digestion, oxidative phosphorylation, citric acid cycle.

21.42 What key metabolic intermediate is formed from the catabolism of all three major classes of foods: carbohydrates, lipids, and proteins?

METABOLISM (SECTIONS 21.4–21.6)

21.43 Why is ATP sometimes called a high-energy molecule?

21.44 What general kind of chemical reaction does ATP participate in?

21.45 What does it mean when we say that two reactions are coupled?

21.46 Show why coupling the reaction for the hydrolysis of 1,3-bisphosphoglycerate to the phosphorylation of ADP is energetically favorable. Combine the equations and calculate ΔG for the coupled process. You need only give names or abbreviations in your equations not chemical structures.

21.47 Write the reaction for the hydrolysis of 1,3-bisphosphoglycerate coupled to the phosphorylation of ADP using the curved-arrow symbolism.

21.48 Is the hydrolysis of fructose 6-phosphate favorable for phosphorylating ADP? Why or why not? Refer to Table 21.1. If not, what would make this reaction favorable?

21.49 FAD is a coenzyme for dehydrogenation.

(a) When a molecule is dehydrogenated, is FAD oxidized or reduced?

(b) Is FAD an oxidizing agent or a reducing agent?

(c) What type of substrate is FAD associated with, and what is the type of product molecule after dehydrogenation?

(d) What is the form of FAD after dehydrogenation?

(e) Use the curved-arrow symbolism to write a general equation for a reaction involving FAD.

21.50 NAD^+ is a coenzyme for dehydrogenation.

(a) When a molecule is dehydrogenated, is NAD^+ oxidized or reduced?

(b) Is NAD^+ an oxidizing agent or a reducing agent?

(c) What type of substrate is NAD^+ associated with, and what type of product molecule is formed after dehydrogenation?

(d) What is the form of NAD^+ after dehydrogenation?

(e) Use the curved-arrow symbolism to write a general equation for a reaction involving NAD^+.

THE CITRIC ACID CYCLE (SECTION 21.7)

21.51 What is the purpose of the citric acid cycle?

21.52 Where in the cell does the citric acid cycle take place?

21.53 What substance acts as the starting point of the citric acid cycle, reacting with acetyl-CoA in the first step and being regenerated in the last step? Draw its structure.

21.54 What is the final fate of the carbons in acetyl-CoA after several turns of the citric acid cycle?

21.55 Look at the eight steps of the citric acid cycle (Figure 21.8) and answer the following questions:

(a) Which steps involve oxidation reactions?

(b) Which steps involve decarboxylation (loss of CO_2)?

(c) Which step or steps involve a hydration reaction?

21.56 How many NADH and how many $FADH_2$ molecules are formed in the citric acid cycle?

21.57 Which reactions of the citric acid cycle transfer energy as $FADH_2$?

21.58 Which reactions of the citric acid cycle transfer energy as NADH?

THE ELECTRON-TRANSPORT CHAIN; OXIDATIVE PHOSPHORYLATION (SECTION 21.8)

21.59 What are the two primary functions of the electron-transport chain?

21.60 How are the processes of the citric acid cycle and the electron-transport chain interrelated?

21.61 What two coenzymes are involved with initial events of the electron-transport chain?

21.62 What are the ultimate products of the electron-transport chain?

21.63 Where are the following found in the cell?

(a) FAD

(b) CoQ

(c) $NADH/H^+$

(d) Cytochrome c

21.64 What do the following abbreviations stand for?

(a) FAD

(b) CoQ

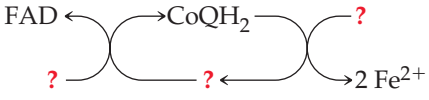
(c) $NADH/H^+$

(d) Cytochrome c

21.65 What atom in the cytochromes undergoes oxidation and reduction in the electron-transport chain? What atoms in coenzyme Q undergo oxidation and reduction in the electron-transport chain?

21.66 Put the following substances in the correct order of their action in the electron-transport chain: cytochrome *c*, coenzyme Q, and NADH.

21.67 Fill in the missing substances in these coupled reactions:



21.68 What would happen to the citric acid cycle if NADH and $FADH_2$ were not reoxidized?

21.69 What does the term "oxidative phosphorylation" mean? What is substrate-level phosphorylation? Are these processes the same? Explain.

21.70 In oxidative phosphorylation, what is oxidized and what is phosphorylated?

21.71 Oxidative phosphorylation has three reaction products.

(a) What is the energy-carrying product?

(b) What are the other two products?

21.72 What supplies the energy to drive oxidative phosphorylation?

21.73 The antibiotic piericidin, a nonpolar molecule, is structurally similar to ubiquinone (coenzyme Q) and can cross the mitochondrial membrane. What effect might the presence of piericidin have on oxidative phosphorylation?

21.74 When oxidative phosphorylation is uncoupled, does oxygen consumption decrease, increase, or stay the same? Explain.

21.75 Which animal would you expect to have more brown fat (provides heat by uncoupling ATP production), a seal or a domestic cat? Explain.

CONCEPTUAL PROBLEMS

21.76 Why must the breakdown of molecules for energy in the body occur in several steps, rather than in one step?

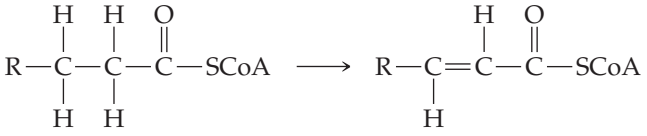
21.77 The first step in the citric acid cycle involves the reaction of acetyl-CoA and oxaloacetate. Show the product of this reaction before hydrolysis to yield citrate.

21.78 Fumarate produced in step 6 of the citric acid cycle must have a *trans* double bond to continue on in the cycle. Suggest a reason why the corresponding *cis* double-bond isomer cannot continue in the cycle.

21.79 With what class of enzymes are the coenzymes NAD^+ and FAD associated?

21.80 We talk of burning food in a combustion process, producing CO_2 and H_2O from food and O_2. Explain how O_2 is involved in the process although no O_2 is directly involved in the citric acid cycle.

21.81 One of the steps that occurs when lipids are metabolized is shown here. Does this process require FAD or NAD^+ as the coenzyme? What is the general class of enzyme that catalyzes this process?



21.82 If you use a flame to burn a pile of glucose completely to give carbon dioxide and water, the overall reaction is identical to the metabolic oxidation of glucose. Explain the differences in the fate of the energy released in each case.

21.83 The mitochondrion pumps H^+ from the matrix into the intermembrane space. Which region is more acidic, the matrix or the intermembrane space? Why?

21.84 Does any step of the citric acid cycle directly produce ATP? Explain.

21.85 The citric acid cycle contains four 4-carbon dicarboxylic acids.

(a) Name them.

(b) Arrange them in order from least oxidized to most oxidized.

21.86 Sometimes, ATP is referred to as the "energy-storage molecule." The cell does not actually store energy as a lot of extra ATP but as glycogen or triacylglycerides. Why do you suppose this is the case?

GROUP PROBLEMS

21.87 Sodium fluoroacetate ($FH_2CCOO^-\ Na^+$) is highly toxic. Patients with fluoroacetate poisoning accumulate citrate and fluorocitrate in their cells. Which enzyme is inhibited by fluoroacetate for this to occur? Explain.

21.88 After running 1.5 kilometers, you stop and breathe heavily for a short period due to oxygen debt. Why do you need to breathe so heavily? (Hint: Look up "oxygen debt" on the Web. Which metabolic pathway requires oxygen?)

21.89 Put in order, from lowest to highest number of mitochondria per cell, the following tissues: adipose tissue (regular), brain, heart muscle, skin, skeletal muscle. Explain your reasoning. You may need to consult the Web.

22

Carbohydrate Metabolism

CONTENTS

CONCEPTS TO REVIEW

A. Phosphorylation (Section 17.6)
B. Function of ATP (Sections 21.4 and 21.8)
C. Oxidized and Reduced Coenzymes (Section 21.6)
D. Carbohydrate Structure (Chapter 20)
E. Enzymes (Chapter 19)

▲ The simple and complex carbohydrates in this meal provide fuel for metabolism.

Maria, age 40 years, has a doctor's appointment because she has been feeling somewhat ill for several months. In addition, she sometimes feels confused, is often thirsty despite adequate fluid intake, and urinates more frequently. One day, while grocery shopping, she realizes her vision is so blurry she cannot read the package labels. Her doctor does a typical exam, noting that Maria is overweight for her height (body mass index [BMI] = 30) and has elevated blood pressure. There is a history of heart disease and

diabetes in her family. Her doctor orders a typical blood panel that includes measuring glucose, cholesterol, and triacylglycerides, as well as enzymes that reflect liver and kidney function. He also orders a glucose tolerance test, an A1C test, which measures the amount of glycated hemoglobin (an indicator of blood glucose levels over several months), and schedules a return visit. He suspects Type II diabetes because of her age and symptoms but must have the test results to confirm it. Type II diabetes more commonly develops in middle age.

Diabetes is a common consequence of faulty glucose metabolism regulation. During carbohydrate metabolism, glucose is converted to acetyl-coenzyme A (acetyl-CoA) for entrance into citric acid cycle. Any excess glucose is stored as glycogen and released for use when glucose is in short supply. Because of the importance of glucose, the body has several strategies for regulating the glucose concentration in blood and providing glucose to cells that depend on it. This chapter discusses those strategies and carbohydrate metabolism as a whole.

22.1 Digestion of Carbohydrates

Learning Objective:

- Describe carbohydrate digestion, where it takes place in the body, the enzymes involved, and name the major products of the process.

The first stage in catabolism is **digestion,** the breakdown of food into small molecules. Digestion entails the physical grinding, softening, and mixing of food, as well as enzyme-catalyzed hydrolysis of carbohydrates, proteins, and fats. Digestion begins in the mouth, continues in the stomach, and concludes in the small intestine.

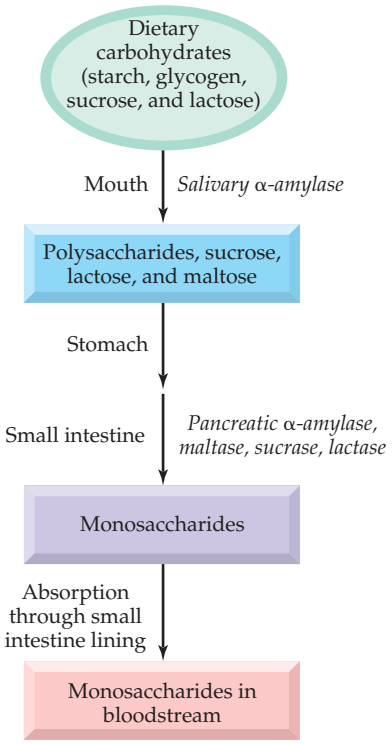
The products of digestion are mostly small molecules that are absorbed from the intestinal tract. Nutrients are absorbed through millions of tiny projections (the *villi*) in the intestinal lining and transferred into the bloodstream. The bloodstream transports these small molecules into target cells, where they may be broken down completely to release energy as their carbon atoms are converted to carbon dioxide. Others are excreted, and some are used as building blocks to synthesize new biomolecules.

The digestion of carbohydrates is summarized in Figure 22.1. Salivary α-amylase catalyzes the hydrolysis of α glycosidic bonds in amylose and amylopectin—plant starches. Starches from plants and glycogen from meat are hydrolyzed to give smaller polysaccharides and the disaccharide maltose. Plant cellulose, with its β glycosidic bonds linking glucose molecules together, is not digested by humans. Salivary α-amylase continues to act upon dietary polysaccharides in the stomach until the enzyme is inactivated by stomach acid. No further carbohydrate digestion takes place in the stomach.

α-Amylase is also secreted by the pancreas and enters the small intestine, where conversion of polysaccharides to maltose continues. Maltase, sucrase, and lactase are secreted from the mucous lining of the small intestine and hydrolyze maltose, sucrose, and lactose to the monosaccharides glucose, fructose, and galactose, which are transported across the intestinal wall into the bloodstream. The focus in this chapter is on the metabolism of glucose; both fructose and galactose can be converted to intermediates that enter the same metabolic pathway followed by glucose.

Digestion A general term for the breakdown of food into small molecules.

CONCEPTS TO REVIEW Recall from Section 20.7 that the plant starches amylose and amylopectin, plant cellulose, and glycogen (animal starch) are all large polymers of glucose. Plant starches and glycogen are digestible, whereas cellulose is not.



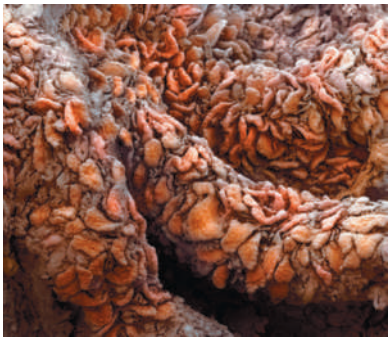
▲ **Figure 22.1**
The digestion of carbohydrates.

22.2 Glucose Metabolism: An Overview

Learning Objective:

- Identify the pathways by which glucose is first synthesized and then broken down, and describe their interrelationships.

Glucose is the major fuel for your body. It is the preferred fuel for the brain, working muscle cells, and red blood cells. Through a series of metabolic oxidations, the energy stored in glucose is converted to ATP energy and used to power other reactions within the cell. The initial metabolic fate of glucose is conversion into pyruvate and then usually to acetyl-CoA, the common intermediate in the catabolism of all foods. Acetyl-CoA delivers



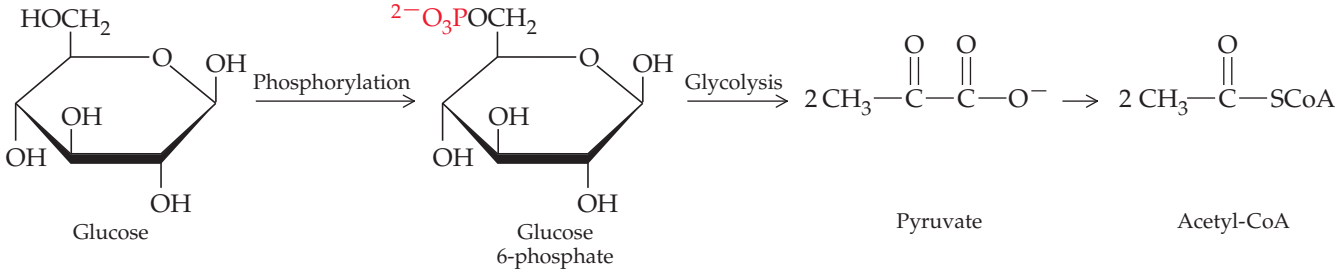
▲ A micrograph showing *villi,* the projections that line the small intestine. Each villus is covered with microvilli, where the digested food molecules are absorbed into the bloodstream.

acetyl groups to the citric acid cycle for oxidation, with the energy captured transferred through the electron transport system, resulting ultimately in the formation of ATP. We discussed the citric acid cycle and the electron transport chain in Chapter 21.

Glycolysis is the first of two sequential, catabolic pathways leading to ATP synthesis as a result of electron transfer. When glucose enters a cell from the bloodstream, it is immediately converted to glucose 6-phosphate. Once phosphorylated, glucose is trapped within the cell because phosphorylated molecules cannot cross the cell membrane unaided by a transporter. Like the first step in many metabolic pathways, the formation of glucose 6-phosphate is highly exergonic and not reversible in the glycolytic pathway, thereby committing the initial substrate to the subsequent reactions.

Several pathways are available to glucose 6-phosphate.

- When energy is needed, glucose 6-phosphate moves down the central catabolic pathway shown in light brown in Figure 22.2, proceeding via the reactions of *glycolysis* to pyruvate and then to acetyl-CoA, which enters the citric acid cycle (discussed in Section 21.7).



- When cells are well supplied with glucose, excess glucose is converted to other forms for storage: into glycogen, the glucose storage polymer, by the *glycogenesis* pathway, or into fatty acids by entrance of acetyl-CoA into the pathways of lipid metabolism (Chapter 24) rather than the citric acid cycle.
- Glucose 6-phosphate can also enter the **pentose phosphate pathway.** This multistep pathway yields two products important to our metabolism. One is a supply of the coenzyme nicotinamide adenine dinucleotide phosphate (NADPH), a reducing agent that is essential for many biochemical reactions. The other is ribose 5-phosphate, which is the precursor for the synthesis of nucleic acids (deoxyribonucleic acid [DNA] and ribonucleic acid [RNA]). Glucose 6-phosphate enters the pentose phosphate pathway when a cell's need for NADPH or ribose 5-phosphate exceeds its need for ATP.

Pentose phosphate pathway The biochemical pathway that produces ribose (a pentose), NADPH, and other sugar phosphates from glucose; an alternative to glycolysis.

PROBLEM 22.1

Name the following pathways:

(a) Pathway for synthesis of glycogen

(b) Pathway for release of glucose from glycogen

(c) Pathway for synthesis of glucose from lactate

PROBLEM 22.2

Name the synthetic pathways that have glucose 6-phosphate as their first reactant.

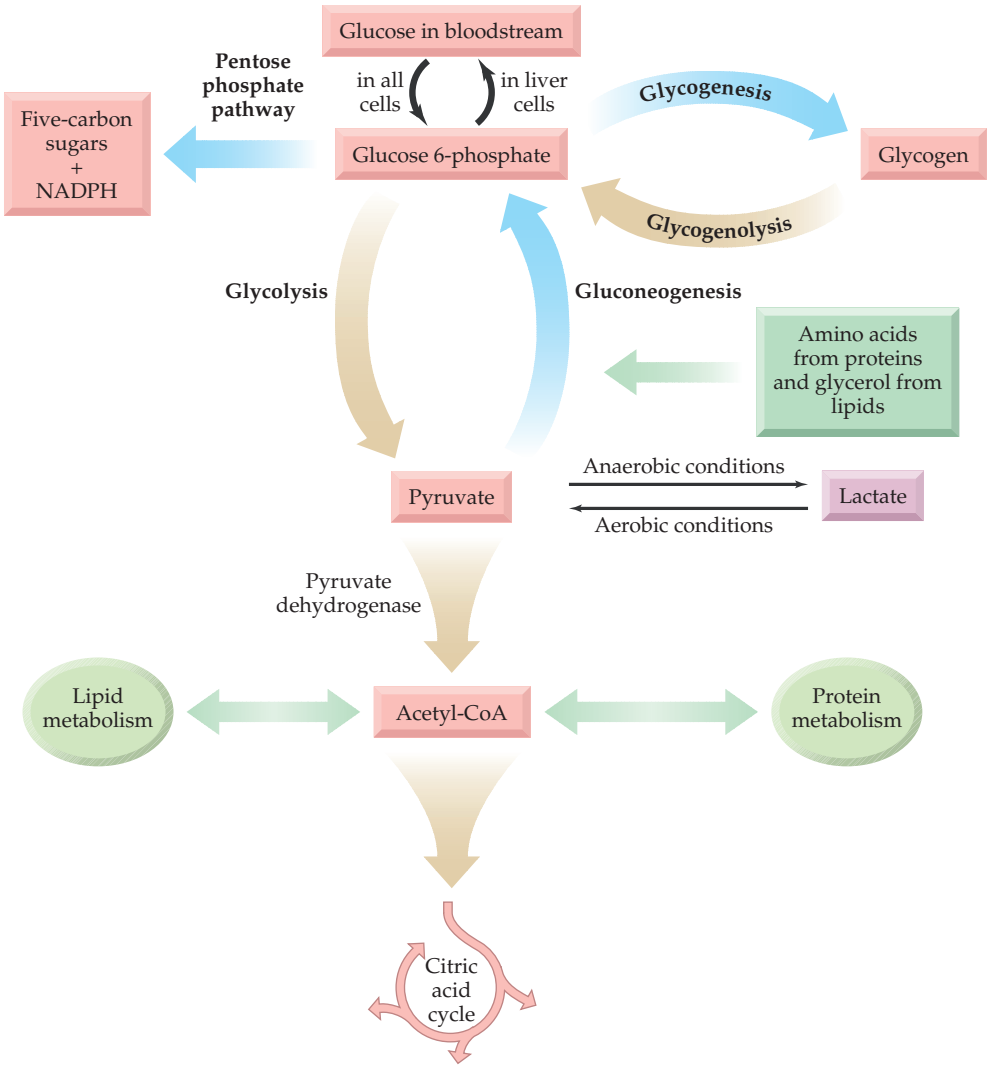
22.3 Glycolysis

Learning Objective:

- Describe the glycolysis pathway and its products.

Glycolysis The biochemical pathway that breaks down a molecule of glucose into two molecules of pyruvate plus energy.

Glycolysis is a series of 10 enzyme-catalyzed reactions that converts a glucose molecule into two pyruvate molecules and in the process yields two ATP molecules and two NADH molecules. The steps of glycolysis are summarized in Figure 22.3, where the reactions and structures of intermediates should be noted as you read the following paragraphs. Almost all organisms carry out glycolysis; in humans it occurs in the cytosol of all cells.



◀ **Figure 22.2**
Glucose metabolism.
Synthetic pathways (anabolism) are shown in blue, pathways that break down biomolecules (catabolism) are shown in light brown, and connections to lipid and protein metabolism are shown in green.

Metabolic Pathways of Glucose

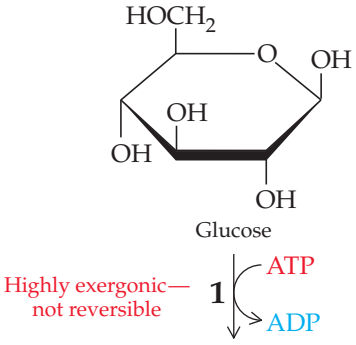
Name	Derivation of Name	Function
Glycolysis (Section 22.3)	*glyco-*, glucose (from Greek, meaning "sweet") *-lysis*, decomposition	Conversion of glucose to pyruvate
Gluconeogenesis (Section 22.9)	*gluco-*, glucose *-neo-*, new *-genesis*, creation	Synthesis of glucose from amino acids, pyruvate, and other noncarbohydrates
Glycogenesis (Section 22.8)	*glyco(gen)-*, glycogen *-genesis*, creation	Synthesis of glycogen from glucose
Glycogenolysis (Section 22.8)	*glycogen-*, glycogen *-lysis*, decomposition	Breakdown of glycogen to glucose
Pentose phosphate pathway (Section 22.2)	*pentose-*, a five-carbon sugar	Conversion of glucose to five-carbon sugar phosphates

Steps 1–5 are referred to as the *energy investment* part of glycolysis. So far, two ATP molecules have been invested and no income earned, but the stage is now set for a small energy profit. Note that since one glucose molecule yields two glyceraldehyde 3-phosphate molecules that pass separately down the rest of the pathway, steps 6–10 of glycolysis each take place twice for every glucose molecule that enters at step 1. *Energy generation,* the second half of glycolysis (steps 6–10) is devoted to generating molecules with phosphate groups that can be transferred to ATP.

◀◀ Phosphorylation is the transfer of a phosphoryl group ($-PO_3^{2-}$) from one molecule to another (see Section 17.6).

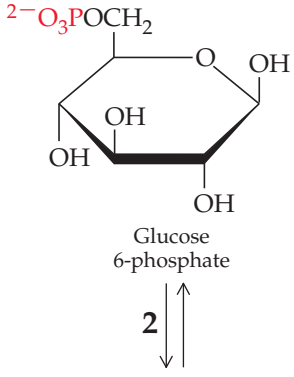
◀◀ Review enzyme regulation by allosteric control in Section 19.7.

Energy Investment Steps in Glycolysis



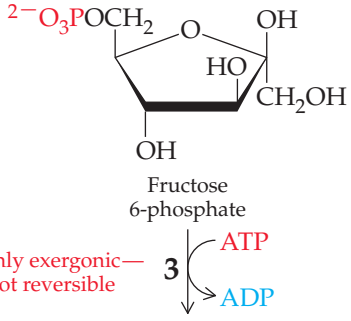
Step 1. Phosphorylation

STEP 1: Phosphorylation Glucose is carried in the bloodstream to cells, where it is transported across the cell membrane into the cytosol. As soon as glucose enters the cell, it is phosphorylated in step 1 of glycolysis, which requires energy investment from ATP. This is the first highly exergonic, irreversible step in glycolysis. The product of step 1, glucose 6-phosphate, is an allosteric inhibitor for the enzyme for this step (*hexokinase*). This is the first control point for glycolysis.



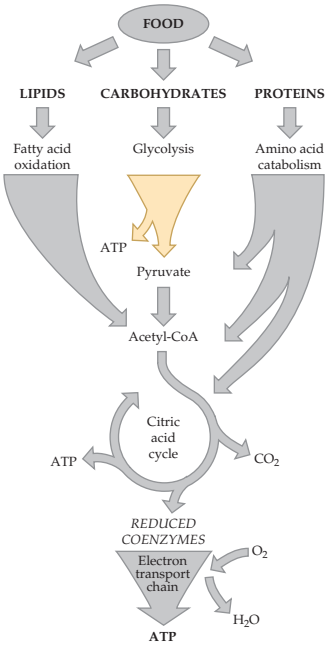
Step 2. Isomerization

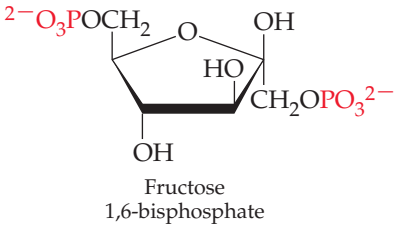
STEP 2: Isomerization The enzyme *glucose 6-phosphate isomerase* converts glucose 6-phosphate (an aldohexose) to fructose 6-phosphate (a ketohexose). This conversion of a six-membered glucose ring to a five-membered ring with a —CH_2OH group prepares the molecule for addition of another phosphoryl group in the next step.



Step 3. Phosphorylation

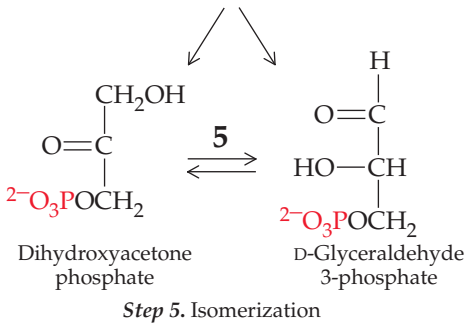
STEP 3: Phosphorylation A second energy investment is made as *phosphofructokinase* converts fructose 6-phosphate to fructose 1,6-bisphosphate by reaction with ATP in an exergonic reaction. This irreversible reaction is another major control point for glycolysis. When the cell is short of energy, adenosine diphosphate (ADP) and adenosine monophosphate (AMP) concentrations build up and activate the step 3 enzyme, *phosphofructokinase*. When energy is in good supply, ATP and citrate build up and allosterically inhibit this enzyme. The outcome of steps 1–3 is the formation of a molecule ready to be split into the two 3-carbon intermediates that will ultimately become two molecules of pyruvate.





Step 4. Cleavage

STEP 4: Cleavage *Aldolase* catalyzes cleavage of the bond between carbons 3 and 4 in fructose 1,6-bisphosphate. The products of this reversible reaction are dihydroxyacetone phosphate and glyceraldehyde 3-phosphate. Only glyceraldehyde 3-phosphate can be used to generate energy, but these two 3-carbon sugar phosphates are interconvertible in an aldose–ketose equilibrium.

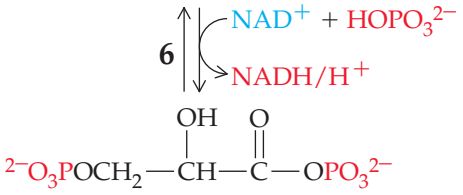


Step 5. Isomerization

STEP 5: Isomerization *Triose phosphate isomerase* catalyzes the conversion of dihydroxyacetone phosphate to glyceraldehyde 3-phosphate. As glyceraldehyde 3-phosphate reacts in step 6, the equilibrium of step 5 shifts to the right. The overall result of steps 4 and 5 is therefore the production of *two* molecules of glyceraldehyde 3-phosphate.

Energy Generation Steps in Glycolysis

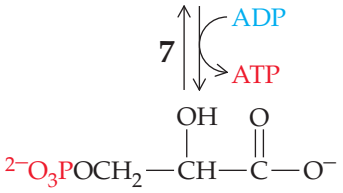
STEP 6: Oxidation Glyceraldehyde 3-phosphate from both steps 4 and 5 is oxidized to 1,3-bisphosphoglycerate by *glyceraldehyde 3-phosphate dehydrogenase*. The enzyme cofactor NAD^+ is the oxidizing agent for this reaction. Some of the energy from the exergonic oxidation is captured in NADH, and some is used in forming the phosphate. This is the first energy-generating step of glycolysis.



1,3-Bisphosphoglycerate

Step 6. Oxidation and Phosphorylation

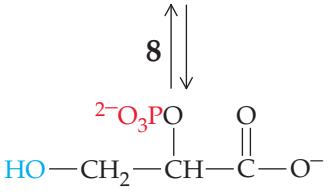
STEP 7: Phosphorylation *Phosphoglycerate kinase* transfers a phosphate group from 1,3-bisphosphoglycerate to ADP. The products of the reaction are 3-phosphoglycerate and ATP, the first ATP generated by glycolysis. Because this step occurs twice for each glucose molecule, the ATP-energy balance sheet in glycolysis is even after step 7. Two ATP molecules were spent in steps 1–5, and now they have been replaced.



3-Phosphoglycerate

Step 7. Phosphate Transfer

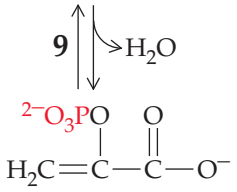
STEP 8: Isomerization *Phosphoglycerate mutase* catalyzes the isomerization of 3-phosphoglycerate to 2-phosphoglycerate. This rearrangement is necessary for the next step.



2-Phosphoglycerate

Step 8. Isomerization

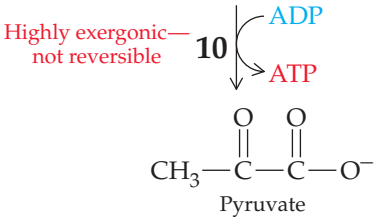
STEP 9: Dehydration *Enolase* catalyzes the dehydration of 2-phosphoglycerate to phosphoenolpyruvate, the second energy-providing phosphate of glycolysis. Water is the other product of this reaction.



Phosphoenolpyruvate

Step 9. Dehydration

STEP 10: Phosphate Transfer *Pyruvate kinase* transfers a phosphate group from phosphoenolpyruvate to ADP forming pyruvate and ATP in a highly exergonic, irreversible reaction. The production of ATP by transfer of a phosphate group to ADP from another molecule is called *substrate-level phosphorylation*.



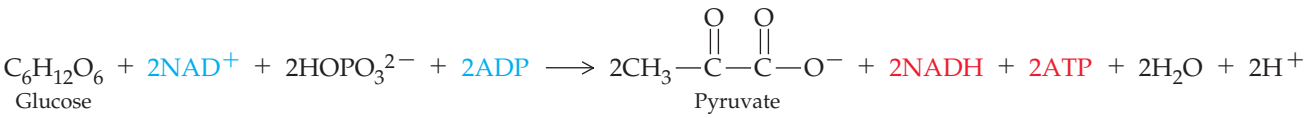
Pyruvate

Step 10. Phosphate Transfer

▲ Figure 22.3
The glycolysis pathway for converting glucose to pyruvate.

The two ATP molecules formed by the reactions in step 10 are pure profit, and the overall results of glycolysis are as follows:

Net result of glycolysis



- Conversion of glucose to two pyruvate molecules
- Net production of two ATP molecules
- Production of two molecules of reduced coenzyme NADH from NAD^+

Worked Example 22.1 Relating Enzyme Names with Reaction Steps of Glycolysis

How do the names of the enzymes involved in the first two steps of glycolysis relate to the reactions involved?

ANALYSIS Look at the names of the enzymes and the reactions. Also recall the enzyme classification scheme from Chapter 19 (Table 19.4).

SOLUTION

In the first reaction, a phosphoryl group is added to glucose. The enzyme name is hexokinase; *kinase* because kinases transfer phosphoryl groups and *hexo-* for a hexose sugar as the substrate. In the second reaction, glucose 6-phosphate is rearranged to fructose 6-phosphate by phosphoglucose isomerase. This enzyme belongs to the enzyme class of isomerases, enzymes that rearrange molecules to an isomer of the original molecule. The phosphoglucose part of the name tells us that a phosphorylated glucose molecule will be rearranged; inspection of the reaction shows that this is true.

PROBLEM 22.3

There are two sets of reactions in glycolysis in which phosphate intermediates are synthesized in the first reaction and their energy harvested as ATP in the second reaction. Identify the two sets of reactions.

PROBLEM 22.4

Identify each step in glycolysis that is an isomerization.

PROBLEM 22.5

Verify the isomerization that occurs in step 2 of glycolysis by drawing the open-chain forms of glucose 6-phosphate and fructose 6-phosphate.

KEY CONCEPT PROBLEM 22.6

In Figure 22.3, compare the starting compound (glucose) and the final product (pyruvate).

(a) Which is oxidized to a greater extent?

(b) Are there any steps in the glycolytic pathway in which an oxidation or reduction occurs? Identify the oxidizing or reducing agents that are involved in these steps.

22.4 Entry of Other Sugars into Glycolysis

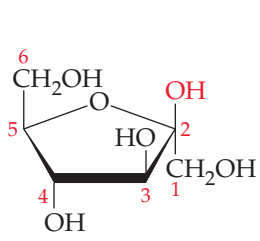
Learning Objective:

- Identify where the major monosaccharides enter glycolysis.

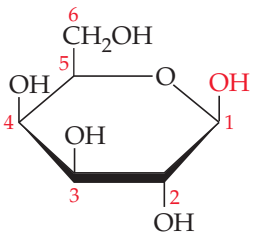
Glucose is not the only monosaccharide that our bodies metabolize. The other major monosaccharides from digestion—fructose, galactose, and mannose—eventually join the glycolysis pathway. Like glucose, these sugars are also metabolized by the bacteria that populate our mouths and digestive systems. The effect of dietary sugars on dental health is explored in the Chemistry in Action "Tooth Decay."

Fructose, from fruits or hydrolysis of the disaccharide sucrose, is converted to glycolysis intermediates in two ways: in muscle cells, it is phosphorylated to fructose 6-phosphate by hexosekinase, and in liver cells, it is converted to glyceraldehyde 3-phosphate. Fructose 6-phosphate is the substrate for step 3 of glycolysis; glyceraldehyde 3-phosphate is the substrate for step 6.

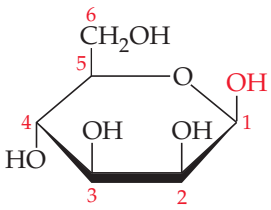




D-Fructose



D-Galactose



D-Mannose

▲ Major dietary monosaccharides other than glucose.

Galactose from hydrolysis of the disaccharide lactose is converted to glucose 6-phosphate, the substrate for step 2 of glycolysis, by a five-step pathway that begins with galactokinase. A hereditary defect affecting any enzyme in this pathway can cause galactosemia (see Table 20.1).

CHEMISTRY IN ACTION

Tooth Decay

Tooth decay is a complex interaction between food, bacteria, and your body. The clinical term for tooth decay is *dental caries.* Dentists recognize it as an infectious microbial disease that results in the destruction of the calcified structures of the teeth.

The mouth is home to many different species of bacteria. Two permanent bacterial residents of the oral cavity, *Streptococcus sanguis* and *Streptococcus mutans,* compete for the same habitat on the biting surfaces of the teeth. *Dental plaque,* bacterial aggregations on the teeth that cannot be removed by a strong water spray, begin to form again immediately after plaque has been removed. First, a coating of organic material composed of glycoproteins from the saliva begins to form; then bacteria quickly colonize this film and secrete a sticky matrix of an insoluble polysaccharide known as *dextran.* The mass of bacteria, their sticky matrix, and the glycoprotein film together comprise dental plaque. Plaque is, therefore, not simply adherent food debris but rather a community of microorganisms (known as a *biofilm*) that forms through an orderly sequence of events.

The bacteria resident in plaque release products consisting of proteins and carbohydrates. Some polysaccharides form intracellular granules that serve as energy storage depots for periods of low nutrient availability (between meals). Other products are toxic to the gums and can promote periodontal disease.

What our dentists and parents told us—that eating candy would create cavities—is true! A diet high in sucrose favors the growth of *S. mutans* over that of *S. sanguis.* Although both bacteria can cause tooth decay, *S. mutans* attacks teeth much more vigorously. It has an enzyme (a glucosyltransferase) that transfers glucose units from sucrose to the dextran polymer. The mature plaque community then metabolizes fructose from the sucrose to lactate, and this acid causes the local pH in the area of the tooth to drop dramatically. If the pH stays low enough for a long enough time, the minerals in the teeth are dissolved away and the tooth begins to decay. The disruption of plaque via oral hygiene and a diet low in sucrose favors the growth of *S. sanguis* over *S. mutans.* To control the decay process, it is necessary to limit both the amount of sucrose in the diet and the frequency with which it is ingested.

CIA Problem 22.1 What is the function of the insoluble polysaccharide known as dextran in the formation of dental plaque?

CIA Problem 22.2 Name four of the major components of dental plaque.

CIA Problem 22.3 How is dental plaque associated with periodontal disease?

CIA Problem 22.4 Explain the chemical process that leads to cavities after dental plaque has formed.

CIA Problem 22.5 Why is table sugar bad for your teeth? Would using honey instead be a better choice for tooth health?

Mannose is a product of the hydrolysis of plant polysaccharides other than starch. It is converted (by hexokinase) to mannose 6-phosphate, which then undergoes a multistep, enzyme-catalyzed rearrangement to fructose 6-phosphate in order to enter glycolysis as the substrate for step 3.

PROBLEM 22.7

Use curved arrows (like those in Figure 22.3) to write an equation for the conversion of fructose to fructose 6-phosphate by ATP. At what step does fructose 6-phosphate enter glycolysis?

PROBLEM 22.8

Compare glucose and galactose (see Table 20.1), and explain how their structures differ.

22.5 The Fate of Pyruvate

Learning Objective:

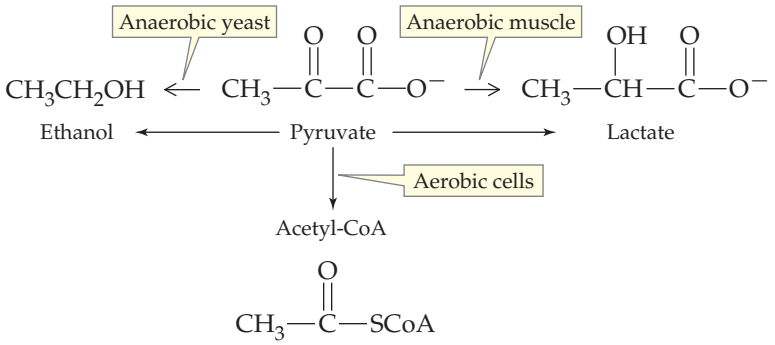
- Describe the pathways involving pyruvate and their respective outcomes.

Aerobic In the presence of oxygen.

Anaerobic In the absence of oxygen.

The conversion of glucose to pyruvate is a central metabolic pathway in most living systems. The further reactions of pyruvate, however, depend on metabolic conditions and the organism. Under normal oxygen-rich **(aerobic)** conditions, pyruvate is converted to acetyl-CoA in mammals. This pathway, however, is short-circuited in some tissues, especially when there is not enough oxygen present (**anaerobic** conditions). Under anaerobic conditions, pyruvate is instead reduced to lactate. When sufficient oxygen again becomes available, lactate is recycled back to pyruvate in muscle cells or to glucose via the Cori cycle in liver cells. A third pathway for pyruvate is conversion back to glucose by *gluconeogenesis,* which also occurs only in liver cells (we will discuss gluconeogenesis and the Cori cycle in Section 22.9). This pathway is essential when the body is starved for glucose. The pyruvate necessary for gluconeogenesis may come not only from glycolysis but also from amino acids or glycerol from lipids. Use of protein and lipid for glucose synthesis occurs when energy needed exceeds energy intake, as in starvation, certain diseases, and some carbohydrate-restricted diets.

Yeast is an organism with a different pathway for pyruvate; it converts pyruvate to ethanol under anaerobic conditions. Humans exploit this property of yeast in leavening bread and brewing beer. We use certain strains of the bacteria *Lactobacillus* and other bacteria, which convert pyruvate to lactate to produce yogurt, kimchee, and sauerkraut. In these and similar products, the lactate produced by these bacteria provide the familiar acidic tang and help preserve the food.

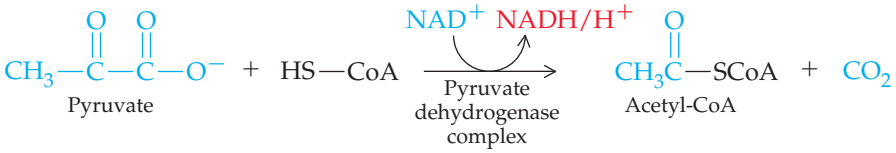


▲ The biochemical transformations of pyruvate.

Aerobic Oxidation of Pyruvate to Acetyl-CoA

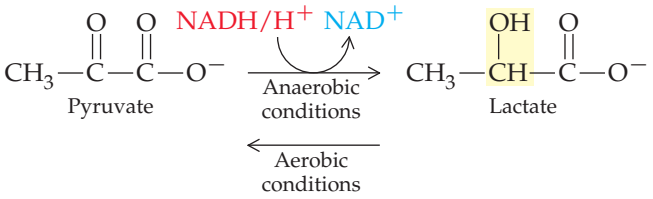
For aerobic oxidation to proceed, pyruvate first moves across the outer mitochondrial membrane from the cytosol where it was produced. Next, a transporter protein carries pyruvate across the otherwise impenetrable inner mitochondrial membrane. Once within the mitochondrial matrix, pyruvate encounters the *pyruvate dehydrogenase*

complex, a large multienzyme complex that catalyzes the conversion of pyruvate to acetyl-CoA, the substrate for the citric acid cycle. The other product of the reaction, CO_2 is exhaled.



Anaerobic Reduction to Lactate

In certain tissues, like muscle, under anaerobic conditions pyruvate is reduced to lactate instead of oxidized to acetyl-CoA. Since glycolysis is anaerobic, why should oxygen be necessary? It does not appear as part of the reaction. Note that for glycolysis to proceed, NAD^+ is necessary for step 6 (Figure 22.3). Under aerobic conditions, NADH is continually reoxidized to NAD^+ during electron transport (see Section 21.8); under anaerobic conditions, electron transport slows and so does the production of NAD^+. The reduction of pyruvate to lactate results in the oxidation of NADH to NAD^+, allowing glycolysis to continue. Lactate is oxidized to pyruvate by another pathway when oxygen is available.



Tissues where oxygen is in short supply also rely on the anaerobic production of ATP by glycolysis. Red blood cells have no mitochondria and thus must always form lactate as the end product of glycolysis. Other examples are the cornea of the eye, where there is little blood circulation, and muscles during intense activity. The resulting buildup of lactate in working muscles causes fatigue and discomfort (see the Chemistry in Action "The Biochemistry of Running" on p. 738).

Alcoholic Fermentation

Microorganisms often must survive in the absence of oxygen and thus have evolved numerous anaerobic strategies for energy production, generally known as **fermentation.** When pyruvate undergoes fermentation by yeast, it is converted into ethanol plus carbon dioxide. This process, known as **alcoholic fermentation,** is used to produce beer, wine, and other alcoholic beverages and also to make bread. The carbon dioxide causes the bread to rise, and the alcohol evaporates during baking.

Fermentation The production of energy under anaerobic conditions.

Alcoholic fermentation The anaerobic breakdown of glucose to ethanol plus carbon dioxide by the action of yeast enzymes.

Worked Example 22.2 Identifying Catabolic Stages

Complete oxidation of glucose produces six molecules of carbon dioxide. Describe the stage of catabolism at which each one is formed.

ANALYSIS Look at each stage of catabolism for the complete oxidation of glucose to carbon dioxide. Notice how many molecules of carbon dioxide are produced and by which step. Pathways to consider (in order) are glycolysis, conversion of pyruvate to acetyl-CoA, and the citric acid cycle. There is no need to consider oxidative phosphorylation because glucose is completely oxidized at the end of the citric acid cycle.

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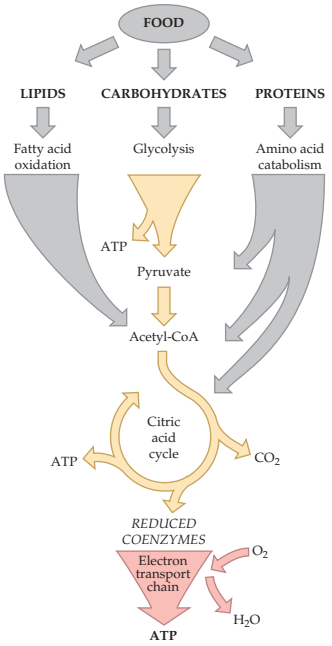
SOLUTION

No molecules of carbon dioxide are produced during glycolysis. Conversion of one molecule of pyruvate to one molecule of acetyl-CoA yields one molecule of carbon dioxide. In the citric acid cycle, two molecules of carbon dioxide are released for each molecule of acetyl-CoA oxidized. One is released in step 3 when isocitrate is converted to α-ketoglutarate and the other when α-ketoglutarate is converted to succinyl-CoA in Step 4. Since each glucose molecule produces two pyruvate molecules, the total is three molecules twice, or six molecules of carbon dioxide.



KEY CONCEPT PROBLEM 22.9

In alcoholic fermentation, each mole of pyruvate is converted to one mole of carbon dioxide and one mole of ethanol. In the process, about 209 kJ/mol of energy is produced. Under the most favorable conditions, more than one-half of this energy is stored as ATP.

(a) What happens to the remaining energy produced in alcoholic fermentation?

(b) Give two reasons why it would be nearly impossible to reverse the reaction that converts pyruvate to ethanol and carbon dioxide.

PROBLEM 22.10

Name three ways humans have exploited the ability of microorganisms to ferment carbohydrates.

PROBLEM 22.11

Pyruvate has three different fates. What are the three different molecules pyruvate is converted into? What conditions exist for the formation of each product?

HANDS-ON CHEMISTRY 22.1

Let's try a fermentation experiment. Look in a cookbook or on the web for a basic yeast bread recipe or buy a frozen, unbaked loaf. Obtain the ingredients and bake a loaf of bread. Observe how it rises—what makes that happen? Dissolve some yeast in water (cold and warm, separately) and observe what happens. What do you smell while the bread rises? While it bakes? If you let it rise too long, you may smell alcohol. Why did this happen?

If you do not have access to an oven, go to a bakery and see if you can find a really fresh bread sample. Or, try to make yogurt from milk and a bit of yogurt containing active cultures. Remember to be very clean with this procedure. Instructions can be found on the web.

22.6 Energy Output in Complete Glucose Catabolism

Learning Objective:

- Calculate the energy produced by partial or total oxidation of glucose.

The total energy output from oxidation of glucose is the combined result of (a) glycolysis, (b) conversion of pyruvate to acetyl-CoA, (c) conversion of two acetyl groups to four molecules of CO_2 in the citric acid cycle, and, finally, (d) the passage of reduced coenzymes from each of these pathways through electron transport and the production of ATP by oxidative phosphorylation.

To determine the total number of ATP molecules generated from one glucose molecule, we first sum the net equations for each pathway that precedes oxidative phosphorylation. Since each glucose yields two pyruvate molecules and two acetyl-CoA

molecules, the net equations for pyruvate oxidation and the citric acid cycle are multiplied by 2.

Net result of catabolism of one glucose molecule

Glycolysis (Section 22.3)

$$\text{Glucose} + 2\text{NAD}^+ + 2\text{HOPO}_3^{2-} + 2\text{ADP} \longrightarrow 2\text{Pyruvate} + 2\text{NADH} + 2\text{ATP} + 2\text{H}_2\text{O} + 2\text{H}^+$$

Pyruvate oxidation (Section 22.5)

$$2\text{Pyruvate} + 2\text{NAD}^+ + 2\text{HSCoA} \longrightarrow 2\text{Acetyl-CoA} + 2\text{CO}_2 + 2\text{NADH} + 2\text{H}^+$$

Citric acid cycle (Section 20.8)

$$2\text{Acetyl-CoA} + 6\text{NAD}^+ + 2\text{FAD} + 2\text{ADP} + 2\text{HOPO}_3^{2-} + 4\text{H}_2\text{O} \longrightarrow 2\text{HSCoA} + 6\text{NADH} + 6\text{H}^+ + 2\text{FADH}_2 + 2\text{ATP} + 4\text{CO}_2$$

$$\text{Glucose} + 10\text{NAD}^+ + 2\text{FAD} + 2\text{H}_2\text{O} + 4\text{ADP} + 4\text{HOPO}_3^{2-} \longrightarrow 10\text{NADH} + 10\text{H}^+ + 2\text{FADH}_2 + 4\text{ATP} + 6\text{CO}_2$$

The summation shows a total of 4 ATP molecules produced per glucose molecule. The remainder of our ATP is generated via electron transport and oxidative phosphorylation. Thus, the total number of ATP molecules produced per glucose molecule is the 4 ATP molecules from glucose catabolism plus the number of ATP molecules produced for each reduced coenzyme that enters electron transport.

Based on an energy-yield assumption of 3 ATP molecules per NADH and 2 ATP molecules per $FADH_2$ the maximum yield for the complete catabolism of one molecule of glucose is 38 ATP molecules, as calculated here:

$$10\text{NADH}\left(\frac{3\text{ATP}}{\text{NADH}}\right) + 2\text{FADH}_2\left(\frac{2\text{ATP}}{\text{FADH}_2}\right) + 4\text{ATP} = 38\text{ATP}$$

PROBLEM 22.12

Glycolysis of one molecule of glucose produces 8 ATP molecules. How many ATP molecules are produced from glycolysis of 10 glucose molecules?

PROBLEM 22.13

Complete catabolism of one glucose molecule yields 38 ATP molecules. How many moles of ATP are produced by the complete catabolism of one mole of glucose?

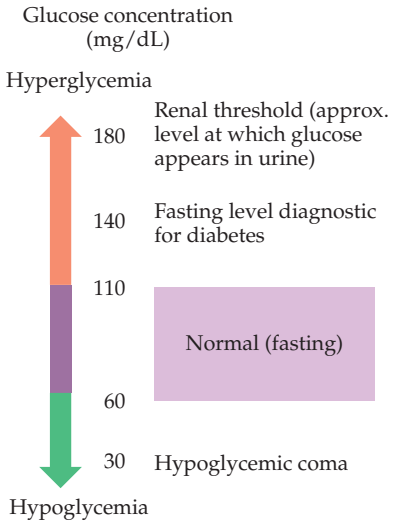
22.7 Regulation of Glucose Metabolism and Metabolism during Stress

Learning Objective:

- Identify the hormones that influence glucose metabolism and describe the changes in metabolism during stress conditions.

A stable blood glucose concentration is vital for proper functioning of the body. Wide fluctuations in glucose levels lead to unwanted side effects. The body uses the hormones insulin and glucagon to control blood glucose levels along with mechanisms to store and release glucose as needed. Glucose is the preferred fuel for brain, muscle during activity, and red blood cells.

Normal blood glucose concentration a few hours after a meal ranges roughly from 65 to 100 mg/dL. When departures from normal occur, specific physiological responses begin to occur (Figure 22.4). Low blood glucose **(hypoglycemia)** causes weakness, sweating, and rapid heartbeat; very low glucose levels in brain cells causes mental



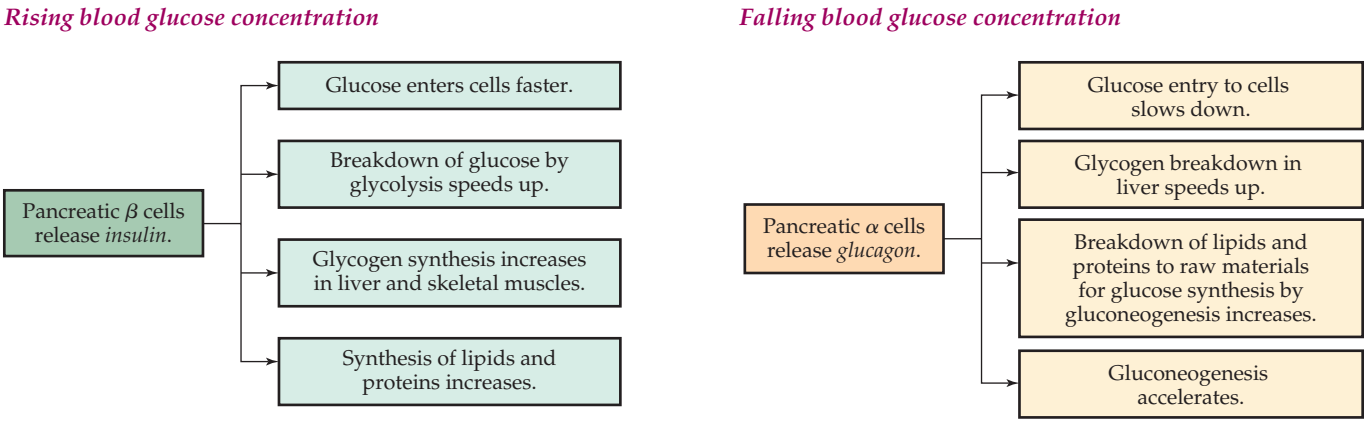
▲ **Figure 22.4**
Blood glucose.
The ranges for low blood glucose (in green; hypoglycemia), normal blood glucose (in purple), and high blood glucose (in orange; hyperglycemia) are indicated.

Hypoglycemia Lower than normal blood glucose concentration.

confusion, convulsions, coma, and eventually death. Glucose is the primary energy source for the brain; alternate fuels are not normally available for brain cells. At a blood glucose level of 30 mg/dL, consciousness is impaired or lost, and prolonged hypoglycemia can cause permanent dementia. High blood glucose (**hyperglycemia**) causes increased urine flow as the normal osmolarity balance of fluids within the kidney is disturbed. Prolonged hyperglycemia can cause low blood pressure, coma, and death.

Hyperglycemia Higher than normal blood glucose concentration.

Two hormones from the pancreas regulate blood glucose levels. The first, insulin, is released when blood glucose concentration rises (Figure 22.5). Its role is to decrease blood glucose concentrations by signaling cells to take in glucose, where it is used for energy production, and by stimulating synthesis of glycogen, proteins, and lipids.



▲ **Figure 22.5**
Regulation of glucose concentration by insulin and glucagon from the pancreas.

The second hormone, glucagon, is released when blood glucose concentration drops. In a reversal of insulin's effects, glucagon stimulates the breakdown of glycogen in the liver and release of glucose. Proteins and lipids are also broken down so that amino acids from proteins and glycerol from lipids can be converted to glucose in the liver by the gluconeogenesis pathways (see Section 22.9). Epinephrine (the "fight-or-flight" hormone) also accelerates the breakdown of glycogen, but primarily in muscle tissue, where glucose is used to generate energy needed for quick action (discussed in Section 28.3).

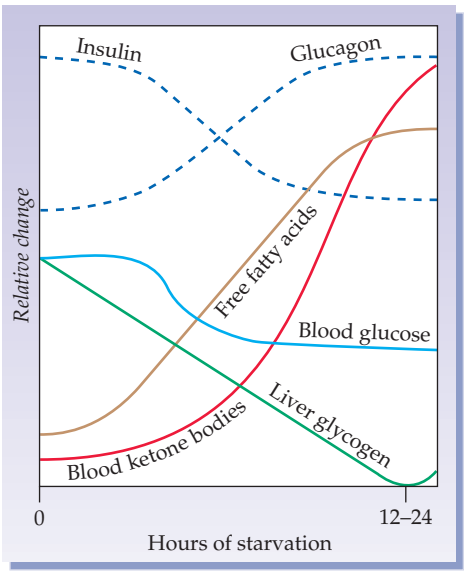
Stress: Dieting, Fasting, and Starvation

Dieting, fasting, and starvation all induce the same metabolic response to an inadequate or nonexistent intake of carbohydrates. Glycogen stored in liver and muscle cells provides glucose for less than 24 hours during fasting conditions, longer while dieting. The primary storage sites for glycogen are liver cells (about 90 g in a 70 kg man) and muscle cells (about 350 g in a 70 kg man). Circulating free glucose and stored glycogen represent less than 1% of our energy reserves and are used up in 15–20 hours of normal activity. Once glycogen stores are exhausted, the liver synthesizes glucose via gluconeogenesis (Section 22.9). This new glucose is delivered preferentially to the brain. The metabolic changes in the absence of food begin with a gradual decline in blood glucose concentration accompanied by an increased release of glucose from glycogen (Figure 22.6 and glycogenolysis, Section 22.8).

Fats are our largest energy reserve, but adjusting to dependence on fat for energy takes several days because there is no direct pathway for generating glucose from the fatty acids in fats (as shown in Figure 22.2). Catabolism of fatty acids to acetyl-CoA, oxidation of acetyl-CoA via the citric acid cycle, and production of ATP energy from electron transport is the path for generating energy from fat. Protein is also broken down into amino acids that can be used to generate energy. Amino acids can enter the citric acid cycle for oxidation to energy or can be used to synthesize glucose in liver cells via the gluconeogenesis pathway (Section 22.9).

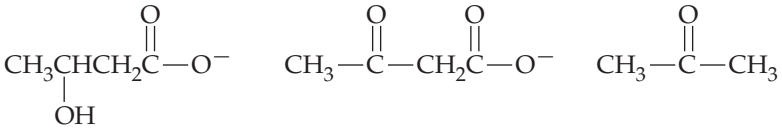
The relationship of changes in amounts of blood glucose, liver glycogen, fatty acids, ketone bodies, insulin, and glucagon present is seen in Figure 22.6.

A body deprived of glucose sources gradually adjusts to producing most of the necessary energy from fat catabolism and begins to conserve protein. As part of the catabolism of fat, acetyl-CoA molecules derived from breakdown of lipids accumulate. Eventually, the citric acid cycle is overloaded and cannot degrade acetyl-CoA as rapidly as it is produced. Acetyl-CoA therefore builds up inside cells and begins to be removed by a new series of metabolic reactions that transform it into a group of compounds collectively known as *ketone bodies*. These ketone bodies enter the bloodstream and the brain and other tissues are able to switch over to producing up to 50% of their ATP from catabolism of ketone bodies instead of glucose. Acetone is so volatile that much of it is excreted through the lungs, giving the breath a fruity odor—an indicator of ketoacidosis in a diabetic.



▲ **Figure 22.6**
Relative changes during early stages of starvation.

Ketone bodies



3-Hydroxybutyrate Acetoacetate Acetone

PROBLEM 22.14

Refer to Figure 22.6 and summarize the changes in liver glycogen and blood glucose during the starvation period represented in the figure.

PROBLEM 22.15

In a diabetic some glucose is converted to sorbitol, an alcohol that accumulates in the eye and can cause cataracts. Draw the open-chain structure of sorbitol, which is identical to that of D-glucose except that the aldehyde group has been reduced to an alcohol group. Can sorbitol form a five- or six-membered cyclic hemiacetal? Explain why or why not. (Hint: The open-chain structure of glucose is found in Section 20.1.)

LOOKING AHEAD The breakdown of triacylglycerols from fatty tissue produces not only ketone bodies but also glycerol, one of the compounds that can be converted to glucose by gluconeogenesis. The production of glycerol and ketone bodies from triacylglycerols is described in Chapter 24, which is devoted to lipid metabolism.

KEY CONCEPT PROBLEM 22.16

Ketoacidosis is relieved by rapid breathing, which converts hydrogen carbonate ions and hydrogen ions in the blood to gaseous carbon dioxide and water, as shown in this equation.

$$H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow H_2O + CO_2\,(\text{Exhaled})$$

(a) Assuming that these reactions can go in either direction, how does a state of acidosis help to increase the generation of carbon dioxide?

(b) What principle describes the effect of added reactants and products on an equilibrium?

HANDS-ON CHEMISTRY 22.2

Go for a run. If you do not run, go for a very fast walk. Monitor your breathing and how your leg muscles feel. If you have exercised long enough and hard enough, you may be in oxygen debt and will breathe heavily for several minutes after coming to a stop. If your leg muscles hurt, it is due to the accumulation of lactic acid generated during exercise. Resting allows lactic acid to be converted into pyruvate by the Cori cycle, and your leg muscles will no longer ache.

CHEMISTRY IN ACTION

The Biochemistry of Running

A runner is poised, tense, and expectant, waiting for the sound of the starting gun. Running requires a constant, rapid source of energy and stresses the entire energy production scheme in the body. Long hours of training have prepared heart, lungs, and red blood cells to deliver the maximum amount of oxygen to the muscles, which have been conditioned to use it as efficiently as possible. In the moments before the race, mounting levels of epinephrine have readied the body for action. Now, everything depends on biochemistry: Chemical reactions in muscle cells will provide the energy to see the race through. How will that energy be produced?

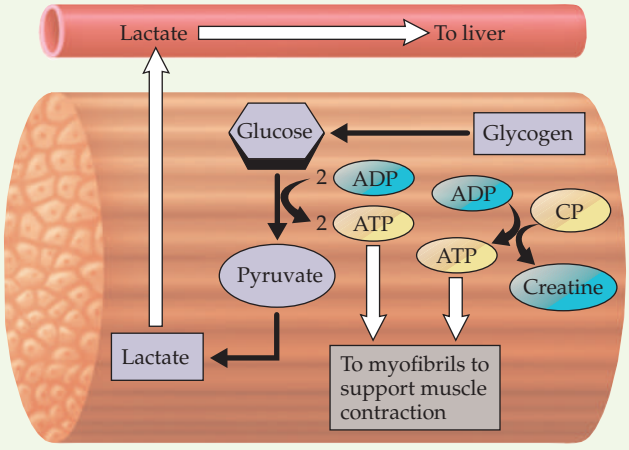
The first source is the supply of immediately available ATP, but this is used up very quickly—probably within a matter of seconds. Additional ATP is then provided by the reaction of ADP with creatine phosphate, an amino acid phosphate in muscle cells that maintains the following equilibrium:

$$\text{ADP} + \text{Creatine phosphate} \rightleftharpoons \text{ATP} + \text{Creatine}$$

After about 30 seconds to a minute, stores of creatine phosphate are depleted, and glucose from glycogenolysis becomes the chief energy source. During maximum muscle exertion, oxygen cannot enter muscle cells fast enough to keep the citric acid cycle and oxidative phosphorylation going. Under these anaerobic conditions, the pyruvate from glycolysis is converted to lactate rather than entering the citric acid cycle.

In a 100 m sprint, all the energy comes from available ATP, creatine phosphate (CP in the figure), and glycolysis of glucose from muscle glycogen. Anaerobic glycolysis suffices for only a minute or two of maximum exertion, because a buildup of lactate causes muscle fatigue.

Beyond this, other pathways must come into action. As breathing and heart rate speed up and oxygen-carrying blood flows more quickly to muscles, the aerobic pathway is activated and ATP is once again generated by oxidative phosphorylation. The trick to avoiding muscle exhaustion in a long race is to run at a speed just under the "anaerobic threshold"—the rate of exertion at which oxygen is in short supply, ATP is supplied only by glycolysis, and lactate is produced.



▲ At peak activity, ATP formation relies on creatine phosphate (CP) and glucose from muscle glycogen. Pyruvate is converted to lactate, which enters the bloodstream for transport to the liver, where it is recycled to pyruvate.

▲ The energy used by these runners is fueled by glycogen stores. The stored glucose is converted to energy through glycolysis, the citric acid cycle, and the electron transport system.

Now the question is, which fuel will metabolism rely on during a long race—carbohydrate or fat? Burning fatty acids from fats is more efficient. Burning a gram of fat yields more than twice as many calories than burning a gram of carbohydrate. When we are sitting quietly, in fact, our muscle cells are burning mostly fat, and the fat in storage could support the exertion of marathon running for several days. By contrast, glycogen alone can provide enough glucose to fuel only 2–3 hours of such running under aerobic conditions.

The difficulty is that fatty acids cannot be delivered to muscle cells fast enough to maintain the ATP level needed for running, so metabolism compromises and the glycogen stored in muscles remains the limiting factor for the marathon runner. Once glycogen is gone, extreme exhaustion and mental confusion set in—the condition known as "hitting the wall." Running speed becomes limited to that sustainable by fats only. To delay this point as long as possible, a runner encourages glycogen synthesis by a diet high in carbohydrates prior to and during a race. In the hours just before the race, however, carbohydrates are avoided. Their effect of triggering insulin release is undesirable at this point because the resulting faster use of glucose will hasten depletion of glycogen.

CIA Problem 22.6 Why is it not possible for a person to sprint for 5 km?

CIA Problem 22.7 Order the following sources of energy (from first used to last used) when muscles are called upon to do extensive work:

(a) Fatty acids from triacylglycerols
(b) ATP
(c) Glycogen
(d) Creatine phosphate
(e) Glucose

CIA Problem 22.8 Why is creatine phosphate a better source of quick energy for a runner than either glucose or glycogen?

22.8 Glycogen Metabolism: Glycogenesis and Glycogenolysis

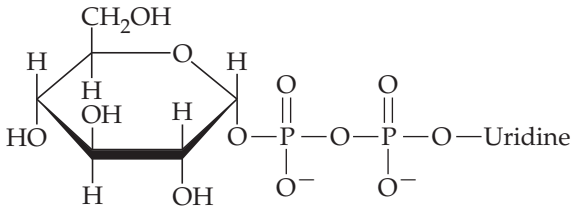
Learning Objective:

- Explain the pathways for glycogen metabolism and their purpose.

Glycogen, the storage form of glucose in animals, is a branched polymer of glucose. **Glycogenesis** (glycogen synthesis) occurs when glucose concentrations are high. It begins with glucose 6-phosphate and occurs via the three steps shown on the right in Figure 22.8.

Glycogenesis The biochemical pathway for synthesis of glycogen, a branched polymer of glucose.

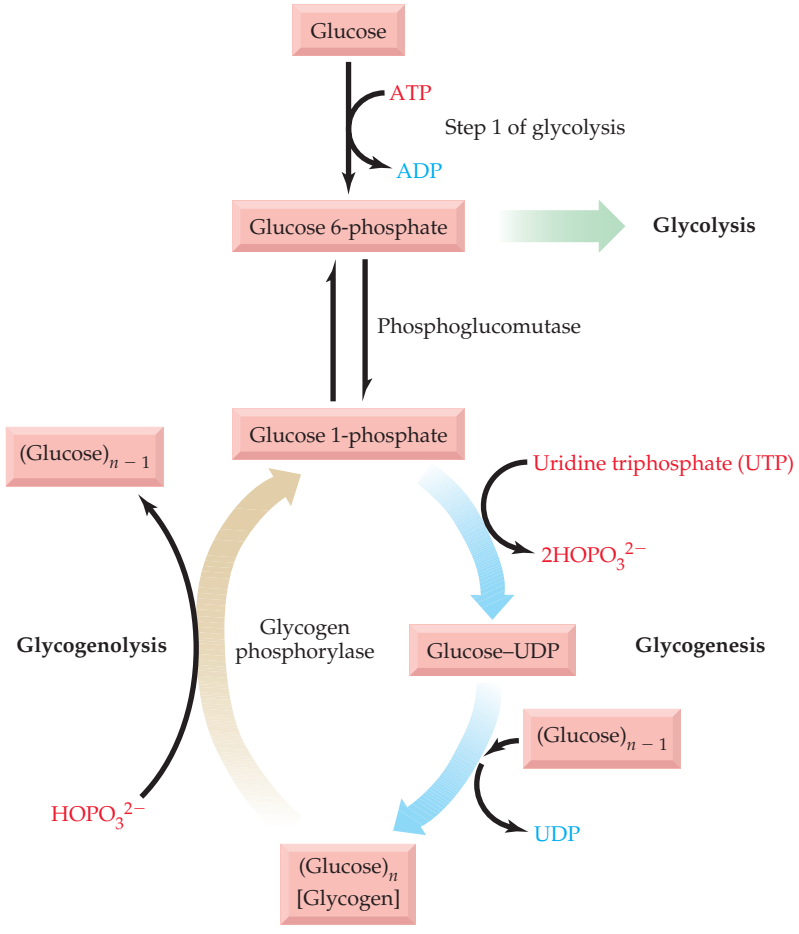
- Step 1: *Phosphoglucomutase* isomerizes glucose 6-phosphate to glucose 1-phosphate.
- Step 2: *Pyrophosphorylase* attaches glucose 1-phosphate to uridine triphosphate (UTP) producing uridine diphosphate (UDP)-glucose in a reaction driven by the release of inorganic pyrophosphate. UTP is a high energy compound similar to ATP. UDP serves as a carrier for glucose.
- Step 3: Glycogen synthase adds UDP-glucose to a glycogen chain, lengthening the chain by one glucose unit and freeing UDP in the process.



UDP-Glucose, the activated carrier of glucose in glycogen synthesis

Glycogenolysis (glucose release) occurs in the two steps on the left in Figure 22.7. In muscle cells, this occurs when there is an immediate need for energy, while in liver cells, it occurs when blood glucose is low.

Glycogenolysis The biochemical pathway for breakdown of glycogen to free glucose.



◂ **Figure 22.7**
Glycogenolysis and glycogenesis. Reading from the top down shows the pathway for glycogen synthesis from glucose (glycogenesis). Reading from the bottom up shows the pathway for release of glucose from glycogen (glycogenolysis).

- Step 1: *Glycogen phosphorylase* simultaneously hydrolyzes α-1, 4 glycosidic bonds and sequentially phosphorylates glucose units. The product is glucose 1-phosphate.
- Step 2a: *Phosphoglucomutase* isomerizes glucose 6-phosphate to glucose 1-phosphate. In muscle cells, glucose 1-phosphate immediately enters glycolysis at step 2. This is the reverse of the same reaction in glycogenesis.
- Step 2b: In liver cells, *glucose 6-phosphatase* hydrolyzes glucose 6-phosphate to glucose that moves out of the liver to blood stream to raise blood sugar levels.

PROBLEM 22.17

What is the difference between glycogenesis and glycogenolysis?

PROBLEM 22.18

Why is glycogenesis necessary? Why is glycogenolysis necessary?

22.9 Gluconeogenesis: Glucose Synthesis from Noncarbohydrates

Learning Objective:

- Explain the pathways for synthesis of glucose from noncarbohydrate molecules.

Gluconeogenesis The biochemical pathway for the synthesis of glucose from noncarbohydrates, such as lactate, amino acids, or glycerol.

Glucose is so important for energy production that there are two pathways involved in the synthesis of glucose from noncarbohydrates. The *Cori cycle* converts lactate into pyruvate, the substrate for **gluconeogenesis,** a pathway that makes glucose from noncarbohydrate molecules (lactate, amino acids, and glycerol) beginning with pyruvate. This pathway becomes critical when glucose is not available.

We noted earlier that for metabolic pathways to be favorable, they must be exergonic. As a result, most are not reversible, because the amount of energy required by the reverse, endergonic pathway would be too large to be supplied by cellular metabolism. Glycolysis and gluconeogenesis provide another good example of this relationship and of the way around it.

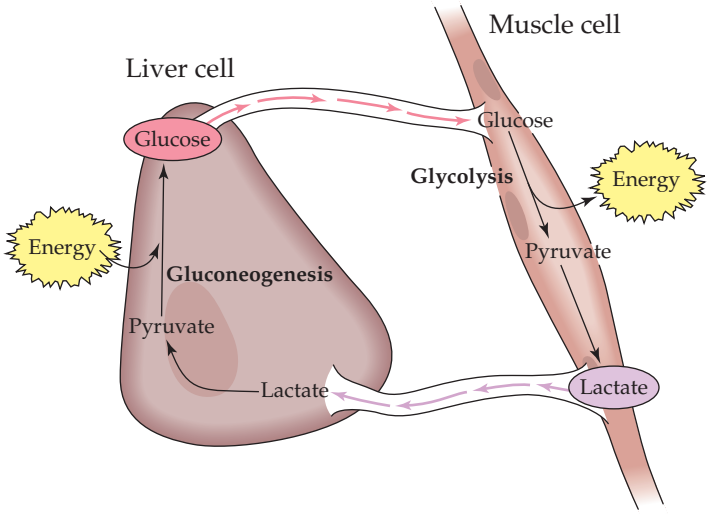
Cori Cycle

Lactate is a normal product of glycolysis in red blood cells and in muscle cells during vigorous exercise. The bloodstream moves lactate from muscle cells to liver cells; it is oxidized to pyruvate by lactate dehydrogenase. Pyruvate is the substrate for an 11-step series of reactions in the gluconeogenesis pathway; the final product is glucose, which is exported to tissues dependent on glucose but lack the gluconeogenesis pathway. The Cori cycle is essentially a recycling pathway. See Figure 22.8.

Gluconeogenesis

Gluconeogenesis, the synthesis of glucose from noncarbohydrate sources, runs when available glucose from the diet and stored glycogen has been used up. Glucose is the preferred energy source for brain and blood cells and must be supplied. Although some of the steps in gluconeogenesis are the reverse of the identical step in glycolysis, the energy requiring steps in gluconeogenesis use different enzymes than the same steps in glycolysis and vice versa. Steps 1, 3, and 10 in Figure 22.3 illustrate this point. These reactions in glycolysis are too exergonic to be directly reversed. The steps in gluconeogenesis are shown in Figure 22.9 and outlined next.

- Step 1: In an energetically expensive step, *pyruvate carboxylase* adds CO_2 to pyruvate forming oxaloacetate. ATP is changed to ADP in this step.
- Step 2: In a second energetically expensive step, *phosphoenolpyruvate carboxylase* removes CO_2 from oxaloacetate while adding a phosphate group from guanosine



◀ Figure 22.8
Glucose production during exercise (the Cori cycle).
L-Lactate produced in muscles under anaerobic conditions during exercise is sent to the liver, where it is converted back to glucose. This new glucose can then return via the bloodstream to the muscles, to be stored as glycogen or used for energy production. Gluconeogenesis requires energy, so shifting this pathway to the liver frees the muscles from the burden of having to produce even more energy.

triphosphate (GTP) (similar to ATP) producing phosphoenolpyruvate and guanosine diphosphate (GDP).

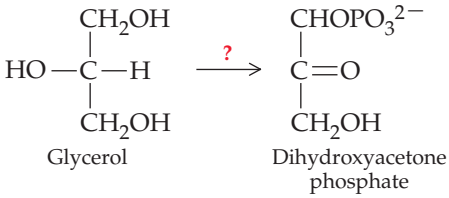
- Steps 3–8: In reversible reactions, *the same set of enzymes as found in glycolysis steps 4–9* convert phosphoenolpyruvate to fructose 1,6-bisphosphate via the same intermediates found in glycolysis.
- Step 9: In a one-way reaction, *fructose 1,6-bisphosphatase* hydrolyzes fructose 1,6-bisphosphate to fructose 6-phosphate.
- Step 10: In a one-way reaction, *phosphohexose isomerase* changes fructose 6-phosphate into glucose 6-phosphate.
- Step 11: In a one-way reaction, *glucose 6-phosphatase* hydrolyzes glucose 6-phosphate to glucose.

Glycerol from triacylglycerol catabolism (Section 24.3) is converted to dihydroxyacetone phosphate and enters the gluconeogenesis pathway at step 7 in Figure 22.9 (or step 5 of glycolysis in Figure 22.3). The carbon atoms from certain amino acids (the glucogenic amino acids, Section 27.5) enter gluconeogenesis as either pyruvate or oxaloacetate.

Glycolysis and gluconeogenesis both occur in the cytoplasm of cells. Recall that the citric acid cycle and electron transport system are found in the mitochondria. Glycogenesis and glycogenolysis occur at the surface of glycogen storage granules in the cytoplasm.

PROBLEM 22.19

What two types of reactions convert glycerol to dihydroxyacetone phosphate?



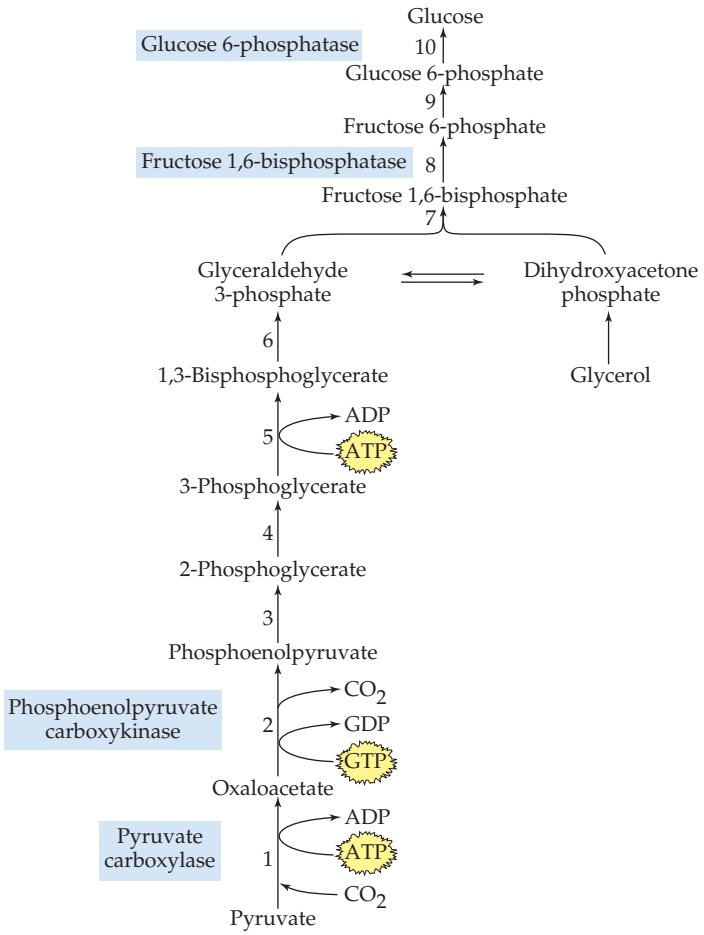
Glycerol — Dihydroxyacetone phosphate

PROBLEM 22.20

What is the purpose of the Cori cycle?

PROBLEM 22.21

Why is gluconeogenesis necessary?



▶ Figure 22.9
Gluconeogenesis. The pathway begins at the bottom of the figure and moves upwards. Each step in the pathway is numbered. Enzymes shaded in blue are those that differ from the enzymes used in glycolysis to achieve the reverse reaction. For the other steps, gluconeogenesis uses the same enzymes as those used in glycolysis.

CHEMISTRY IN ACTION

Diagnosis and Monitoring of Diabetes

Diabetes mellitus is one of the most common metabolic diseases. Although often thought of only as a disease of glucose metabolism, diabetes affects protein and fat metabolism as well, and in some ways the metabolic response resembles starvation. Type I diabetes, an autoimmune disease, is caused by failure of pancreatic β cells to produce insulin. Type II diabetes is caused by "insulin resistance" of target cells; insulin is in good supply but fails to promote the passage of glucose across cell membranes. In both cases, diabetes is not the inability to metabolize glucose but the inability of sufficient glucose to enter cells to be metabolized. A prediabetic condition named metabolic syndrome has been characterized by a set of physical symptoms and blood indicators. Any diabetic as well as a prediabetic with metabolic syndrome is more likely to develop heart disease than nondiabetics. The following table gives typical symptoms, physician observations, and treatment for both types of diabetes.

Diabetes Comparison

	General Symptoms	Type I Diabetes	Type II Diabetes
Physician Observations	Abnormal thirst Frequent urination Unusually hungry Injuries heal slowly Persistently tired Dry mouth and itchy skin Blurry vision	Thin Losing weight Usually under 20 years of age Rapid, severe onset	Overweight Gaining weight slowly Usually over 40 years of age Slow, mild onset
Treatment		Exercise and diet control Insulin injections (several times daily)	Exercise and diet control Oral medications or insulin as needed

▲ **Glucose blood test.** A tiny drop of blood is absorbed on the test strip in the blood glucose monitor. The results of the test are read in less than 10 seconds by most modern monitors and displayed on an LCD screen.

Glucose measurements are essential in the diagnosis of diabetes mellitus and in the management of diabetic patients, both in a clinical setting and on a day-to-day basis by patients themselves. The *glucose-tolerance test* is among the clinical laboratory tests usually done to pin down a diagnosis of diabetes mellitus. The patient must fast for 10–16 hours, and after a fasting blood sample is drawn, is challenged with a controlled dose sugar drink, and additional blood samples are taken at regular intervals thereafter. The results show an immediate blood glucose rise, followed by a drop in blood glucose. A difference is apparent after 2 hours, when the concentration in a normal individual has dropped to close to the fasting level but that in a diabetic individual remains high. The metabolic syndrome, prediabetic patient has an intermediate response. The fasting glucose level is greater than 100 mg/dL and the challenge response is intermediate between that of the diabetic and nondiabetic patient. A fasting blood glucose concentration of 140 mg/dL or higher and/or a glucose tolerance test concentration that remains above 200 mg/dL beyond 1 hour are considered diagnostic criteria for diabetes. For a firm diagnosis, the glucose tolerance test is usually given more than once. This test does not distinguish between Type I and Type II diabetes. A physician must make that decision based on other information.

An additional test, the A1C test, determines the percent of glycated hemoglobin (glucose covalently bonded to hemoglobin, making it a glycoprotein) present. This value indicates a several month history of blood glucose levels and is used both in diagnosis and in evaluating success and compliance with treatment. Values of 6.5% and higher indicate diabetes; high numbers indicate poor control of the disease.

Individuals with diabetes must monitor their blood glucose levels at home daily, often several times a day. Most tests for glucose rely on detecting a color change that accompanies the oxidation of glucose. Because glucose and its oxidation product, gluconate, are colorless, the oxidation must be tied chemically to the color change of a suitable indicator. Modern methods for glucose detection rely on the action of an enzyme specific for glucose. The most commonly used enzyme is glucose oxidase, and the products of the oxidation are gluconate and hydrogen peroxide (H_2O_2). A second enzyme in the reaction mixture, a peroxidase, catalyzes the reaction of hydrogen peroxide with a dye that gives a detectable color change.

$$\text{Glucose} + O_2 \xrightarrow{\text{Glucose oxidase}} \text{Gluconate} + H_2O_2$$

$$H_2O_2 + \underset{\text{(colorless)}}{\text{Reduced dye}} \xrightarrow{\text{Peroxidase}} H_2O_2 + \underset{\text{(colored)}}{\text{Oxidized dye}}$$

The enzymes needed for the reactions are embedded in the test strip itself and only a miniscule drop of blood is needed. The blood test is desirable because it is specific and quick. It is used to achieve tighter control of blood glucose levels to help those with diabetes live longer, healthier lives.

Remember Maria from the beginning of the chapter? At her follow-up appointment with her physician, her blood tests following a glucose tolerance test showed a classic response for diabetes. The patient history indicated a high probability that she had developed Type II diabetes. She was prescribed exercise and an oral medication designed to improve glucose uptake by cells, and given an appointment with a dietician to help improve her diet. Maria is at increased risk for heart disease because her blood lipids were also elevated, a common complication of Type II diabetes.

CIA Problem 22.9 Briefly describe the enzymatic process used in home glucose monitors for determination of blood glucose levels.

CIA Problem 22.10 How do fasting glucose levels in a diabetic person compare to those in a nondiabetic person?

CIA Problem 22.11 Discuss the differences in the response of a diabetic person compared to those of a nondiabetic person after drinking a glucose solution.

CIA Problem 22.12 If your doctor suspects that you have diabetes, what tests would he or she order to confirm the presence of diabetes?

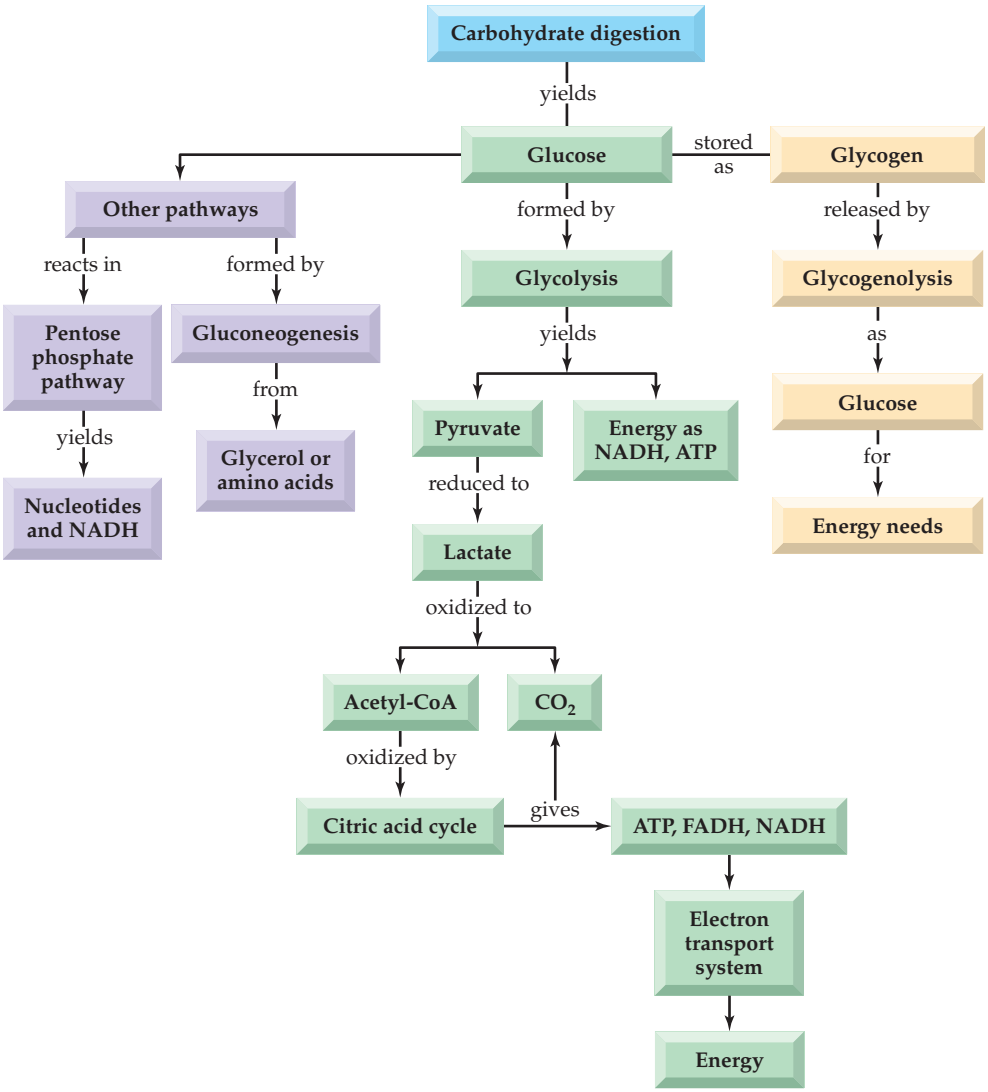
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Describe carbohydrate digestion, where it takes place in the body, the enzymes involved, and name the major products of the process.** Carbohydrate *digestion,* the hydrolysis of disaccharides and polysaccharides, begins in the mouth and continues in the stomach and small intestine. The products that enter the bloodstream from the small intestine are monosaccharides—mainly glucose, fructose, and galactose *(see Problems 31–40)*.
- **Identify the pathways by which glucose is first synthesized and then broken down, and describe their interrelationships.** The major catabolic pathway for glucose is *glycolysis*. Pyruvate, the end product of glycolysis, enters the citric acid cycle via acetyl-CoA. An alternative pathway for glucose is *glycogenesis*, the synthesis of glycogen, which is stored mainly in the liver and muscles. Another alternative is the *pentose phosphate pathway*, which provides NADPH and the 5-carbon sugars needed for the synthesis of nucleotides (see Figure 22.2) *(see Problems 23–25, 39, and 40).*
- **Describe the glycolysis pathway and its products.** Glycolysis (Figure 22.3) is a 10-step pathway that produces two molecules of pyruvate, two molecules of reduced coenzyme (NADH), and two ATP molecules for each molecule of glucose metabolized. Glycolysis begins with phosphorylation (steps 1–3) to form fructose 1,6-bisphosphate, followed by cleavage, and isomerization reactions that produce two molecules of glyceraldehyde 3-phosphate (steps 4–5). Each glyceraldehyde 3-phosphate then proceeds through the energy-generating steps (steps 6–10) in which phosphates are alternately created and then donate their phosphate groups to ADP to yield ATP *(see Problems 22, 26, 30, 41–46, 48, 70–72, and 76)*.
- **Identify where the major monosaccharides enter glycolysis.** Dietary monosaccharides other than glucose enter glycolysis at various points—fructose as fructose 6-phosphate or glyceraldehyde 3-phosphate, galactose as glucose 6-phosphate, and mannose as fructose 6-phosphate *(see Problems 51, 52, 73, 83, and 85)*.
- **Describe the pathways involving pyruvate and their respective outcomes.** Under aerobic conditions, pyruvate is transported into mitochondria and converted to acetyl-CoA for energy generation via the citric acid cycle and oxidative phosphorylation. When there is insufficient oxygen, pyruvate is reduced to lactate, with the production of NAD^+. Production of NAD^+ compensates for the shortage of NAD^+ created by the slowdown of electron transport under anaerobic conditions. Lactate produced in muscle is transported to the liver and is oxidized back to pyruvate. In yeast, pyruvate undergoes *anaerobic fermentation* to yield ethanol *(see Problems 36, 49, 50, 69, 77, and 84).*
- **Calculate the energy produced by partial or total oxidation of glucose.** Sum the reactions to determine the total number of ATP, NADH, and $FADH_2$ molecules produced. Use the appropriate multipliers to find the total number of ATP molecules for the reaction *(see Problems 47, 73, 74, and 85).*
- **Identify the hormones that influence glucose metabolism and describe the changes in metabolism during stress conditions.** *Insulin*, produced when blood glucose concentration rises, accelerates glycolysis and glycogen synthesis to remove glucose from the bloodstream. *Glucagon*, produced when blood glucose concentration drops, accelerates production of glucose in the liver from stored glycogen and from other precursors via the *gluconeogenesis* pathway. Adaptation to stress conditions like fasting and running begins with glucagon mobilizing glucose from storage as glycogen and proceeds to energy production from protein and fat *(see Problems 27, 53–56, 75, and 78–81).*
- **Explain the pathways for glycogen metabolism and their purpose.** *Glycogenesis* (Figure 22.8), the synthesis of glycogen, puts excess glucose into storage, mainly in muscle and the liver cells. *Glycogenolysis* is the release of stored glucose from glycogen. Glycogenolysis occurs in muscles when there is an immediate need for energy, producing glucose 6-phosphate for intracellular glycolysis. When blood glucose concentration is low, liver cells can convert glucose 6-phosphate to glucose and release it to the bloodstream *(see Problems 38, and 57–60).*
- **Explain the pathways for synthesis of glucose from noncarbohydrate molecules.** *Gluconeogenesis* (Figure 22.9) maintains glucose levels by synthesizing new glucose from lactate, from certain amino acids derived from proteins, and from glycerol derived from fatty tissue; this pathway, found in liver cells, is part of normal metabolism and is critical during fasting and starvation. The gluconeogenesis pathway uses alternate enzymes for the reverse of the three highly exergonic steps of glycolysis, but otherwise utilizes the same enzymes for reactions that run in reverse of their direction in glycolysis *(see Problems 28, 29, 37, 61–68, 76, and 82).*

KEY WORDS

Aerobic, *p. 732*
Alcoholic fermentation, *p. 733*
Anaerobic, *p. 732*
Digestion, *p. 725*
Fermentation, *p. 733*
Gluconeogenesis, *p. 740*
Glycogenesis, *p. 739*
Glycogenolysis, *p. 739*
Glycolysis, *p. 726*
Hyperglycemia, *p. 736*
Hypoglycemia, *p. 735*
Pentose phosphate pathway, *p. 726*

CONCEPT MAP: GLUCOSE METABOLISM



▲ **Figure 22.10 Concept Map.** Glucose is the primary fuel for energy production when pyruvate, the product of glycolysis, is converted to acetyl-CoA and subsequently completely oxidized via the citric acid cycle and oxidative phosphorylation, as seen in Chapter 21. This chapter also explores the relationship between the catabolism and anabolism of glucose. These relationships are shown in the concept map.

UNDERSTANDING KEY CONCEPTS

22.22 What class of enzymes catalyzes the majority of the reactions involved in carbohydrate digestion?

22.23 Glucose 6-phosphate is in a pivotal position in metabolism. Depending on conditions, glucose 6-phosphate follows one of several pathways. Under what conditions do the following occur?

(a) Glycolysis

(b) Hydrolysis to free glucose

(c) Pentose phosphate pathway

(d) Glycogenesis

22.24 What "chemical investments" are made to get glycolysis started, and why are they made? What happens in the middle of the pathway to generate two 3-carbon compounds? What are the outcomes of the reactions of these 3-carbon compounds?

22.25 Outline the conditions that direct pyruvate toward the following:

(a) Entry into the citric acid cycle

(b) Conversion to ethanol and CO_2

(c) Conversion to lactate

(d) Glucose synthesis (gluconeogenesis)

In what tissues or organisms is each pathway present?

22.26 Classify each enzyme of glycolysis into one of the six classes of enzymes. What class of enzymes has the most representatives in glycolysis? Why is this consistent with the goals of glycolysis? Why are ligases *not* represented in glycolysis?

22.27 When blood glucose levels rise following a meal, the following events occur. Arrange these events in the appropriate sequence.

(a) Glucagon is secreted.

(b) Glycolysis replenishes ATP supplies.

(c) Glucose is absorbed by cells.

(d) The liver releases glucose into the bloodstream.

(e) Glycogen synthesis (glycogenesis) occurs with excess glucose.

(f) Blood levels pass through normal to below normal (hypoglycemic).

(g) Insulin levels rise.

22.28 Name the molecules used for gluconeogenesis. What are the sources of these molecules? Under what conditions would gluconeogenesis occur?

22.29 Fatty acids from stored triacylglycerols (fat) are *not* available for gluconeogenesis. Speculate why we do not have the enzymes to directly convert fatty acids into glucose. Plants (especially seeds) *do* have enzymes to convert fatty acids into carbohydrates. Why are they so lucky?

22.30 The pathway that converts glucose to acetyl-CoA is often referred to as an "aerobic oxidation pathway." (a) Is molecular oxygen involved in any of the steps of glycolysis? (b) Thinking back to Chapter 20, where does molecular oxygen enter the picture?

ADDITIONAL PROBLEMS

DIGESTION AND METABOLISM (SECTIONS 22.1 AND 22.2)

22.31 Where does digestion occur in the body, and what kinds of chemical reactions does it involve?

22.32 Complete the following word equation:

$$\text{Lactose} + H_2O \longrightarrow ? + ?$$

Where in the digestive system does this process occur?

22.33 What are the major monosaccharide products produced by digestion of carbohydrates?

22.34 What are the products of digestion of proteins, triacylglycerols, maltose, sucrose, lactose, and starch?

22.35 What do the words *aerobic* and *anaerobic* mean?

22.36 What three products are formed from pyruvate under aerobic, anaerobic, and fermentation conditions?

22.37 Name the substrate and the product of (a) glycolysis and (b) gluconeogenesis.

22.38 Name the substrate and the product of (a) glycogenesis and (b) glycogenolysis.

22.39 What is the major purpose of the pentose phosphate pathway? What cofactor (coenzyme) is used?

22.40 Depending on the body's needs, into what type of compounds is glucose converted in the pentose phosphate pathway?

GLYCOLYSIS (SECTIONS 22.3, 22.4, AND 22.5)

22.41 Where in a liver cell do the following pathways occur?

(a) Glycolysis

(b) Gluconeogenesis

(c) Glycogenesis

(d) Glycogenolysis

22.42 Which cells, liver, muscle, or brain, use the following pathways?

(a) Glycolysis

(b) Gluconeogenesis

(c) Glycogenesis

(d) Glycogenolysis

22.43 Although the catabolism of glucose produces energy, the first step uses energy. Explain why.

22.44 Glycolysis can occur under both aerobic and anaerobic conditions. Why is glycolysis called an anaerobic pathway?

22.45 Which glycolysis reactions are catalyzed by the following enzymes?

(a) Pyruvate kinase

(b) Glyceraldehyde 3-phosphate dehydrogenase

(c) Hexokinase

(d) Phosphoglycerate mutase

(e) Aldolase

22.46 Review the 10 steps in glycolysis (Figure 22.3) and then answer the following questions:

(a) Which steps involve phosphorylation?

(b) Which step is an oxidation?

(c) Which step is a dehydration?

22.47 How many moles of ATP are produced by phosphorylation in the following?

(a) Glycolysis of 1 mol of glucose

(b) Aerobic conversion of 1 mol of pyruvate to 1 mol of acetyl-CoA

(c) Catabolism of 1 mol of acetyl-CoA in the citric acid cycle

22.48 For each reaction in Problem 22.47, tell if the ATP formed is produced by oxidative phosphorylation or substrate-level phosphorylation. What is the difference in the two types of ATP formation?

22.49 Why is pyruvate converted to lactate under anaerobic conditions?

22.50 Lactate can be converted into pyruvate by the enzyme lactate dehydrogenase and the coenzyme NAD^+. Write the reaction in the standard biochemical format, using a curved arrow to show the involvement of NAD^+.

22.51 How many moles of CO_2 are produced by the complete catabolism of 1 mol of sucrose?

22.52 How many moles of acetyl-CoA are produced by the complete catabolism of 1 mol of sucrose?

REGULATION OF GLUCOSE METABOLISM AND METABOLISM DURING STRESS (SECTION 22.7)

22.53 Differentiate between the effect of insulin and glucagon on blood sugar concentration.

22.54 Differentiate between blood sugar levels and resulting symptoms in hyperglycemia and hypoglycemia.

22.55 What molecules are used initially during starvation or fasting to produce glucose?

22.56 (Fill in the blank) As starvation continues, acetyl-CoA is converted to _____ to prevent buildup of acetyl-CoA in the cells.

GLYCOGEN CATABOLISM AND ANABOLISM (SECTION 22.8)

22.57 Where is most of the glycogen in the body stored?

22.58 What major site of glycogen storage is not able to release glucose to the bloodstream?

22.59 How is UTP used in the formation of glycogen from glucose?

22.60 Why does glycogenolysis use fewer steps than the reverse process, glycogenesis? Which process uses less energy?

GLUCOSE FROM NONCARBOHYDRATES (SECTION 22.9)

22.61 Name the anabolic pathway for making glucose.

22.62 Name the two molecules that serve as starting materials for glucose synthesis.

22.63 (Fill in the blanks.) Pyruvate is initially converted to _____ in the anabolism of glucose. That molecule in turn is converted to _____.

22.64 Explain why pyruvate cannot be converted to glucose in an exact reverse of the glycolysis pathway.

22.65 Explain how the energy-releasing steps of glycolysis are reversed in gluconeogenesis.

22.66 How many steps in gluconeogenesis are not the exact reversal of the steps in glycolysis? What kind of conversion of substrate to product does each involve? What is the common theme in each of these reactions?

22.67 What is the Cori cycle?

22.68 Explain why the Cori cycle is necessary and when your cells would use this cycle.

CONCEPTUAL PROBLEMS

22.69 Why can pyruvate cross the mitochondrial membrane but no other molecule after step 1 in glycolysis can?

22.70 Look at the glycolysis pathway (Figure 22.3). With what type of reactions are kinase enzymes usually associated?

22.71 Explain why one more ATP is produced when glucose is obtained from glycogen rather than used directly from the blood.

22.72 Why is it important that glycolysis be tightly controlled by the cell?

22.73 How many moles of ATP are generated from the catabolism of fructose (by glycolysis) in (a) liver cells and (b) muscle cells?

22.74 Which of the following conversions would you expect to consume energy and which would you expect to yield energy based on the final oxidation state of the coenzymes involved in each reaction?

(a) pyruvate $\longrightarrow$ lactate

(b) pyruvate $\longrightarrow$ acetyl-CoA + CO_2

22.75 Why is it important for muscle cells to export lactate into the bloodstream during heavy exercise?

22.76 Under which physiological condition is the following pathway the predominant one?

(a) glycolysis

(b) gluconeogenesis

22.77 Why is it important for the cell that the NADH produced when pyruvate is converted to lactate be converted back to NAD^+?

22.78 What are the characteristics of Type I diabetes?

22.79 What are the characteristics of Type II diabetes?

22.80 Explain the relationship between metabolic syndrome and diabetes.

22.81 Many diabetics suffer blindness due to cataracts. Why is this condition associated with this disease?

GROUP PROBLEMS

22.82 A primary function of liver cells is to synthesize new glucose via gluconeogenesis, while working muscle cells use glucose via glycolysis. Why is this a good physiological strategy for your body?

22.83 In liver cells, galactose is converted to glucose 6-phosphate in a four-step process; it then enters glycolysis. People with the genetic disease galactosemia lack one or more of the enzymes necessary to convert galactose to glucose 6-phosphate; galactose instead is converted to undesirable molecules that damage various organs. This disease can be controlled by a careful diet. What food or foods are a major source of galactose in the diet?

22.84 It is important to avoid air when making wine, so a novice winemaker added yeast to fresh grape juice and placed it in a sealed bottle to avoid air. Several days later, the lid exploded off the bottle. Explain the biochemistry responsible for the exploding lid.

22.85 Is the same net production of ATP observed in the complete oxidation of fructose as is observed in the complete oxidation of glucose? Why or why not?

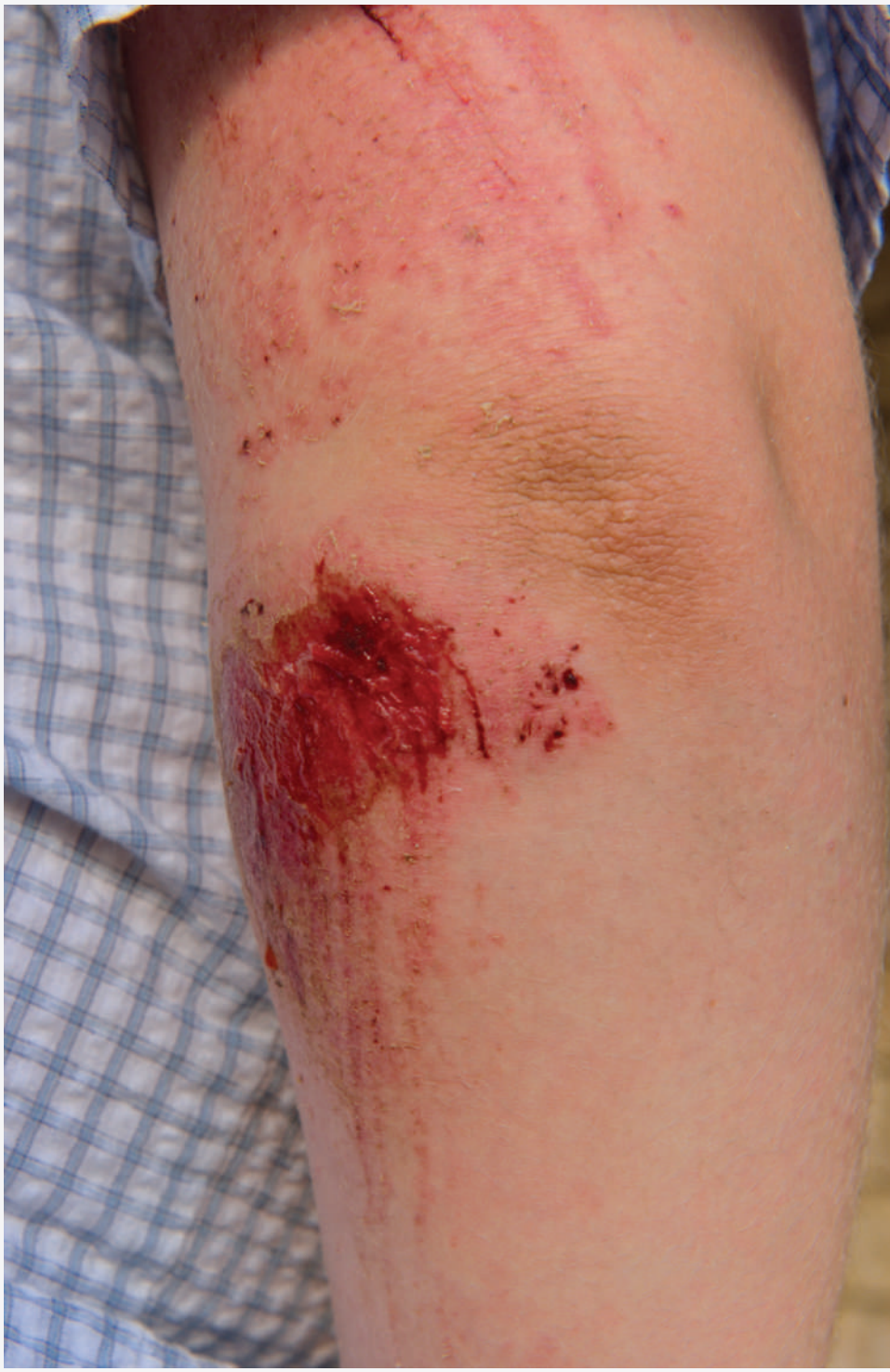
23

Lipids

CONTENTS

CONCEPTS TO REVIEW

A. Intermolecular Forces (Section 8.2)
B. Cis–Trans Isomerism (Section 13.3)
C. Esters and Amides (Sections 17.4 and 17.6)
D. Phosphoric Acid Derivatives (Section 17.8)
E. Carboxylic Acids (Sections 17.1 and 17.2)



▲ The red, raised but unbroken skin around this abrasion is a local reaction caused by a class of lipids called prostaglandins, a type of eicosanoid.

Lipids are less well known than carbohydrates and proteins, yet lipids are just as essential to our diet and well-being. They have three major roles in human biochemistry: (1) Within fat cells *(adipocytes)*, they store energy from metabolism of food. (2) As part of all cell membranes, they keep separate the different chemical environments inside and outside the cells. (3) In the endocrine system and elsewhere, lipids serve as chemical messengers;

steroids and eicosanoids are two such examples. Steroids serve as chemical messengers circulating throughout the body, whereas certain eicosanoids are responsible for the localized minor pain you may experience from scrapes and abrasions from falls, or the redness, heat, and swelling from tangling with a rose bush. One response to alleviate minor pain is to take aspirin to lessen the discomfort because it has analgesic, antipyretic (fever reducing), and anti-inflammatory properties. Why does aspirin, one of the oldest known analgesics, alleviate pain and hasten the disappearance of redness, heat, and swelling of a scrape or cut when other nonsteroidal anti-inflammatory drugs (NSAIDs) do not? The Chemistry in Action "Eicosanoids: Prostaglandins and Leukotrienes" at the end of this chapter has the answer, which lies in a lipid.

23.1 Structure and Classification of Lipids

Learning Objective:

- Describe the chemical structures and general properties of fatty acids, waxes, sterols, fats, and oils.

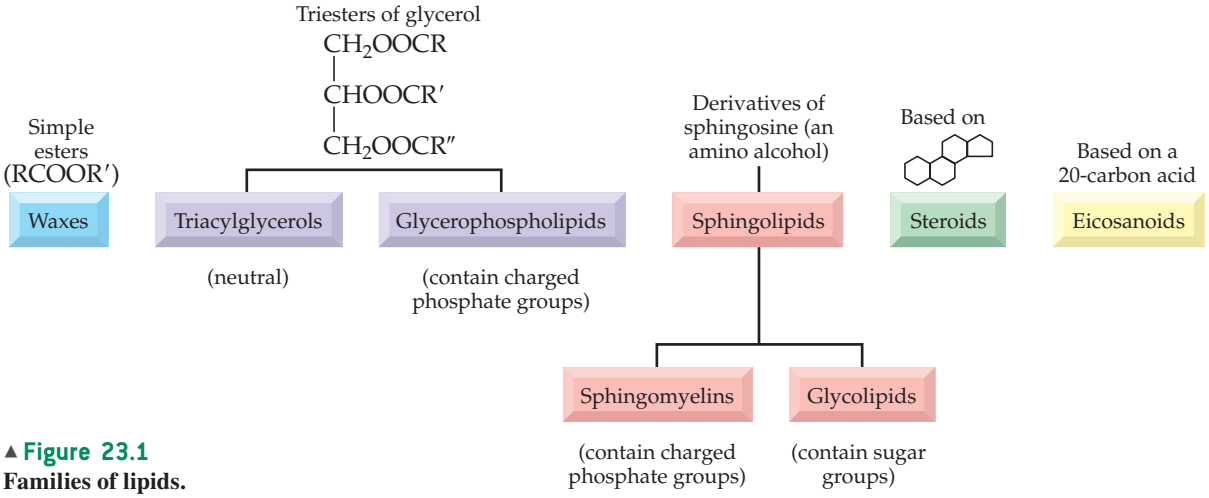
Lipids are naturally occurring organic molecules that are nonpolar and therefore dissolve in nonpolar organic solvents but not in water. For example, if a sample of plant or animal tissue is placed in a kitchen blender, finely ground, and then treated with ether, any molecule that dissolves in ether is a lipid and any molecule that does not dissolve in ether (including carbohydrates, proteins, and inorganic salts) is not a lipid.

Since **lipids** are defined by solubility in nonpolar solvents (a physical property) rather than by chemical structure, it should not surprise you that there are a great many different kinds and that they serve a variety of functions in the body. In the following examples of lipid structures, note that the molecules contain large hydrocarbon portions and not many polar groups, which accounts for their solubility behavior. Many lipids have hydrocarbon or modified hydrocarbon structures, properties, and behavior. This similarity to hydrocarbons and their derivatives unifies a set of highly diverse molecules into one class.

Lipid A naturally occurring molecule from a plant or animal that is soluble in nonpolar organic solvents.

Figure 23.1 organizes the classes of lipids discussed in this chapter according to their chemical structures. Many lipids are esters or amides of carboxylic acids with long, unbranched hydrocarbon chains, known as **fatty acids.** The fatty acids that contain unbranched hydrocarbon chains are loosely referred to as *straight-chain fatty acids.*

Fatty acid A long-chain carboxylic acid; those in animal fats and vegetable oils often have 12–22 carbon atoms.

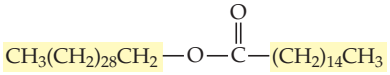


▲ **Figure 23.1**
Families of lipids.

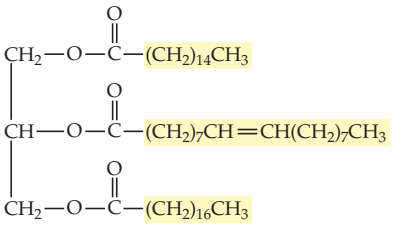
Lipids That Are Esters or Amides of Fatty Acids

- *Waxes* are carboxylic acid esters (RCOOR′) with long, straight hydrocarbon chains in both R groups; they are secreted by sebaceous glands in the skin of animals and perform mostly external protective functions (Section 23.2).

- *Triacylglycerols* are carboxylic acid triesters of glycerol, a three-carbon trialcohol. Triacylglycerols (Sections 23.2–23.3) are found in most dietary fats and oils and are also the fat storage molecules in our body. They are a major source of biochemical energy, a function described in Chapter 24.



A wax



A triacylglycerol

- *Glycerophospholipids* (Section 23.5) are triesters of glycerol that contain charged phosphate-diester groups and are abundant in cell membranes. Together with other lipids, they help to control the flow of molecules into and out of cells.
- *Sphingomyelins* are amides derived from an amino alcohol *(sphingosine)* that also contain charged phosphate-diester groups; they are essential to the structure of cell membranes (Section 23.5) and are especially abundant in nerve cell membranes.
- *Glycolipids* are different amides derived from *sphingosine* that contain polar carbohydrate groups; on cell surfaces the carbohydrate portion is recognized and interacts with intercellular messengers (Section 23.5).

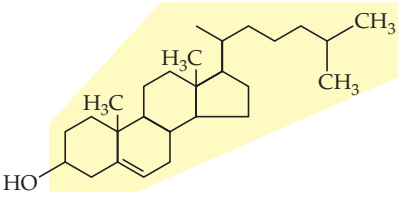
Other Types of Lipids

There are also two groups of lipids that are not esters or amides:

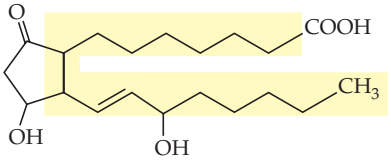
- *Sterols* are a family of molecules that all contain the four-ring steroid nucleus structure. Important sterols are cholesterol, found in cell membranes; bile salts, necessary for fat emulsification in digestion; and sex hormones (Section 23.6).

Eicosanoid A lipid derived from a 20-carbon unsaturated carboxylic acid.

- *Eicosanoids.* The eicosanoids are carboxylic acids that are a special type of localized intercellular chemical messenger (see the Chemistry in Action "Eicosanoids: Prostaglandins and Leukotrienes").



Cholesterol, a sterol

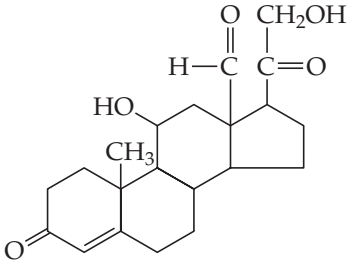


A prostaglandin

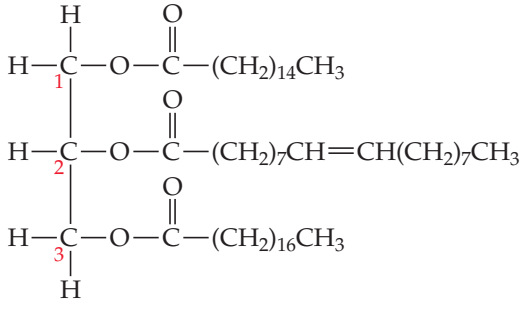
Worked Example 23.1 Identifying Lipid Families

Use Figure 23.1 to identify the family of lipids to which each of these molecules belongs.

(a)



(b)



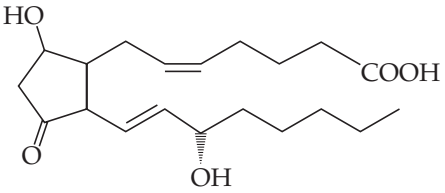
ANALYSIS Inspect the molecules and note their distinguishing characteristics. Molecule (a) has a four-member fused-ring system. Only sterols have this structure. Molecule (b) has three fatty acids esterified to a single backbone molecule—glycerol. Thus, (b) must be a member of the triacylglycerol family.

SOLUTION
Molecule (a) is a sterol, and molecule (b) is a triacylglycerol.

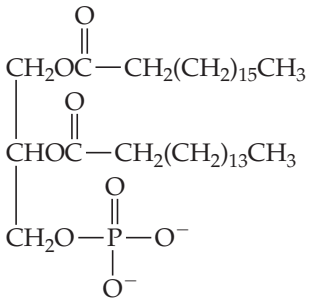
PROBLEM 23.1

Use Figure 23.1 to identify the family of lipids to which each of these molecules belongs.

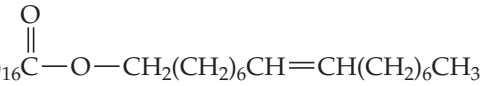
(a)



(b)



(c)



23.2 Fatty Acids and Their Esters

Learning Objective:

- Describe the characteristics of fatty acids and fatty acid esters.

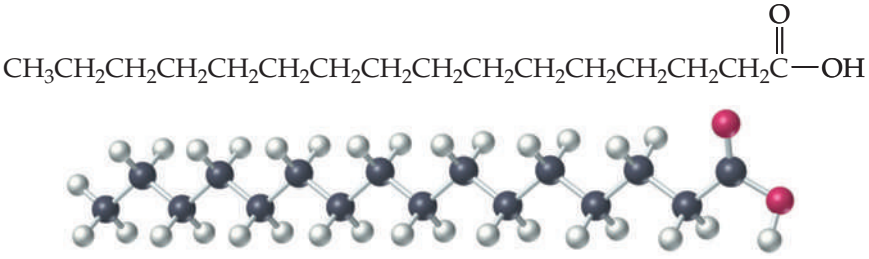
Naturally occurring fats and oils are triesters formed between glycerol and fatty acids. Fatty acids are long, unbranched hydrocarbon chains with a carboxylic acid group at one end. Most have even numbers of carbon atoms. Fatty acids may or may not contain carbon–carbon double bonds. Those containing only carbon–carbon single bonds are known as **saturated fatty acids;** those containing one or more carbon–carbon double bonds are known as **unsaturated fatty acids.** If double bonds are present in naturally occurring fats and oils, the double bonds are usually *cis* rather than *trans*.

CONCEPTS TO REVIEW Recall that an ester, RCOOR′, is formed from a carboxylic acid and an alcohol (Section 17.4).

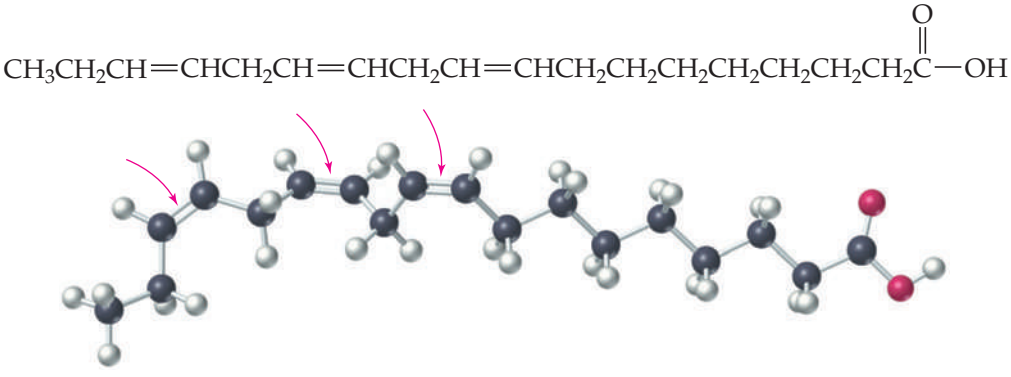
In the *cis* configuration, the groups attached to the double-bond carbons are on the same side of the double bond (Section 13.3).

Saturated fatty acid A long-chain carboxylic acid containing only carbon–carbon single bonds.

Unsaturated fatty acid A long-chain carboxylic acid containing one or more carbon–carbon double bonds.



A saturated fatty acid
(palmitic acid)



A cis unsaturated fatty acid
(linolenic acid)

Polyunsaturated fatty acid A long-chain carboxylic acid that has two or more carbon–carbon double bonds.

Degree of unsaturation The number of carbon–carbon double bonds in a molecule.

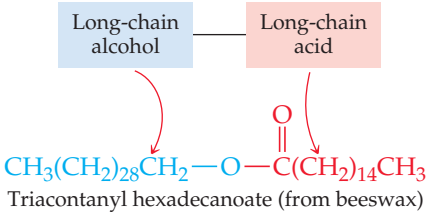
Some of the common fatty acids are listed in Table 23.1. Chemists use a shorthand nomenclature for fatty acids that avoids using the common names. This notation uses C for carbon followed by the number of carbon atoms present in the fatty acid, a colon, and the number of unsaturated bonds present. For example, lauric acid, which contains 12 carbon atoms and no double bonds, is represented by C12:0. Oleic acid is *monounsaturated,* that is, it has only one carbon–carbon double bond. The **polyunsaturated fatty acids** have more than one carbon–carbon double bond. The number of double bonds present in a fatty acid is referred to as the **degree of unsaturation.**

Table 23.1 Structures of Some Common Fatty Acids

Name	Typical Source	Number of Carbons	Number of Double Bonds	Condensed Formula	Condensed Notation	Melting Point (K)
Saturated						
Lauric	Coconut oil	12	0	$CH_3(CH_2)_{10}COOH$	C12:0	317
Myristic	Butter fat	14	0	$CH_3(CH_2)_{12}COOH$	C14:0	331
Palmitic	Most fats and oils	16	0	$CH_3(CH_2)_{14}COOH$	C16:0	336
Stearic	Most fats and oils	18	0	$CH_3(CH_2)_{16}COOH$	C18:0	343
Unsaturated						
Oleic	Olive oil	18	1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$ (*cis*)	C18:1	277
Linoleic	Vegetable oils	18	2	$CH_3(CH_2)_3(CH_2CH{=}CH)_2(CH_2)_7COOH$ (all *cis*)	C18:2	268
Linolenic	Soybean and canola oils	18	3	$CH_3(CH_2CH{=}CH)_3(CH_2)_7COOH$ (all *cis*)	C18:3	262
Arachidonic	Animal fat	20	4	$CH_3(CH_2)_4(CH_2CH{=}CH)_4(CH_2)_2COOH$ (all *cis*)	C18:4	223

Wax A mixture of monoesters of long-chain carboxylic acids with long-chain alcohols.

Example of a wax



Triacontanyl hexadecanoate (from beeswax)

Two of the polyunsaturated fatty acids, linoleic and linolenic, are essential in the human diet because the body does not synthesize them, even though these omega-6 and omega-3 fatty acids are needed for the synthesis of other lipids. Infants grow poorly and develop severe skin lesions if fed a diet lacking these acids. Adults usually have sufficient reserves in body fat to avoid such problems. A deficiency in adults can arise, however, after long-term intravenous feeding that contains inadequate essential fatty acids or among those surviving on limited and inadequate diets.

▲ This grebe is coated with oil spilled by a tanker that sank off Brittany on the northwest coast of France. If the oil is not removed from its feathers, the bird will perish.

Waxes

The simplest fatty acid esters in nature are waxes. A **wax** is a mixture of fatty acids and long-chain alcohol esters. The acids usually have an even number of carbon atoms, generally from 16 to 36 carbons, whereas the alcohols have an even number of carbon atoms ranging from 24 to 36 carbons. For example, a major component in beeswax is the ester formed from a 30-carbon alcohol (triacontanol) and a 16-carbon acid (palmitic acid). The waxy protective coatings on most fruits, berries, leaves, and animal furs have similar structures. Aquatic birds have a water-repellent waxy coating on their feathers. When caught in an oil spill, the waxy coating dissolves in the oil and the birds lose their buoyancy.

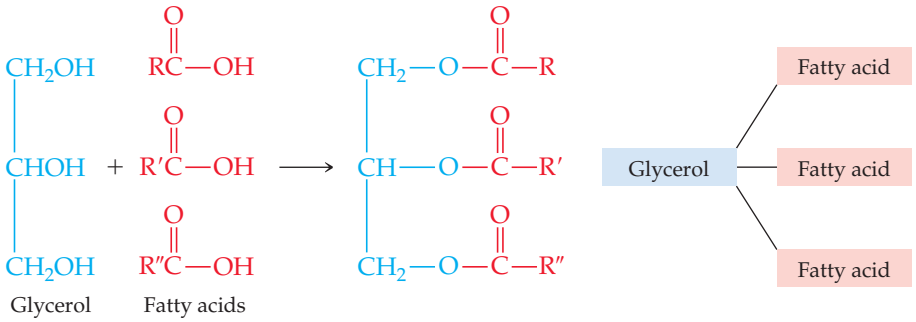
Triacylglycerols

Animal fats and vegetable oils are the most plentiful lipids in nature. Although they appear different—animal fats like butter and lard are solid, whereas vegetable oils like corn, olive, soybean, and peanut oil are liquid—their structures are

closely related. All fats and oils are composed of triesters of glycerol (propane-1,2,3-triol, also known as glycerin) with three fatty acids. They are named chemically as **triacylglycerols** but are often called **triglycerides.**

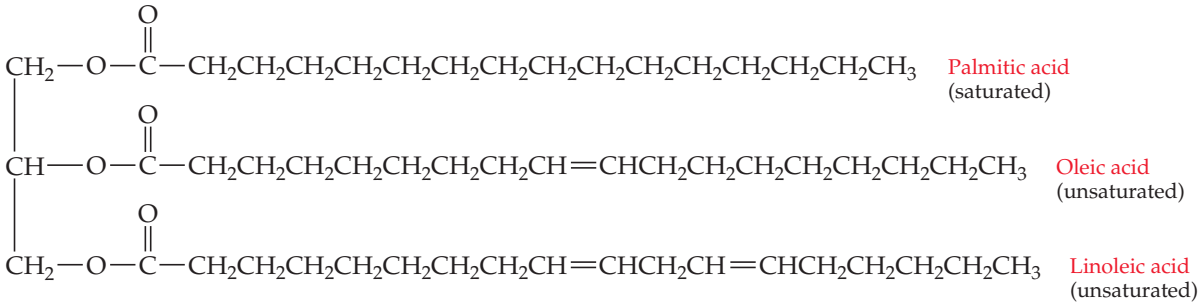
Triacylglycerol (triglyceride) A triester of glycerol with three fatty acids.

Triacylglycerols



The three fatty acids of any specific triacylglycerol are not necessarily the same, as is the case in the following molecule.

Example of a triacylglycerol



Furthermore, the fat or oil from a given natural source is a complex mixture of many different triacylglycerols. Table 23.2 lists the average composition of fats and oils from several different sources. Note particularly that vegetable oils consist almost entirely of unsaturated fatty acids, whereas animal fats contain a much larger percentage of saturated fatty acids. This difference in composition is the primary reason for the different melting points of fats and oils, as explained in the next section.

Table 23.2 Approximate Composition of Some Common Fats and Oils*

	Saturated Fatty Acids (mass %)			Unsaturated Fatty Acids (mass %)		
	C12:0	C14:0	C16:0	C18:0	C18:1	C18:2
Source	Lauric	Myristic	Palmitic	Stearic	Oleic	Linoleic
Animal Fat						
Lard	—	1	25	15	50	6
Butter	2	10	25	10	25	5
Human fat	1	3	25	8	46	10
Whale blubber	—	8	12	3	35	10
Vegetable Oil						
Corn	—	1	8	4	46	42
Olive	—	1	5	5	83	7
Peanut	—	—	7	5	60	20
Soybean	—	—	7	4	34	53

**Where totals are less than 100%, small quantities of several other acids are present, with cholesterol also present in animal fats.*

PROBLEM 23.2

One of the constituents of the carnauba wax used in floor and furniture polish is an ester of a 32-carbon straight-chain alcohol with a C20:0 straight-chain carboxylic acid. Draw the structure of this ester. (Use subscripts to show the numbers of connected CH_2 groups.)

PROBLEM 23.3

Draw the structure of a triacylglycerol whose components are glycerol and three oleic acid acyl groups.

KEY CONCEPT PROBLEM 23.4

(a) Which animal fat has the largest percentage of saturated fatty acids?
(b) Which vegetable oil has the largest percentage of polyunsaturated fatty acids?
(c) Which fat or oil has the largest percentage of the essential fatty acid linoleic acid?

Oil A mixture of triacylglycerols that is liquid because it contains a high proportion of unsaturated fatty acids.

Fat A mixture of triacylglycerols that is solid because it contains a high proportion of saturated fatty acids.

23.3 Properties of Fats and Oils

Learning Objective:

- List the physical properties of fats and oils and explain why they are different.

Table 23.1 shows that as the number of double bonds in a fatty acid increases, the melting point decreases. For example, the saturated 18-carbon acid (stearic) melts at 70°C (343 K), the monounsaturated 18-carbon acid (oleic) melts at 4°C (277 K), and the diunsaturated 18-carbon acid (linoleic) melts at –5°C (268 K). The same trend also holds true for triacylglycerols: the more highly unsaturated the acyl groups in a triacylglycerol, the lower its melting point. The dissimilarity in melting points between fats and oils is a consequence of this difference. Vegetable **oils** are lower melting because oils generally have a higher proportion of unsaturated fatty acids than animal **fats.**

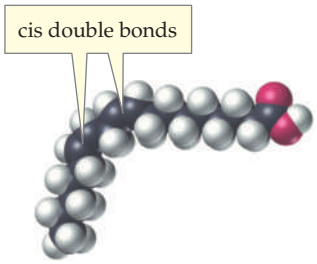
How do the double bonds make such a significant difference in the melting point? Compare the shapes of a saturated and an unsaturated fatty acid molecule in the margin.

The hydrocarbon chains in saturated acids are uniform in shape with identical angles at each carbon atom, and the chains are flexible, allowing them to nestle together. By contrast, the carbon chains in unsaturated acids have rigid kinks wherever they contain *cis* double bonds. The kinks make it difficult for such chains to fit next to each other in the orderly fashion necessary to form a solid. The more double bonds there are in a triacylglycerol, the harder it is for it to solidify. The shapes of the molecular models in Figure 23.2 further illustrate this concept.

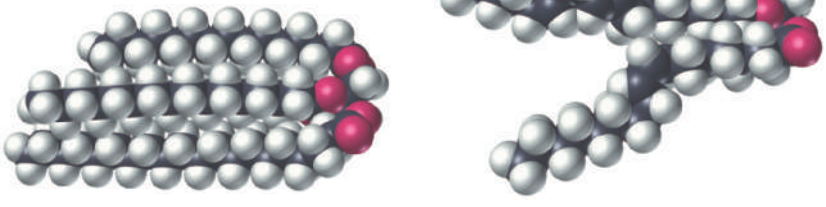
A saturated fat has only single C–C bonds and appears straight

Stearic acid, an 18-carbon saturated fatty acid

Unsaturated fats bend due to cis double bonds



Linoleic acid, an 18-carbon unsaturated fatty acid



A fat An oil

▲ **Figure 23.2**
Triacylglycerols from a fat and an oil.

CHEMISTRY IN ACTION

Lipids in the Diet

The major recognizable sources of fats and oils in our diet are butter and margarine, vegetable oils, the visible fat in meat, and chicken skin. In addition, triacylglycerols in meat, poultry, fish, dairy products, and eggs add saturated fats to our diet, along with small quantities of cholesterol. Vegetable oils, such as those in nuts, seeds, and whole-grain cereals, have a higher unsaturated fatty acid content and no cholesterol. Vegetable oils never contain cholesterol because plants do not synthesize cholesterol.

Fats and oils are a popular component of our diet: they taste good, give a pleasant texture to food, and, because they are digested slowly, give a feeling of satisfaction after a meal. The percentage of energy from fats and oils in the average U.S. diet has declined from 40–45%, to around 35%, a number approaching the recommended 30%. Excess energy from dietary fats and oils is mostly stored as fat in adipose tissue.

Concern for the relationships among saturated fats, cholesterol levels, and various diseases—most notably heart disease and cancer (see the Chemistry in Action "Fat Storage, Lipids, and Atherosclerosis," Chapter 24)—caused a reevaluation of the kinds of fats recommended for consumption. The consumption of butter, eggs, beef, and whole milk (all containing relatively high proportions of saturated fat and cholesterol) decreased in response to new nutrition guidelines. This decrease in fat intake is relative, however; at the same time, the total amount of energy consumed increased. The increase is attributed to an increase in carbohydrates eaten. So, unfortunately, the change in fat intake did not coincide with a reduction in obesity, which is a mass 20% over the desirable mass for a person's height, sex, and activity level or a body mass index (BMI) of 30 or greater. In fact, concern has been accelerating in recent years over a rise in obesity in the U.S. population and its inevitable association with heart disease and diabetes.

Several organizations, including the U.S. Food and Drug Administration (FDA), recommend a diet with not more than 30% of its energy from fats and oils. In a daily diet of 9200 J, which is about right for teenage girls, active women, and sedentary men, 30% from fats and oils is approximately 73 grams, the amount in 6 tablespoons of butter. Men and very active women require more daily energy and can include proportionately more fats in their diets.

▲ A selection of appealing but high-fat foods.

The Nutrition Facts labels (see the Chemistry in Action "Vitamins, Minerals, and Food Labels," Chapter 19) list the energy (in J) from fat, grams of fat (which includes all triacylglycerols), and grams of saturated fat in a single serving of a commercially prepared food. The FDA further recommends that not more than 10% of daily energy come from saturated fat and not more than 300 mg of cholesterol be included in the daily diet. For those with the goal of 9200 J/day, the limit is 24 g of saturated fats. In order to reduce dietary intake of saturated fats you should choose low-fat varieties of foods and foods that contain different kinds of fats. The foods highest in cholesterol are high-fat dairy products, liver, and egg yolks.

CIA Problem 23.1 Fats and oils are major sources of triacylglycerols. List some other foods that are associated with high-lipid content.

CIA Problem 23.2 According to the FDA, what is the maximum percentage of your daily energy that should come from fats and oils?

CIA Problem 23.3 Which one should you choose for a treat—a small dipped ice cream cone from kiosk A or two oatmeal cookies from kiosk B? Some of the nutrition facts for these choices are listed in the following table. To decide, consider which snack would best help you stay within the nutrition guidelines regarding daily intake of total fat and saturated fat in the diet.

Food	Total Energy (J)	Total Fat (g)	Saturated Fat (g)	% energy from Fat	Carbohydrates (g)	% energy from Carbohydrates
Cone	1420 J	17	9	45	42	49
Two Cookies	1250 J	12	2	36	46	61

HANDS-ON CHEMISTRY 23.1

How can you tell if a food contains fat? Use this simple test. Place a small amount of your sample (cookie, cracker, cereal, candy bar, carrot, etc.) on a piece of paper (notebook, newspaper, or napkin). Observe the paper and sample in 15 minute intervals for an hour. What did you see? Did you expect this? Foods containing a lot of fat will leave a large "grease" spot while foods that contain little fat will leave either no greasy spot or a small one.

▲ Where the fat goes? Each of these adipose tissue cells holds a globule of fat (magnified more than 500 times).

LOOKING AHEAD Triacylglycerols from plants and animals are a major component of our diet. In our bodies, they are the depots for energy storage. Therefore, in considering the metabolism of lipids, it is the metabolism of triacylglycerols that is of greatest interest. This topic is discussed in Chapter 24.

Triacylglycerols are uncharged, nonpolar, hydrophobic molecules. When stored in fatty tissue they coalesce, and the interior of an adipocyte (fat cell) is occupied by one large fat droplet with the cell's nucleus pushed to one side. The primary function of triacylglycerols is long-term storage of energy for the organism. In addition, adipose tissue serves to provide thermal insulation and protective padding. Most fatty tissue is located under the skin or in the abdominal cavity, where it cushions the organs.

We are accustomed to the characteristic yellow color and flavors of cooking oils, but these are caused by natural materials carried along during production of the oils from plants; pure oils are colorless and odorless. Overheating, or exposure to air or oxidizing agents, causes decomposition to products with unpleasant odors or flavors, creating what we call a *rancid oil*. Antioxidants such as phenolic compounds are added to prepared foods to prevent oxidation of their oils.

Properties of the Triacylglycerols in Natural Fats and Oils

- Nonpolar and hydrophobic
- No ionic charges
- Solid triacylglycerols (fats)—high proportion of saturated fatty acid chains
- Liquid triacylglycerols (oils)—high proportion of unsaturated fatty acid chains

Worked Example 23.2 Comparing Melting Points

Which of these two fatty acids has the higher melting point?

(a) $CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2(CH_2)_6\overset{\overset{O}{\|}}{C}{-}OH$ **(b)** $CH_3(CH_2)_5CH{=}CHCH_2(CH_2)_6\overset{\overset{O}{\|}}{C}{-}OH$

ANALYSIS First, determine the chain length (number of carbon atoms) and the number of unsaturated bonds present. In general, the more carbon atoms present in a molecule, the higher the melting point. However, the higher the number of unsaturated bonds, the lower the melting point. The degree of unsaturation is more important than the number of carbon atoms when the number of carbon atoms is identical or similar.

SOLUTION

Molecule (a) has 18 carbon atoms and two unsaturated bonds. Molecule (b) has 16 carbon atoms and one unsaturated bond. Although molecule (a) is slightly larger than molecule (b) and would be expected to have a higher melting point, molecule (a) has two double bonds, whereas molecule (b) has only one double bond. Since the degree of unsaturation is more important in these similarly sized molecules, molecule (b) has the higher melting point.

PROBLEM 23.5

Draw the complete structural formula of arachidonic acid (Table 23.1) in a way that shows the *cis* stereochemistry of its four double bonds.

PROBLEM 23.6

Can there be any chiral carbon atoms in triacylglycerols? If so, which ones can be chiral and what determines their chirality?

KEY CONCEPT PROBLEM 23.7

What noncovalent interactions (covered in Section 8.2) hold lipid molecules together? Are these forces generally weak or strong? Why do lipids not mix readily with water?

23.4 Chemical Reactions of Triacylglycerols

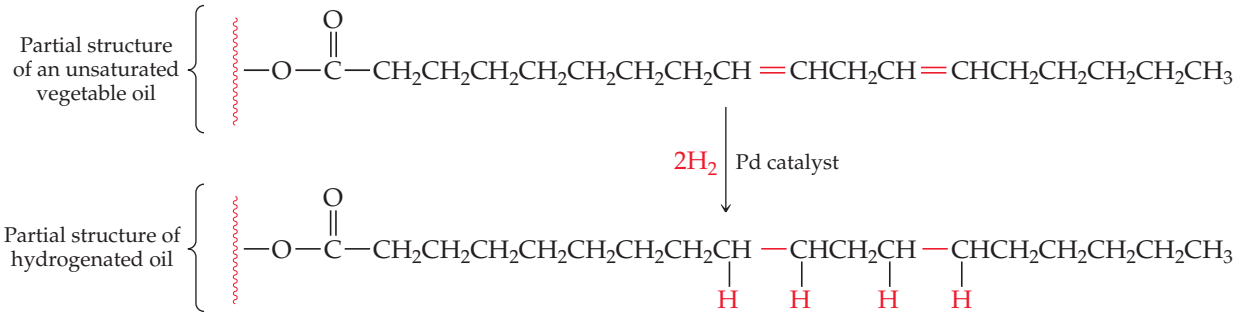
Learning Objective:

- Describe hydrogenation and hydrolysis reactions of triacylglycerols, and, given the reactants, predict the products.

Hydrogenation

The carbon–carbon double bonds in unsaturated fatty acids such as those found in triacylglycerides in vegetable oils can be hydrogenated to yield saturated fats in the same way

that any alkene can react with hydrogen to yield an alkane (see Section 13.6). Margarine and solid cooking fats (shortenings) are produced commercially by hydrogenation of vegetable oils to give a product chemically similar to that found in animal fats.



The extent of hydrogenation varies with the number of double bonds in the unsaturated acids and their locations. In general, the number of double bonds is reduced in a stepwise fashion from three to two to one. By controlling the extent of hydrogenation and monitoring the composition of the product, it is possible to control consistency. In margarine, for example, only about two-thirds of the double bonds present in the starting vegetable oil are hydrogenated. Most of the remaining double bonds, which vary in their locations, are left intact so that the margarine has exactly the right consistency to remain soft in the refrigerator and melt on warm toast. However, partial hydrogenation, to create margarine, results in the rearrangement of *cis* bonds to *trans* bonds in the partially hydrogenated fatty acids. Research indicates consumption of *trans* fats, which do not occur naturally, poses health risks.

PROBLEM 23.8

Write an equation for the complete hydrogenation of triolein, the triacylglycerol with three oleic acid acyl groups for which you drew the structure in Problem 23.3. Name the fatty acid from which the resulting acyl groups are derived.

PROBLEM 23.9

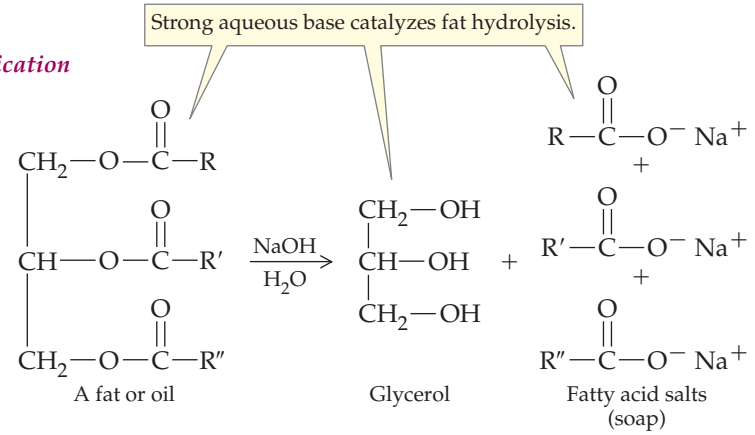
Butter and an equally solid margarine both contain an abundance of saturated fatty acids. What lipid that has been identified as a health hazard is not present in margarine but is present in butter? Conversely, what other lipid that may cause health problems is present in large amounts in some margarines but is present in small amounts in butter as a naturally occurring lipid?

Hydrolysis of Triacylglycerols

Triacylglycerols, like all esters, can be hydrolyzed—that is, they can react with water to form their carboxylic acids and alcohols. In the body, this hydrolysis is catalyzed by enzymes (hydrolases) and is the first reaction in the digestion of dietary fats and oils.

Commercial hydrolysis of fats and oils is usually carried out by strong aqueous bases (NaOH or KOH) and is called *saponification* (pronounced sae-*pon*-if-i-*ka*-tion, from the Latin *sapon,* soap [see Section 17.6]). The initial products of saponification of a fat or oil molecule are one molecule of glycerol and three molecules of fatty acid carboxylate salts:

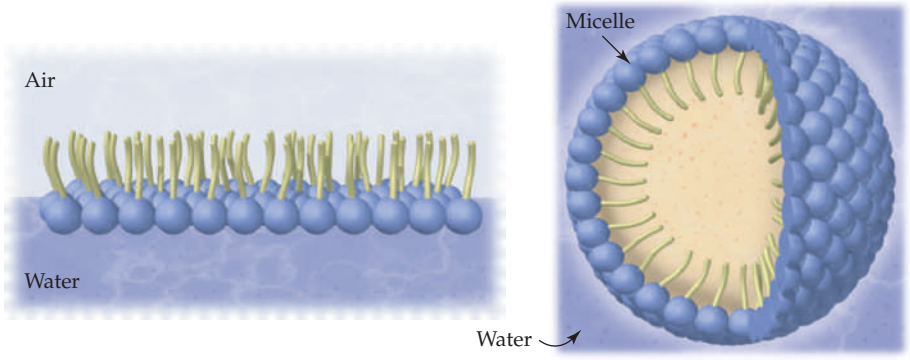
Saponification



Soap The mixture of salts of fatty acids formed by saponification of animal fat.

The fatty acid salts produced by base hydrolysis of triacylglycerols are referred to as **soaps.** Soaps can sequester other molecules because the two ends of a soap molecule are so different. The sodium salt end is ionic and therefore hydrophilic (water-loving); it tends to dissolve in water. The long hydrocarbon chain portion of the molecule, however, is nonpolar and therefore hydrophobic (water-fearing). When soap is dispersed in water, the big, organic anions cluster together so that their long, hydrophobic hydrocarbon tails are in contact, creating a nonpolar microenvironment. At the same time, their hydrophilic ionic heads on the surface of the cluster stick out into the water. The resulting spherical clusters are called **micelles** (Figure 23.3). Grease and dirt become coated by the nonpolar tails of the soap molecules and trapped in the center of the micelles as they form. Once suspended within micelles, the grease and dirt can be rinsed away. In exactly the same way soaps sequester greasy dirt, polar lipids form micelles in the bloodstream to transport neutral lipids trapped inside the micelles through the body.

Micelle A spherical cluster formed by the aggregation of soap or detergent molecules so that their hydrophobic ends are in the center and their hydrophilic ends are on the surface.



▶ Figure 23.3
Soap or detergent molecules in water.
The hydrophilic ionic ends (blue spheres) remain in the water. At the surface of the water, a film forms with the hydrocarbon chains (yellow tails) on the surface. Within the solution, the hydrocarbon chains cluster together at the centers of micelles. Greasy dirt is dissolved in the oily center and carried away. Lipids are transported in the bloodstream in similar micelles, as described in Section 24.2.

PROBLEM 23.10

Draw a saturated fatty acid salt that could participate in micelle formation. Indicate the hydrophilic head and the hydrophobic tail. Which end will be on the interior of the micelle and which end will be on the exterior of the micelle?

PROBLEM 23.11

Write the complete equation for the hydrolysis of a triacylglycerol in which the fatty acids are two molecules of stearic acid and one of oleic acid (see Table 23.1).

23.5 Phospholipids and Glycolipids

Learning Objective:

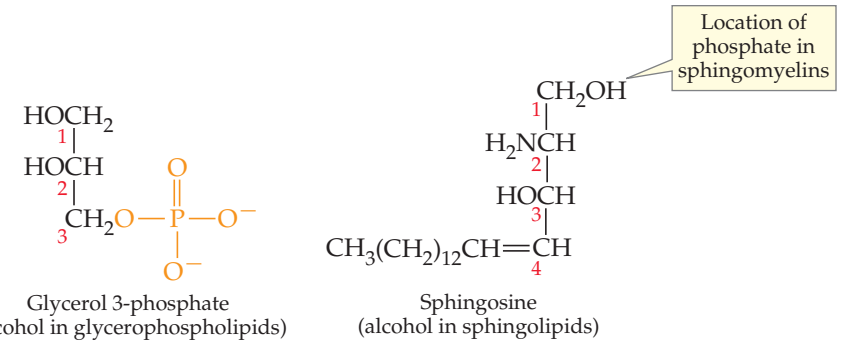
- Recognize phospholipids and glycolipids and describe their functions.

Cell membranes separate the aqueous interior of cells from the aqueous environment surrounding the cells. To accomplish this, the membranes establish a hydrophobic barrier between the two watery environments. Lipids are ideal for this function. The three major kinds of cell membrane lipids in animals are *phospholipids, glycolipids,* and *cholesterol.*

Phospholipids

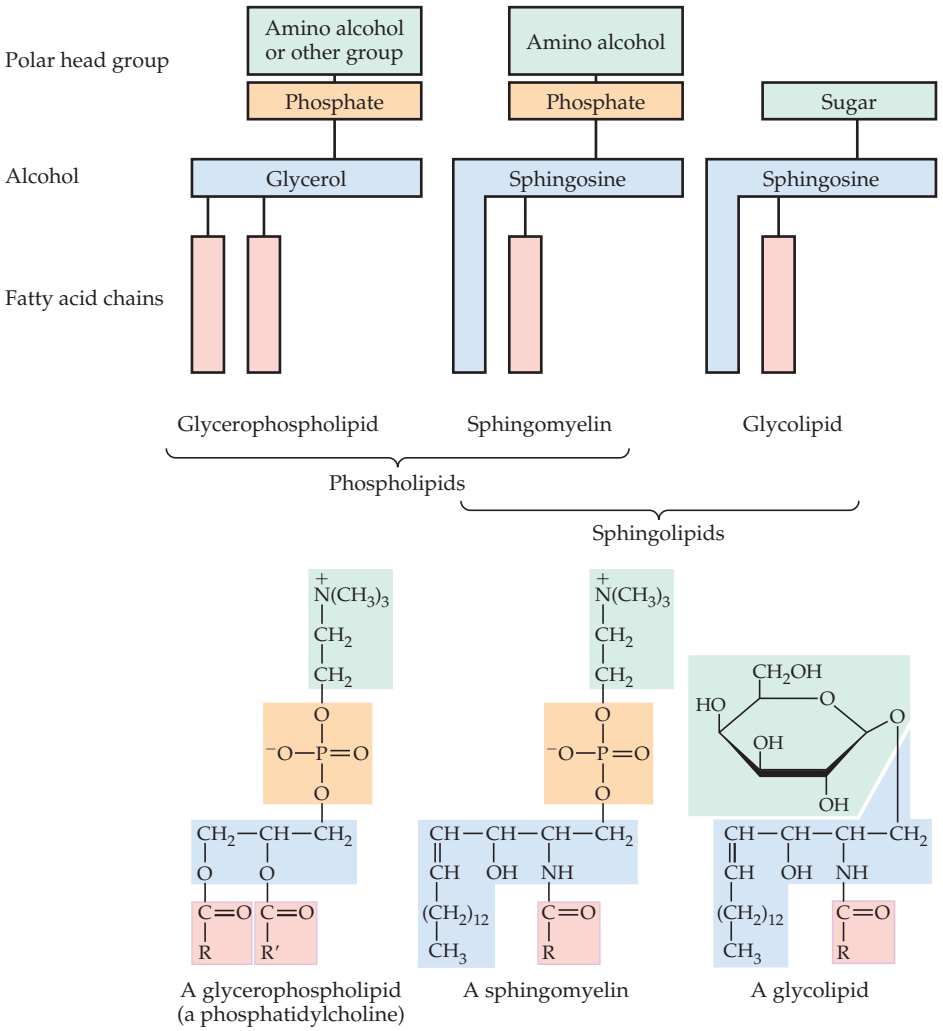
Phospholipid A lipid that has an ester link between phosphoric acid and an alcohol (either glycerol or sphingosine).

Phospholipids contain a phosphate ester link between phosphoric acid and an alcohol. They are built up from either glycerol (to give *glycerophospholipids*) or from the alcohol sphingosine (to give *sphingomyelins*). The general structures of these lipids and the relationships of their classification are shown in Figure 23.4. Because phospholipids have ionized phosphate groups at one end, they are similar to soap molecules in having ionic, hydrophilic heads and hydrophobic tails (see Figure 23.3). They differ, however, in having *two* tails instead of one.



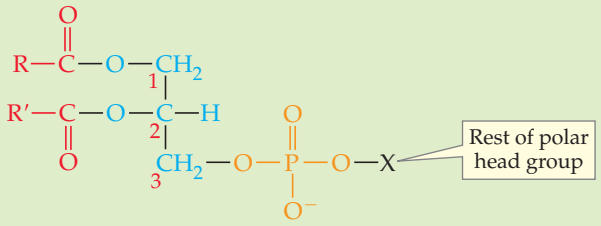
Glycerophospholipids (also known as **phosphoglycerides**) are triesters of glycerol 3-phosphate and are the most abundant membrane lipids. Two of the ester bonds are with fatty acids, which provide the two hydrophobic tails (pink in the general glycerophospholipid structure in Figure 23.4). The fatty acids may be any of the fatty acids normally present in fats or oils. The fatty acid acyl group (R—C=O) bonded to C1 of glycerol is usually saturated, whereas the fatty acyl group at C2 is usually unsaturated. At the third position in glycerophospholipids, there is a phosphate ester group (orange in Figure 23.4). This phosphate has a second ester link to one of several different OH-containing compounds, often ethanolamine, choline, or serine (green in Figure 23.4; see structures in Table 23.3).

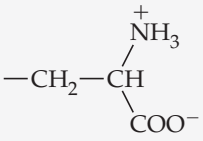
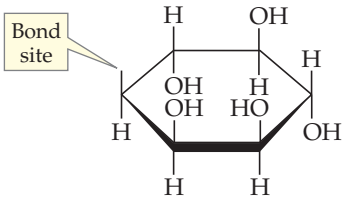
Glycerophospholipid (phosphoglyceride) A lipid in which glycerol is linked by ester bonds to two fatty acids and one phosphate, which is in turn linked by another ester bond to an amino alcohol (or other alcohol).



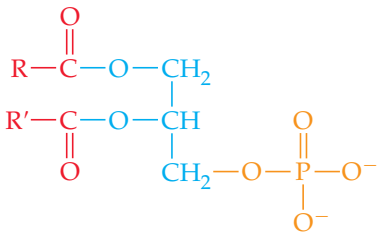
◀ **Figure 23.4**
Membrane lipids.
The top row shows the identity of the components of each class of membrane lipid. The bottom row shows a structural example of each class. Note that all classes have two hydrocarbon tails and polar, hydrophilic head groups. In the sphingolipids (sphingomyelins and glycolipids), one of the two hydrocarbon tails is part of the alcohol sphingosine (blue).

Table 23.3 Some Glycerophospholipids

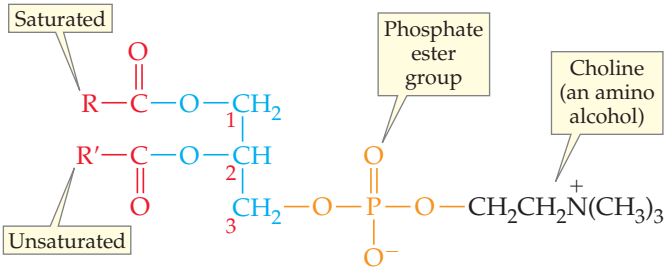


Precursor of X (HO–X)	Formula of X	Name of Resulting Glycerophospholipid Family	Function
Water	—H	Phosphatidate	Basic structure of glycerophospholipids
Choline	$-CH_2CH_2\overset{+}{N}(CH_3)_3$	Phosphatidylcholine	Basic structure of lecithins; most abundant membrane phospholipids
Ethanolamine	$-CH_2CH_2\overset{+}{N}H_3$	Phosphatidylethanolamine	Membrane lipids
Serine		Phosphatidylserine	Present in most tissues; abundant in brain
myo-Inositol		Phosphatidylinositol	Relays chemical signals across cell membranes

The glycerophospholipids are named as derivatives of phosphatidic acids. In the following molecule on the right, for example, the phosphate ester link to the right of the phosphorus atom is the amino alcohol choline, $HOCH_2CH_2N^+(CH_3)_3$. Lipids of this type are known as either *phosphatidylcholines* or *lecithins*. (A substance referred to in the singular as either lecithin or phosphatidylserine, or any of the other classes of phospholipids, is usually a mixture of molecules with different R and R′ tails.) Examples of some other classes of glycerophospholipids are included in Table 23.3.



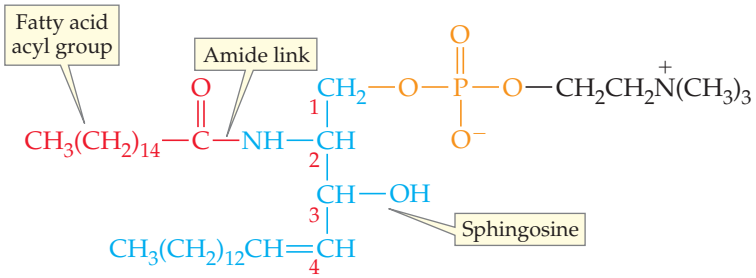
A phosphatidate



A phosphatidylcholine
(a glycerophospholipid that is a lecithin)

Because of their combination of hydrophobic tails and hydrophilic head groups, the glycerophospholipids are *emulsifying agents*—substances that surround droplets of nonpolar liquids and hold them in suspension in water (see the micelle diagram in Figure 23.3). You will find lecithin, usually obtained from soybean oil, listed as an ingredient in chocolate bars and other foods, where it is added to keep oils from separating out. It is the lecithin in egg yolk that emulsifies the oil droplets in mayonnaise.

In **sphingolipids,** the amino alcohol sphingosine provides one of the two hydrophobic hydrocarbon tails (blue here and in Figure 23.4). The second hydrocarbon tail is from a fatty acid acyl group connected by an amide link to the $-NH_2$ group in sphingosine (red in the following diagram; pink in Figure 23.4).



A sphingomyelin (a sphingolipid)

Sphingomyelins are sphingosine derivatives with a phosphate ester group at C1 of sphingosine. The sphingomyelins are major components of the coating around nerve fibers (the *myelin sheath*) and are present in large quantities in brain tissue. A diminished amount of sphingomyelins and phospholipids in brain myelin has been associated with multiple sclerosis. Whether this is a cause or a result of multiple sclerosis is unclear. The orientation of the hydrophilic and hydrophobic regions of a sphingomyelin is shown in Figure 23.5, together with a general representation of this and other types of cell membrane lipids used in drawing cell membranes.

PROBLEM 23.12

Lecithins are often used as food additives to provide emulsification. How do they accomplish this purpose?

PROBLEM 23.13

Identify the products formed by complete hydrolysis of all ester bonds in (a) the phosphatidylcholine on page 760 and (b) the sphingomyelin in Figure 23.5.

Glycolipids

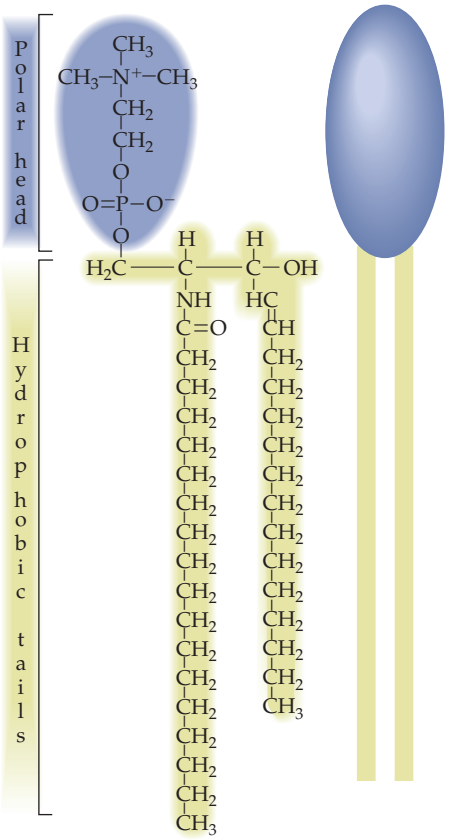
Glycolipids, like sphingomyelins, are derived from sphingosine, a diol with an amine group. They differ from phospholipids by having a carbohydrate group at C1 (orange in the glycolipid in Figure 23.4) instead of a phosphate bonded to an amino alcohol.

Like glycoproteins (see Section 22.8), glycolipids reside in cell membranes with their short carbohydrate chains extending into the fluid surrounding the cells. Here, they function as receptors that, as you will see in Chapter 28, are essential for recognizing chemical messengers, other cells, pathogens, and drugs. The general structures of these lipids and the relationships of their classification are shown at the top in Figure 23.4. Note the overlapping classes of membrane lipids. Glycolipids and sphingomyelins both contain sphingosine and are therefore classified as sphingolipids, whereas glycerophospholipids and sphingomyelins both contain phosphate groups and are therefore classified as phospholipids.

The glycolipid molecule is classified as a *cerebroside*. Cerebrosides, which contain a single monosaccharide, are particularly abundant in nerve cell membranes in the brain, where the monosaccharide is D-galactose. They are also found in other cell membranes, where the sugar unit is D-glucose.

Sphingolipid A lipid derived from the amino alcohol sphingosine.

▲ Lecithin (phosphatidylcholine) is the emulsifying agent in most chocolates.

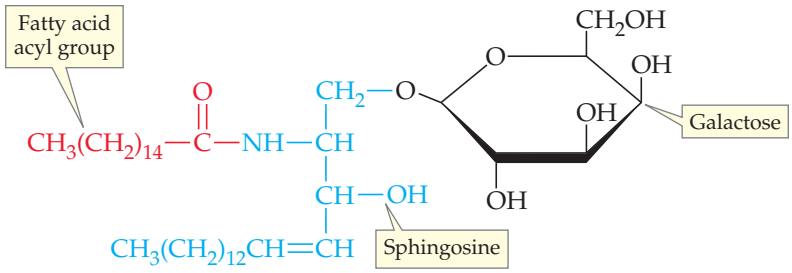


A sphingomyelin

▲ **Figure 23.5**
A sphingomyelin, showing its polar, hydrophilic head group and its two hydrophobic tails.
The drawing on the right is the representation of phospholipids used in picturing cell membranes. It shows the relative positions of the hydrophilic head and the hydrophobic tails.

Glycolipid A lipid with a fatty acid bonded to the C2 $-NH_2$ group and a sugar bonded to the C1 $-OH$ group of sphingosine.

A glycolipid



A glycolipid
(a cerebroside)

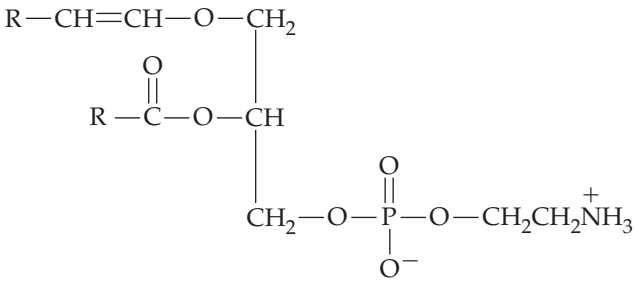
Gangliosides are glycolipids in which the carbohydrate is a small polysaccharide (an oligosaccharide) rather than a monosaccharide. Over 60 different gangliosides are known. The oligosaccharides responsible for blood types are ganglioside molecules (see the Chemistry in Action "Cell-Surface Carbohydrates and Blood Type" in Chapter 20).

Tay-Sachs disease, a genetic disorder found mainly in persons of Eastern European Jewish descent, Cajuns, and French Canadians, is the result of a deficiency in the enzyme β-hexosaminidase A, which causes an elevated concentration of a particular ganglioside in the brain. An infant born with this defect suffers mental retardation and liver enlargement and usually dies by age 3. Tay-Sachs is one of a group of sphingolipid storage diseases. Another well-known, fatal disease in this group is Niemann-Pick disease, in which sphingomyelin accumulates due to a deficiency in the enzyme sphingomyelinase. These metabolic diseases result from deficiencies in the supply of enzymes that break down sphingolipids.

Currently there is no known therapy for either Tay-Sachs disease or Niemann-Pick disease. The harmful consequences result from the *storage* of the excess sphingolipids. A more promising outcome may be available for those with Gaucher's disease, the most common lipid storage disease. In Gaucher's patients, fats accumulate in many organs (liver, lungs, and brain) due to a deficiency in the enzyme glucocerebrosidase. Enzyme replacement therapy allows many of these patients to avoid some of the nonneurological effects of Gaucher's disease.

Worked Example 23.3 Identifying Complex Lipid Components

A class of membrane lipids known as *plasmalogens* has the general structure shown here. Identify the component parts of this lipid and choose the terms that apply to it: phospholipid, glycerophospholipid, sphingolipid, glycolipid. Is it most similar to a phosphatidylethanolamine, a phosphatidylcholine, a cerebroside, or a ganglioside?



ANALYSIS Compare each part of the molecule with the basic components found in complex lipids and decide which lipid component the part resembles most. The molecule contains a phosphate group and thus is a phospholipid. The glycerol backbone of three carbon atoms bonded to three oxygen atoms is also present, so the compound is a glycerophospholipid, but one in which there is an ether linkage ($—CH_2—O—CH=CHR$) in place of one of the ester linkages. The phosphate group is bonded to ethanolamine ($HOCH_2CH_2NH_2$).

This compound is not a sphingolipid or a glycolipid because it is not derived from sphingosine; for the same reason it is not a cerebroside or a ganglioside. Except for the ether group in place of an ester group, the compound has the same structure as a phosphatidylethanolamine.

SOLUTION

The terms that apply to this plasmalogen are *phospholipids* and *glycerophospholipid*. It has a structure nearly identical to phosphatidylethanolamine, so it is most similar to phosphatidylethanolamine.

PROBLEM 23.14

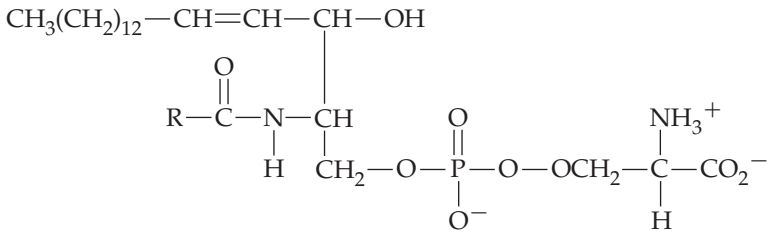
Draw the structure of the sphingomyelin that contains a myristic acid acyl group. Identify the hydrophilic head group and the hydrophobic tails in this molecule.

PROBLEM 23.15

Draw the structure of the glycerophospholipid that contains a stearic acid acyl group, an oleic acid acyl group, and a phosphate bonded to ethanolamine.

PROBLEM 23.16

Which of the following terms apply to the compound shown below? (Hint: Look at the functional groups and the bonds involved to begin analyzing the compound part by part in comparison to the lipids discussed in this chapter.)



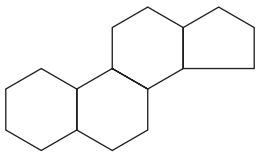
(a) A phospholipid
(b) A steroid
(c) A sphingolipid
(d) A glycerophospholipid
(e) A lipid
(f) A phosphate ester
(g) A ketone

23.6 Sterols

Learning Objective:

- Identify sterols and their derivatives and describe their structures and roles.

The steroid nucleus



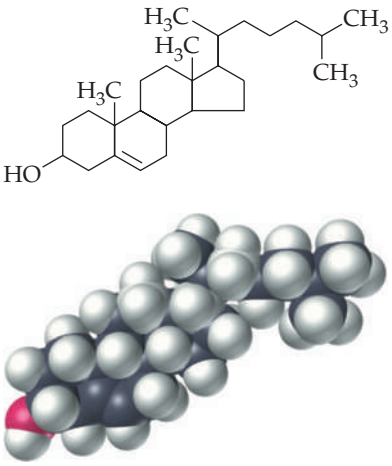
All **sterols** have a common central structure composed of the four connected rings, as shown in the margin. Because they are soluble in hydrophobic solvents and not in water, sterols are classified as lipids.

Sterol A lipid whose structure is based on a fused tetracyclic (four-ring) carbon skeleton.

Sterols have many roles throughout both the plant and animal kingdoms. In human biochemistry, the main sterol is cholesterol, which is an important component of cell membranes. The major functions of sterols other than cholesterol are as the bile acids that are essential for the digestion of fats and oils in the diet (Section 24.1) and as hormones.

Sterols are discussed in their role as hormones in Chapter 28 and their connection to heart disease in the Chemistry in Action "Fat Storage, Lipids, and Atherosclerosis" in Chapter 24.

Cholesterol



▲ Cholesterol is shown here in the line structure (upper image) and in the space filling structure (lower image).

Cholesterol has the molecular structure and shape shown in the margin.

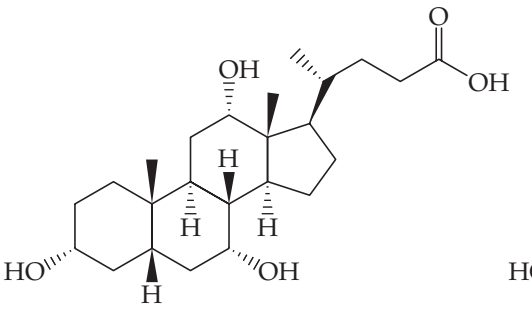
Cholesterol is the most abundant animal sterol. The body of a 60 kg person contains about 75 g of cholesterol, which serves two important functions: as a component of cell membranes and as the starting material for the synthesis of all other sterols. "Cholesterol" has become a household word because of its presence in the arterial plaque that contributes to heart disease. Some cholesterol is obtained from the diet, but most of our cholesterol is synthesized in the liver. Even on a strict no-cholesterol diet, an adult's organs can manufacture approximately 800 mg of cholesterol per day.

The molecular model of cholesterol reveals the nearly flat shape of the molecule. Except for its —OH group, cholesterol is hydrophobic. Within a cell membrane, cholesterol molecules are distributed among the hydrophobic tails of the phospholipids. Because cholesterol is more rigid than hydrophobic phospholipid tails, the cholesterol molecules help to maintain the structural rigidity of the membrane. Approximately 25% of liver cell membrane lipid is cholesterol.

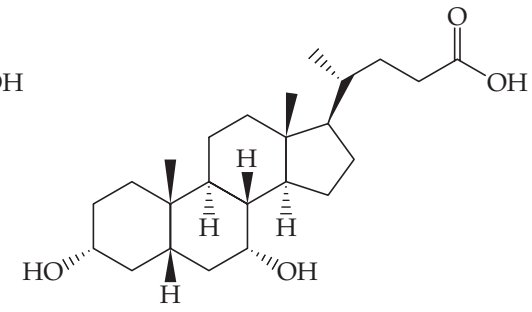
Bile Acids

Bile acids are essential for the emulsification of fats during digestion. Synthesized in liver cells from cholesterol and stored in the gall bladder until release into the small intestine is stimulated by a meal, these molecules have a polar end and a nonpolar end. Solubility of bile acids is increased by conjugation with taurine, a cysteine derivative, or glycine. This structural alteration increases solubility and enhances the formation of micelles of bile acids and fats in the digestive system, with the polar heads exposed to the aqueous medium of the small intestine and the nonpolar ends and fats on the interior of the micelle. Formation of micelles is essential for the digestion of dietary fat, as you will see in Chapter 24.

Note the acidic group added to cholesterol in each of the two most common bile acids, cholic acid and chenodeoxycholic acid. In the intestinal tract, these acids are ionized to anions and referred to as *bile* salts.

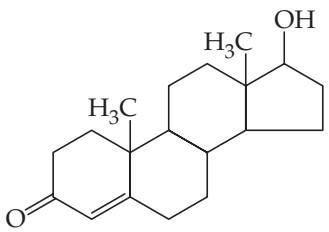


Cholic acid



Chenodeoxycholic acid

Steroid Hormones

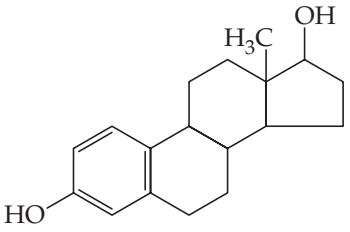


Testosterone
(an androgen)

The steroid hormones are divided according to function into three types. *Mineralocorticoids,* such as *aldosterone,* regulate the delicate cellular fluid balance between Na^+ and K^+ ions (hence the "mineral" in their name). The second type, *glucocorticoids,* such as cortisol (also known as *hydrocortisone*) and its close relative cortisone, help to regulate glucose metabolism and inflammation. You have probably used an anti-inflammatory ointment containing hydrocortisone to reduce the swelling and itching of poison ivy or some other skin irritation. The third type of steroid hormones is the family of *sex hormones.* The two most important male sex hormones, or *androgens,* are *testosterone* and *androsterone.* They are responsible for the development of male secondary sex characteristics during puberty and for promoting tissue and muscle growth. *Estrone* and *estradiol,* the female hormones known as *estrogens,* are synthesized from testosterone,

primarily in the ovaries but also to a small extent in the adrenal cortex. Estrogens govern development of female secondary sex characteristics and participate in regulation of the menstrual cycle. We will learn more about the signaling properties of the sex hormones in Chapter 28. The structures of testosterone and estradiol are shown in the margin. Note the steroid ring system common to these molecules.

In addition to the several hundred known steroids isolated from plants and animals, a great many more have been synthesized in the laboratory in the search for new drugs. You will discover more about steroids as cellular signals in Chapter 28.



Estradiol
(an estrogen)

23.7 Cell Membranes: Structure and Transport

Learning Objectives:

- Identify the membrane lipids and describe their structures and roles.
- Describe the general structure of a cell membrane and its chemical composition.
- Distinguish between passive transport and active transport and between simple diffusion and facilitated diffusion.

Every cell in your body is surrounded by a membrane. Cell membranes keep the interior of the cell separate from the exterior world, selectively permitting ions and molecules to enter or leave the cell. Lipids comprise most of the cell membrane, but proteins are also involved as are carbohydrates bonded either to lipids or proteins.

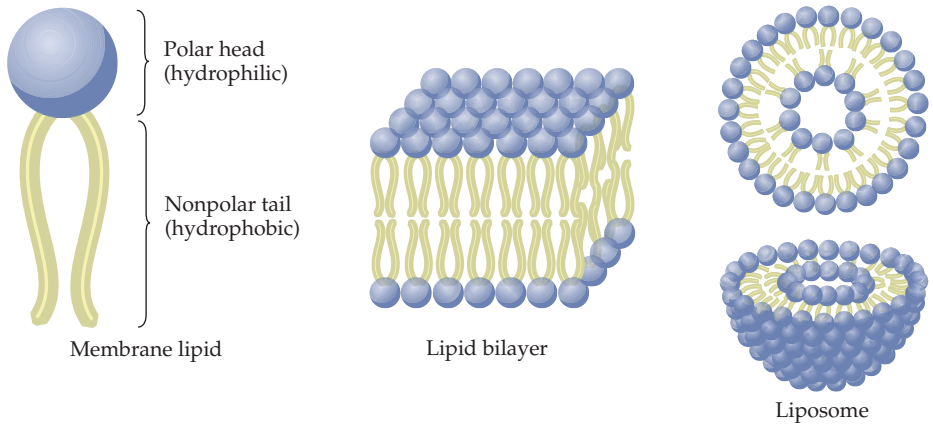
Membrane Structure

Phospholipids provide the basic structure of cell membranes, where they aggregate in a closed, sheet-like, *double leaflet* structure—the **lipid bilayer** (Figure 23.6). The bilayer is formed by two parallel layers of lipids oriented so that the ionic head groups are exposed to the aqueous environments on either side of the bilayer. The nonpolar tails cluster together in the middle of the bilayer, where they interact and avoid water. Each half of the bilayer is termed a *leaflet*.

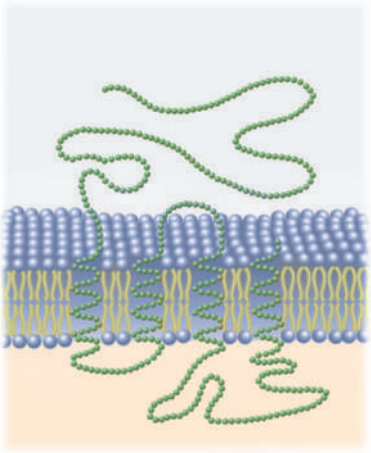
Lipid bilayer The basic structural unit of cell membranes; composed of two parallel sheets of membrane lipid molecules arranged tail to tail.

The bilayer is a favorable arrangement for phospholipids—it is highly ordered and stable but still flexible. When phospholipids are shaken vigorously with water, they spontaneously form **liposomes**—small spherical vesicles with a lipid bilayer surrounding an aqueous center, as shown in Figure 23.6. Water-soluble substances can be trapped in the center of liposomes, and lipid-soluble substances can be incorporated into the bilayer. Liposomes are potentially useful as carriers for drug delivery because they can fuse with cell membranes and empty their contents into the cell. One approved medical use of liposomes targets systemic fungal infections. Individuals with compromised immune systems due to acquired immunodeficiency syndrome (AIDS) are especially

Liposome A spherical structure in which a lipid bilayer surrounds a water droplet.



◀ **Figure 23.6**
Aggregation of membrane lipids. The lipid bilayer provides the basic structure of a cell membrane.



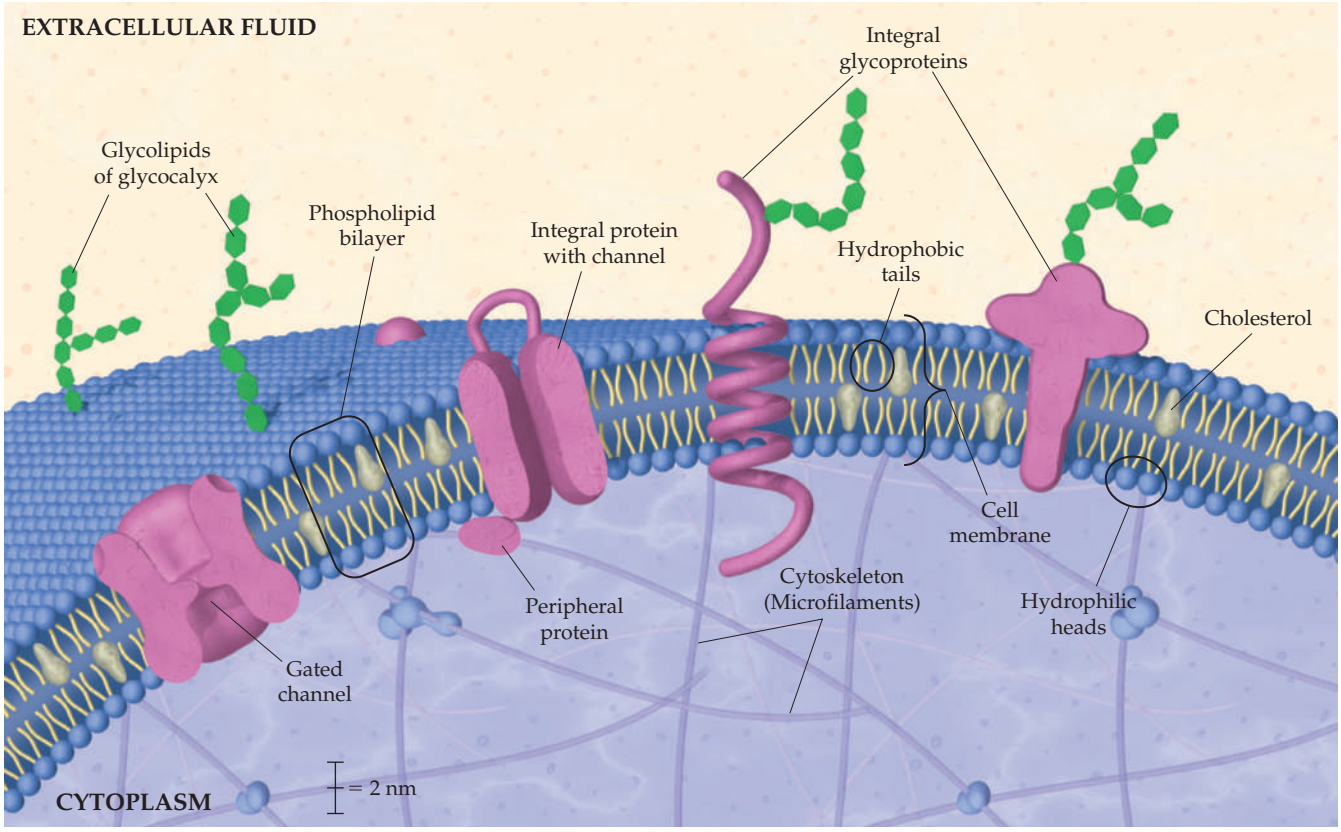
▲ **An example of an integral membrane protein.** The green circles represent amino acids. Many membrane proteins pass in and out of the membrane numerous times.

susceptible to this kind of infection. The liposomes carry amphotericin B, an antibiotic that attacks the fungal cell membrane. By delivering amphotericin to the fungal cells, the liposomal drug diminishes the serious side effects of attack by this antibiotic on kidney cells and cells in other healthy organs. Current medical research includes investigation of liposomes as delivery agents for other drugs.

The overall structure of cell membranes is represented by the *fluid-mosaic model*. The membrane is described as *fluid* because it is not rigid and molecules can move around within it and as a *mosaic* because it contains many kinds of molecules. The components of the cell membrane are shown in Figure 23.7.

Glycolipids and cholesterol are present in cell membranes, and 20% or more of the mass of a membrane consists of protein molecules, many of them glycoproteins (p. 684). *Peripheral proteins* are associated with just one face of the bilayer (i.e., with one leaflet) and are held within the membrane by noncovalent interactions with the hydrophobic lipid tails or the hydrophilic head groups. *Integral proteins* extend completely through the cell membrane and are anchored by hydrophobic regions that extend through the bilayer. In some cases, the hydrophobic amino acid chain may traverse the membrane many times before ending on the exterior of the membrane with a hydrophilic sugar group. The carbohydrate parts of glycoproteins and glycolipids mediate the interactions of the cell with outside agents. Some integral proteins form channels to allow specific molecules or ions to enter or leave the cell.

Because the bilayer membrane is fluid rather than rigid, it is not easily ruptured. The lipids in the bilayer simply flow back together to repair any small hole or puncture. The effect is similar to what is observed in cooking when a thin film of oil or melted butter floats on water in a cooking pot. The film can be punctured and broken, but it immediately flows together when left alone.



▲ **Figure 23.7**
The cell membrane.
Cholesterol forms part of the membrane, proteins are embedded in the lipid bilayer, and the carbohydrate chains of glycoproteins and glycolipids extend into the extracellular space, where they act as receptors. Integral proteins form channels to the outside of the cell and also participate in transporting large molecules across the membrane.

One consequence of membrane fluidity is the movement of proteins within the membrane. For example, low-density lipoprotein receptors, which are glycoproteins that interact with lipoproteins in the extracellular fluid (discussed in Section 24.2), move sideways within the membrane to form clusters of receptors on the cell surface. The glycoproteins move sideways in the membrane layers continuously, not unlike floating on a pond; this is an energetically neutral motion. However, phospholipids and other membrane components do not flip from the inside leaflet of the membrane to the outside leaflet or vice versa. That is an energetically unfavored action because it would force polar and nonpolar interactions between membrane components.

Two other consequences of bilayer fluidity are that small *nonpolar* molecules can easily enter the cell through the membrane and that some individual lipid or protein molecules can diffuse rapidly from place to place within the membrane.

The fluidity of the membrane varies with the relative amounts of saturated and unsaturated fatty acids in the glycerophospholipids. Such variation is put to use in the adaptation of organisms to their environment. In reindeer, for example, the membranes of cells near the hooves contain a higher proportion of unsaturated fatty acid chains than in other cells. These chains do not pack tightly together. The result is a membrane that remains fluid while the animals stand in snow.

KEY CONCEPT PROBLEM 23.17

Integral membrane proteins are not water-soluble. Why? How must these proteins differ from globular proteins?

Transport Across Cell Membranes

The cell membrane must accommodate opposing needs in allowing the passage of molecules and ions into and out of a cell. The membrane surrounding a living cell cannot be impermeable, because nutrients must enter and waste products must leave the cell. However, the membrane cannot be completely permeable, or substances would just move back and forth until their concentrations were equal on both sides—hardly what is required for the maintenance of a constant internal environment in the body or *homeostasis* (see the Chemistry in Action "Homeostasis," Chapter 28, p. 868).

The problem is solved by two modes of passage across the membrane (Figure 23.8). In **passive transport,** substances move across the membrane freely by diffusion from regions of higher concentration to regions of lower concentration. In **active transport,** substances can cross the membrane only when energy is supplied because they must go in the reverse direction—from lower to higher concentration regions.

Passive transport Movement of a substance across a cell membrane without the use of energy, from a region of higher concentration to a region of lower concentration.

Active transport Movement of substances across a cell membrane with the assistance of energy (e.g., from ATP).

Passive Transport by Simple Diffusion

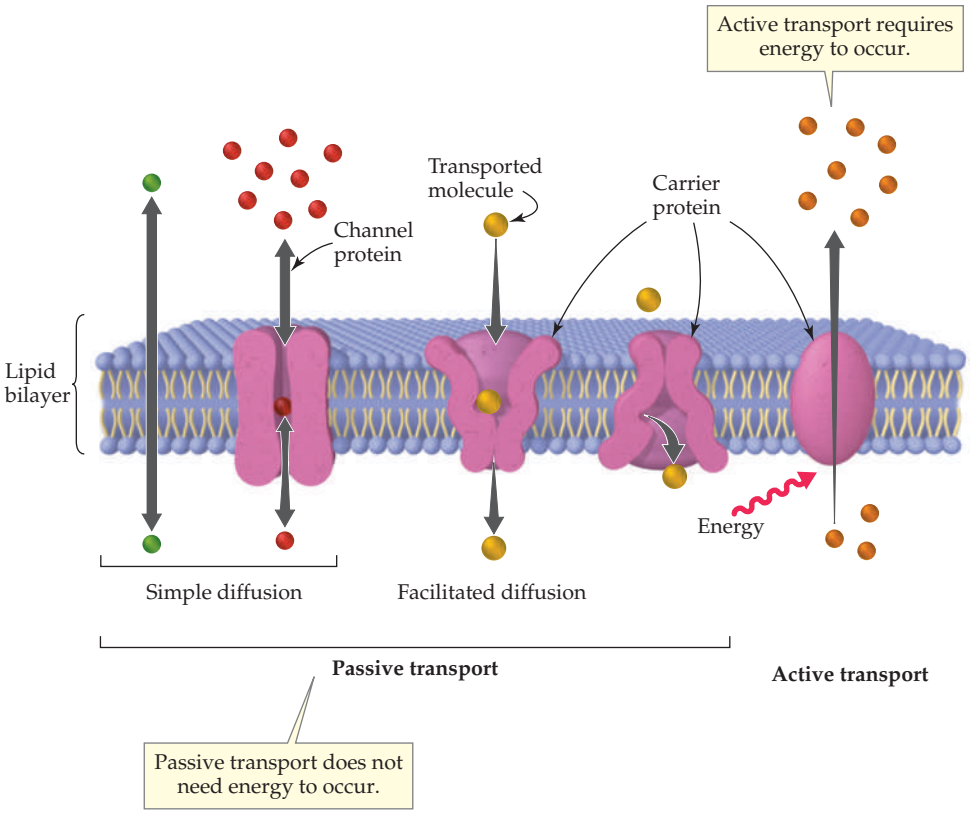
Some solutes enter and leave cells by **simple diffusion**—they move by normal molecular motion into areas of lower concentration. Small, nonpolar molecules, such as CO_2 and O_2, and lipid-soluble substances, including steroid hormones, move through the hydrophobic lipid bilayer in this way. Hydrophilic substances similarly pass through the aqueous environment inside channels formed by integral proteins. What passes through the protein channels is limited by the size of the molecules relative to the size of the openings. The lipid bilayer is essentially impermeable to ions and larger polar molecules, which are not soluble in the nonpolar hydrocarbon region.

Simple diffusion Passive transport by the random motion of diffusion through the cell membrane.

Passive Transport by Facilitated Diffusion

Like simple diffusion, **facilitated diffusion** is passive transport and requires no energy input. However, in facilitated diffusion solutes are moved across the membrane by proteins. The interaction is similar to that between enzymes and substrates. The molecule to be transported binds to a membrane protein, which changes shape so that

Facilitated diffusion Passive transport across a cell membrane with the assistance of a protein that changes shape.



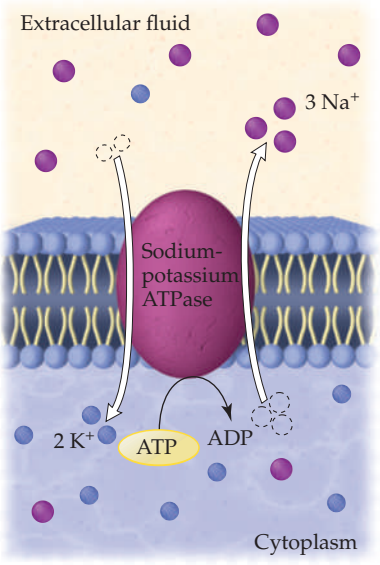
▶ **Figure 23.8**
Modes of transport across cell membranes.

the transported molecule is released on the other side of the membrane. Glucose is transported into cells in this fashion.

Concentration gradient A difference in concentration within the same system.

Active Transport

It is essential to life that the concentrations of some solutes be different inside and outside cells. Such differences are contrary to the natural tendency of solutes to move about until the concentration equalizes. Therefore, maintaining **concentration gradients** (differences in concentration within the same system) requires the expenditure of energy. An important example of active transport is the continuous movement of sodium and potassium ions across cell membranes. This is the only way to maintain homeostasis, which requires low Na^+ concentrations within cells and higher Na^+ concentrations in extracellular fluids, with the opposite concentration ratio for K^+. Energy from the conversion of adenosine triphosphate (ATP) to adenosine diphosphate (ADP) is used to change the shape of an integral membrane protein (an ATPase referred to as the sodium/potassium pump), simultaneously bringing two K^+ ions into the cell and moving three Na^+ ions out of the cell (Figure 23.9).



▲ **Figure 23.9**
An example of active transport.
A protein known as sodium–potassium ATPase uses energy from ATP to move Na^+ and K^+ ions across cell membranes against their concentration gradients.

Properties of Cell Membranes

- Cell membranes are composed of a fluid-like phospholipid bilayer.
- The bilayer incorporates cholesterol, proteins (including glycoproteins), and glycolipids.
- Small nonpolar molecules cross by simple diffusion through the lipid bilayer.
- Small ions and polar molecules diffuse across the membrane via protein pores *(simple diffusion)*.
- Glucose and certain other substances (including amino acids) cross with the aid of proteins and without energy input *(facilitated diffusion)*.
- Na^+, K^+, and other substances that maintain concentration gradients across the cell membrane cross with expenditure of energy and the aid of proteins *(active transport)*.

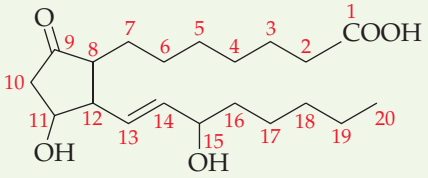
CHEMISTRY IN ACTION

Eicosanoids: Prostaglandins and Leukotrienes

Have you ever cut yourself, hit your fingers with a hammer, or scratched your skin on thorns while picking blackberries? Did the injured area swell and hurt? If so, that is a response mediated by an **eicosanoid.** This group of compounds, derived from the 20-carbon polyunsaturated fatty acid arachidonic acid and synthesized throughout the body, function as short-lived chemical messengers that act near their points of synthesis ("local hormones").

The *prostaglandins* (named for their discovery in prostate cells) and the *leukotrienes* (named for their discovery in leukocytes) are two classes of eicosanoids that differ somewhat in their structure. The prostaglandins all contain a five-membered ring, which the leukotrienes lack.

Prostaglandins and leukotrienes are synthesized in the body from the 20-carbon unsaturated fatty acid arachidonic acid. Arachidonic acid, in turn, is synthesized from linolenic acid, an essential fatty acid.

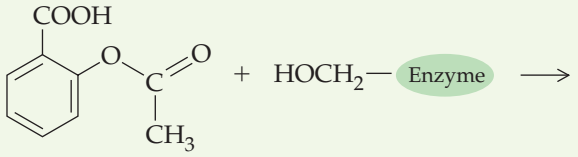


PGE_1, a prostaglandin

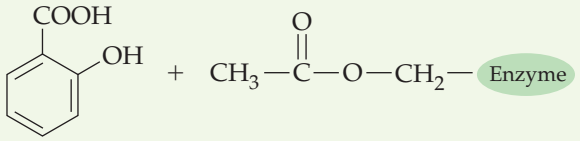
The several dozen known prostaglandins have an extraordinary range of biological effects. They can lower blood pressure, influence platelet aggregation during blood clotting, stimulate uterine contractions, and lower the extent of gastric secretions. In addition, they are responsible for some of the pain and swelling that accompany inflammation.

Aspirin's anti-inflammatory and fever-reducing *(antipyretic)* action results in part from its irreversible inhibition of prostaglandin synthesis by transferring its acetyl group to a serine side chain in cyclooxygenase (COX), the enzyme that catalyzes the first step in conversion of arachidonic acid to prostaglandins. This inhibition is also thought to explain the effect of aspirin on combating heart attacks. COX is present in two forms in cells, referred to as COX-1 and COX-2. Aspirin's effect is short lived, so other drugs have been designed to inhibit either one or the other of these enzymes. Of great interest are drugs that block the activity of COX-2, the enzyme responsible for synthesizing prostaglandins involved in inflammation and pain responses in diseases such as arthritis. While basic research seeking alternative COX-2 inhibitors continues, current medical practice prescribes these drugs sparingly and depends on older, better-understood analgesics such as aspirin and acetaminophen to lessen pain and fever.

There is also great medical interest in leukotrienes. Leukotriene release has been found to trigger the asthmatic



Aspirin (acetylsalicylic acid) Active enzyme (cyclooxygenase)

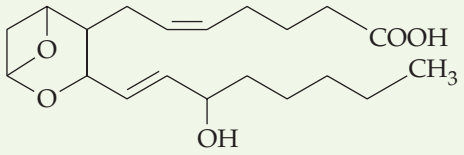


Salicylic acid Inactive enzyme

response, severe allergic reactions, and inflammation. Asthma treatment with drugs that inhibit leukotriene synthesis is being studied, although the available drugs are not yet as effective as standard steroid treatments.

As it turns out, the lipid responsible for localized minor pain, heat, and inflammation is a prostaglandin, and the discomfort is effectively treated with aspirin but not other NSAIDs. Because aspirin, unlike other NSAIDs, irreversibly inhibits COX, the enzyme that catalyzes the first reaction in a pathway that converts arachidonic acid into a prostaglandin.

CIA Problem 23.4 In the eicosanoid shown here, identify all the functional groups. Which groups are capable of hydrogen bonding? Which are most acidic? Is this molecule primarily nonpolar, polar, or something in between?



CIA Problem 23.5 The molecule in CIA Problem 23.4 is *Thromboxane* A_2—a lipid involved in the blood-clotting process. To what category of lipids does thromboxane A_2 belong? What fatty acid do you think serves as a biological precursor of thromboxane A_2?

CIA Problem 23.6 How does aspirin disrupt the synthesis of prostaglandins?

CIA Problem 23.7 Why are the eicosanoids often called "local hormones"?

CIA Problem 23.8 List some of the functions prostaglandins serve in the body.

CIA Problem 23.9 Which two of the following would involve a prostaglandin response?

(a) The itchy bump from a mosquito bite
(b) A sunburn after spending the day at the beach
(c) A strep throat caught from your sibling
(d) The sneezing, stuffy nose, and itchy eyes after working in the rose garden

HANDS-ON CHEMISTRY 23.2

Either alone or with a partner, build a model of a cell membrane. Gather up any arts and crafts supplies you may have and be creative. Suggested supplies are colored paper, cardboard, pipe cleaners (these make good transmembrane proteins), beads, pins with round heads (phospholipid), yarn, balloons, scissors, tape, and glue. Or head for the various types of dry pasta in the grocery store and use different kinds for different membrane structures. Make a key for your model and explain this model to someone not taking this class. Was your explanation understood? How might you improve your explanation? (Hint: Search the web for model ideas if you are stuck.)

PROBLEM 23.18

Does an NO molecule cross a lipid bilayer by simple diffusion? Explain.

PROBLEM 23.19

As noted earlier (Section 22.3), the first step in glycolysis, which occurs within cells, is phosphorylation of glucose to glucose 6-phosphate. Why does this step prevent passive diffusion of glucose back out of the cell?

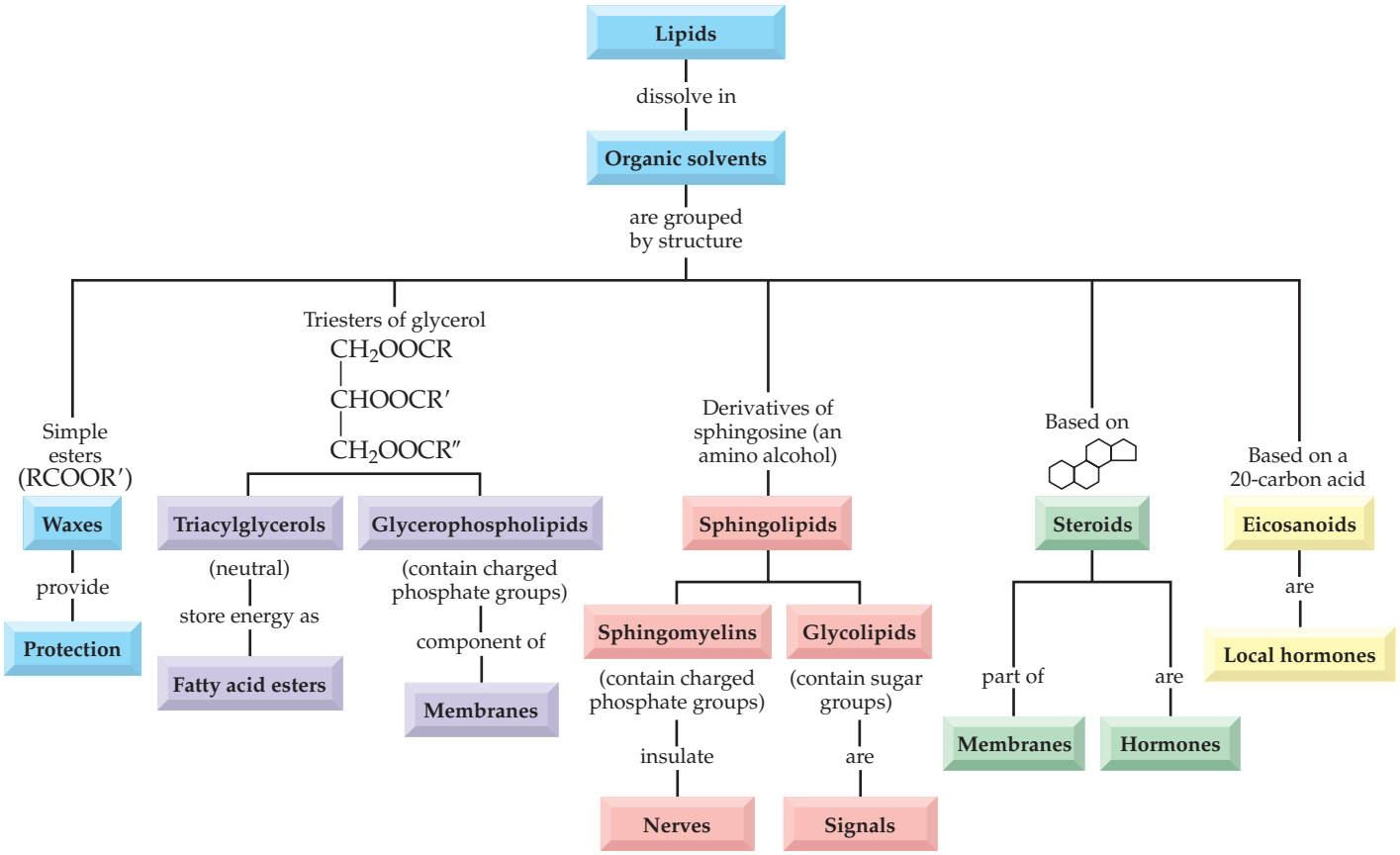
KEY CONCEPT PROBLEM 23.20

The compositions of the inner and outer surfaces of the lipid bilayer are different. Why do these differences exist and how might they be of use to a living cell?

SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Describe the chemical structures and general properties of fatty acids, waxes, sterols, fats, and oils.** *Fatty acids* are long-chain carboxylic acids. *Waxes* are esters of unbranched fatty acids and alcohols. *Sterols* contain four interconnecting rings. *Fats* and *oils* are *triacylglycerols*—triesters of glycerol and fatty acids. In fats, the fatty acid chains are mostly saturated; in oils, the proportions of unsaturated fatty acid chains vary *(see Problems 26, 27, 77, and 88).*
- **Describe the characteristics of fatty acids and fatty acid esters.** Fatty acids are long-chain alkanes or alkenes with a carboxyl group. They have a polar "head" and a nonpolar "tail" and can aggregate into micelles in water. Fatty acid esters have an alcohol esterified to the carboxyl group on the fatty acid. Esters are neutral in charge *(see Problems 28–35 and 76).*
- **List the physical properties of fats and oils and explain why they are different.** Fats are solid because the saturated hydrocarbon chains pack together neatly; oils are liquids because the kinks at the *cis* double bonds prevent such packing *(see Problems 36–45, 79, and 80).*
- **Describe hydrogenation and hydrolysis reactions of triacylglycerols, and, given the reactants, predict the products.** The principal reactions of triacylglycerols are catalytic *hydrogenation* and *hydrolysis.* Hydrogen adds to the double bonds of unsaturated hydrocarbon chains in oils, thereby thickening the consistency of the oils and raising their melting points. Treatment of a fat or oil with a strong base such as NaOH hydrolyzes the triacylglycerols to give glycerol and salts of fatty acids. Such *saponification* reactions produce soap, a mixture of fatty acid salts *(see Problems, 22, 46–53, 76, and 86).*
- **Recognize phospholipids and glycolipids and describe their functions.** *Phospholipids,* which are either *glycerophospholipids* (derived from glycerol) or *sphingomyelins* (derived from the amino alcohol sphingosine), have charged phosphate-diester groups in their hydrophilic heads. Glycolipids have carbohydrate head groups. These lipids are found in cell membranes *(see Problems 25, 44, and 45).*
- **Identify sterols and their derivatives and describe their structures and roles.** The unifying feature of sterols is a fused four-ring system. Sterols include cholesterol, an important participant in membrane structure. Bile acids and salts, necessary for the emulsification of fats during digestion, are synthesized from cholesterol. The third major group of sterols includes steroid hormones, including the sex hormones, which function as signaling molecules *(see Problems 64–67, 81–85, and 87).*
- **Identify the membrane lipids and describe their structures and roles.** The membrane lipids include *phospholipids* and *glycolipids* (which have hydrophilic, polar head groups and two hydrophobic tails) and cholesterol (a steroid). See the learning objectives earlier for structural descriptions *(see Problems 23, 77, and 83–85).*
- **Describe the general structure of a cell membrane and its chemical composition.** The basic structure of cell membranes is a *bilayer of lipids,* with their hydrophilic heads in the aqueous environment outside and inside the cells, and their hydrophobic tails clustered together in the center of the bilayer. *Cholesterol* molecules fit between the hydrophobic tails and help maintain membrane structure and rigidity. The membrane also contains *glycoproteins* and *glycolipids* (with their carbohydrate segments at the cell surface, where they serve as receptors) as well as *proteins.* Some of the proteins extend through the membrane (*integral proteins*), and others are only partially embedded at one surface *(peripheral proteins) (see Problems 24, 17–20, and 68–70).*
- **Distinguish between passive transport and active transport and between simple diffusion and facilitated diffusion.** Small, nonpolar molecules and lipid-soluble substances can cross the lipid bilayer by simply diffusing through it. Ions and hydrophilic substances can move through aqueous fluid-filled channels in membrane proteins. Some substances cross the membrane by binding to an integral protein, which then releases them inside the cell. These modes of crossing are all *passive transport*—they do not require energy because the substances move from regions of higher concentration to regions of lower concentration. Passive transport takes the form of *simple diffusion,* crossing the membrane by passing through it unimpeded, or *facilitated diffusion,* crossing the membrane with the aid of a protein embedded in the membrane. *Active transport,* which requires energy and is carried out by certain integral membrane proteins, moves substances against their *concentration gradients (see Problems 71–75).*

CONCEPT MAP



▲ **Figure 23.10 Concept Map.** This lipid concept map connects the disparate categories of lipids and indicates important functions and the importance of lipids in membrane structure.

KEY WORDS

Active transport, *p. 767*
Concentration gradient, *p. 768*
Degree of unsaturation, *p. 752*
Eicosanoid, *p. 750*
Facilitated diffusion, *p. 767*
Fat, *p. 754*
Fatty acid, *p. 749*
Glycerophospholipid (phosphoglyceride), *p. 759*
Glycolipid, *p. 761*
Lipid, *p. 749*
Lipid bilayer, *p. 765*
Liposome, *p. 765*
Micelle, *p. 758*
Oil, *p. 754*
Passive transport, *p. 767*
Phospholipid, *p. 758*
Polyunsaturated fatty acid, *p. 752*
Saturated fatty acid, *p. 751*
Simple diffusion, *p. 767*
Soap, *p. 758*
Sphingolipid, *p. 761*
Sterol, *p. 763*
Triacylglycerol (triglyceride), *p. 753*
Unsaturated fatty acid, *p. 751*
Wax, *p. 752*

UNDERSTANDING KEY CONCEPTS

23.21 The fatty acid composition of three triacylglycerols (A, B, and C) is reported below. Predict which one has the highest melting point. Which one do you expect to be liquid (oil) at room temperature? Explain.

	Palmitic Acid	Stearic Acid	Oleic Acid	Linoleic Acid
A	21.4%	27.8%	35.6%	11.9%
B	12.2%	16.7%	48.2%	22.6%
C	11.2%	8.3%	28.2%	48.6%

23.22 Complete hydrogenation of triacylglycerol C in Problem 23.20 yields a triacylglycerol of what fatty acid composition? Would the hydrogenation product of triacylglycerol C be more like the hydrogenation product of triacylglycerol A or B? Explain.

23.23 A membrane lipid was isolated and completely hydrolyzed. The following products were detected: ethanolamine, phosphate, glycerol, palmitic acid, and oleic acid. Propose a structure for this membrane lipid, and name the family (Table 23.3) to which it belongs.

23.24 According to the fluid-mosaic model (Figure 23.7), the cell membrane is held together mostly by hydrophobic interactions. Considering the forces applied, why does the cell membrane not rupture as you move, press against objects, etc.?

23.25 Dipalmitoylphosphatidylcholine (DPPC) is a surfactant on the surface of the alveoli in the lungs. What is the nature of its fatty acid groups? In what arrangement is it likely to exist at the lung surfaces?

ADDITIONAL PROBLEMS

WAXES, FATS, AND OILS (SECTION 23.1)

23.26 What makes a molecule a lipid?

23.27 Name two classes of lipids found in your body.

FATTY ACIDS AND THEIR ESTERS (SECTION 23.2)

23.28 Draw an 18-carbon saturated fatty acid. Is this a "straight-chain" molecule or a "bent" molecule?

23.29 Draw an 18-carbon unsaturated fatty acid that contains two carbon–carbon double bonds, one on carbon 6 and one on carbon 9 (count starting with the carboxyl carbon). Is this a "straight-chain" molecule or a "bent" molecule?

23.30 Differentiate between saturated, monounsaturated, and polyunsaturated fatty acids.

23.31 Are the carbon–carbon double bonds in naturally occurring fatty acids primarily *cis* or *trans*?

23.32 What is an essential fatty acid?

23.33 Name two essential fatty acids. What are good sources of these fatty acids?

23.34 Which of these fatty acids has the lower melting point? Explain why.

(a) Linoleic acid **(b)** Stearic acid

23.35 Which of these fatty acids has the higher melting point? Explain why.

(a) Linolenic acid **(b)** Stearic acid

FATS AND OILS (SECTION 23.3)

23.36 What are the chemical and physical differences between fats and oils?

23.37 List typical food sources for oils and fats. Are there similarities or differences in the sources for each?

23.38 Draw the structure of glyceryl trilaurate, which is made from glycerol and three lauric acid molecules.

23.39 There are two isomeric triacylglycerol molecules whose components are glycerol, one palmitic acid unit, and two stearic acid units. Draw the structures of both, and explain how they differ.

23.40 What function does a wax serve in a plant or animal?

23.41 What functions do fats serve in an animal?

23.42 *Spermaceti,* a fragrant substance isolated from sperm whales, was commonly used in cosmetics until it was banned in 1976 to protect the whales from extinction. Chemically, spermaceti is cetyl palmitate, the ester of palmitic acid with cetyl alcohol (the straight-chain 16-carbon alcohol). Draw the structure of spermaceti.

23.43 What kind of lipid is spermaceti—a fat, a wax, or a sterol?

23.44 A major ingredient in peanut butter cup candy is soy lecithin. Draw the structure of lecithin.

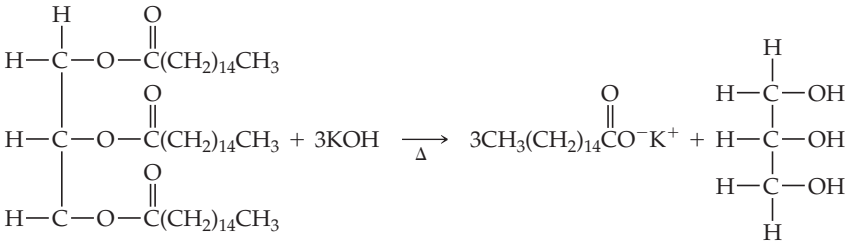
23.45 Which kind of lipid is lecithin?

CHEMICAL REACTIONS OF LIPIDS (SECTION 23.4)

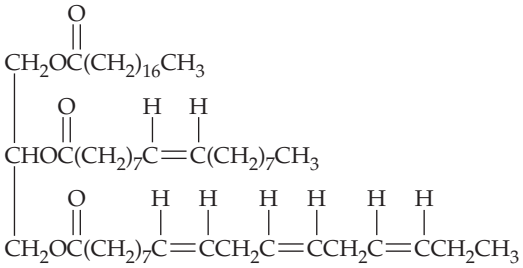
23.46 What is the name of the reaction that converts unsaturated fatty acids to saturated fatty acids?

23.47 When a vegetable oil is converted to a soft margarine, a nonnatural product is synthesized. What is this product?

23.48 Is the reaction shown here esterification, hydrogenation, hydrolysis, saponification, or substitution?



23.49 Draw the structures of all products you would obtain by saponification of the following lipid with aqueous KOH. What are the names of the products?



23.50 Draw the structure of the product you would obtain on complete hydrogenation of the triacylglycerol in Problem 23.49. What is its name? Does it have a higher or lower melting temperature than the original triacylglycerol?

23.51 Tell how many different products you would obtain on hydrogenation of the triacylglycerol in Problem 23.49 if:

(a) One double bond was converted to a single bond

(b) Two double bonds were converted to single bonds

(c) Three double bonds were converted to single bonds

(d) All four double bonds were converted to single bonds

23.52 Dietary guidelines suggest we limit our intake of butter due to the cholesterol content and substitute oils or margarine. The following table shows the major fatty acid distribution for a typical stick of margarine and also for butter. Values are percentages.

Sample	Myristic Acid (C14:0)	Palmitic Acid (C16:0)	Stearic Acid (C18:0)	Oleic Acid (C18:1)	Linoleic Acid (C18:2)
Margarine	0.7	14.1	7.0	60.7	17.0
Butter	12	31	11	24	3

(a) Which contains more monounsaturated fatty acids?

(b) Which contains more polyunsaturated fatty acids?

(c) Which is likely to contain fewer *trans*-fatty acids

23.53 Recently it has been suggested that using oils with more monounsaturated fatty acids (e.g., oleic acid) is better for our health than those with polyunsaturated fatty acids or saturated fatty acids. What are good sources of oils with predominantly monounsaturated fatty acids? (Hint: See Table 23.2.)

PHOSPHOLIPIDS AND GLYCOLIPIDS (SECTION 23.5)

23.54 Describe the difference between a triacylglycerol and a phospholipid.

23.55 Why are glycerophospholipids, rather than triacylglycerols, found in cell membranes?

23.56 How do sphingomyelins and cerebrosides differ structurally?

23.57 Name the two different kinds of sphingosine-based lipids.

23.58 Why are glycerophospholipids more soluble in water than triacylglycerols?

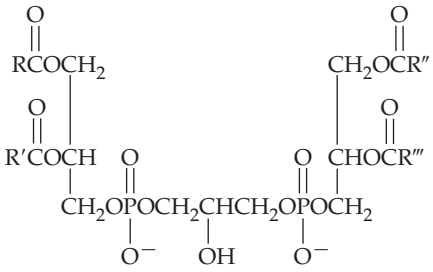
23.59 What are the functions of glycerophospholipids in the human body? Of triacylglycerides in the human body?

23.60 Show the structure of a cerebroside made up of D-galactose, sphingosine, and myristic acid.

23.61 Draw the structure of a sphingomyelin that contains a stearic acid unit.

23.62 Draw the structure of a glycerophospholipid that contains palmitic acid, oleic acid, and the phosphate bonded to propanolamine.

23.63 *Cardiolipin,* a compound found in heart muscle, has the following structure. What products are formed if all ester bonds in the molecule are saponified by treatment with aqueous NaOH?



Cardiolipin

STEROLS (SECTION 23.6)

23.64 What is a major function of cholesterol in your body?

23.65 What is the function of the bile acids?

23.66 Name a male sex hormone and a female sex hormone.

23.67 Compare the structures of the sex hormones named in Problem 23.66. What portions of the structures are the same? Where do they differ?

CELL MEMBRANES (SECTION 23.7)

23.68 Explain how a micelle differs from a membrane bilayer.

23.69 Describe the similarities and differences between a liposome and a micelle.

23.70 What constituents besides phospholipids are present in a cell membrane?

23.71 What would happen if cell membranes were freely permeable to all molecules?

23.72 Which process requires energy—passive or active transport? Why is energy sometimes required to move solute across the cell membrane?

23.73 How does facilitated diffusion differ from simple diffusion?

23.74 Based on the information in Section 23.7, how would you expect each of these common metabolites to cross the cell membrane?

(a) NO (nitrous oxide) **(b)** Fructose

(c) Ca^{2+}

23.75 Based on the information in Section 23.7, how would you expect each of these common metabolites to cross the cell membrane?

(a) Galactose **(b)** CO **(c)** Mg^{2+}

CONCEPTUAL PROBLEMS

23.76 Which of the following are saponifiable lipids? (Recall that ester bonds are broken by base hydrolysis.)

(a) Progesterone **(b)** Glyceryl trioleate

(c) A sphingomyelin **(d)** Prostaglandin E_1

(e) A cerebroside **(f)** A lecithin

23.77 Identify the component parts of each saponifiable lipid listed in Problem 23.76.

23.78 Draw the structure of a triacylglycerol made from two molecules of myristic acid and one molecule of linolenic acid.

23.79 Would the triacylglycerol described in Problem 23.78 have a higher or lower melting temperature than the triacylglycerol made from one molecule each of linolenic, myristic, and stearic acids? Why?

23.80 Common names for some triacylglycerols depend on their source. Identify the source. Choices are plant oils (soybean, canola, corn, sunflower, and so on), beef fat, and pork fat.

(a) Tallow **(b)** Cooking oil **(c)** Lard

23.81 Explain why cholesterol is not saponifiable.

23.82 Draw cholesterol acetate. Is this molecule saponifiable? Explain.

23.83 Which three types of lipids are particularly abundant in brain tissue?

23.84 What is the function of sphingomyelin?

23.85 In what disease is a decrease in sphingomyelin observed?

23.86 If the average molar mass of a sample of soybean oil is 1500 g/mol, how many grams of NaOH are needed to saponify 5.0 g of the oil?

GROUP PROBLEMS

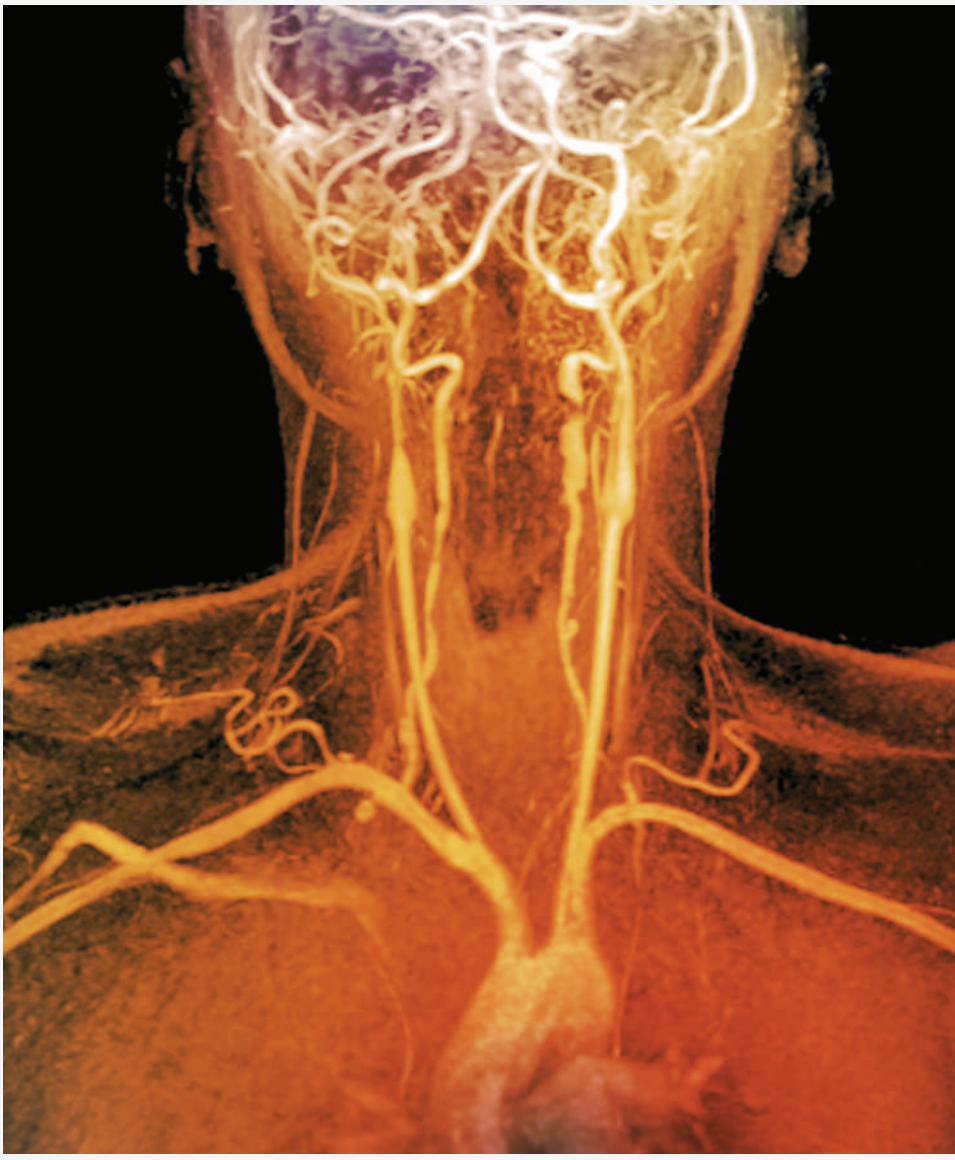
23.87 The concentration of cholesterol in the blood serum of a normal adult is approximately 200 mg/dL. How many grams of cholesterol does a person with a blood volume of 5.75 L have circulating in his or her blood? (You may need to review Chapter 1.)

23.88 Jojoba wax, used in candles and cosmetics, is partially composed of the ester of stearic acid and a straight-chain 22-carbon atom alcohol. Draw the structure of this wax component. Compare this structure with the structure drawn for spermaceti in Problem 23.42. Do you think jojoba wax could replace spermaceti in the cosmetic industry?

24

Lipid Metabolism

CONTENTS



▲ Narrowed portions of blood vessels, generally caused by fatty deposits, are shown in this imaging of blood flow in the head and neck of an adult.

CONCEPTS TO REVIEW

A. Types of Lipids (Section 23.1)
B. Cell Membranes (Section 23.7)
C. Metabolism and Energy Production (Section 21.4)

Carbohydrate metabolism (discussed in Chapter 22) is one of our two major sources of energy. Lipid metabolism, the topic of this chapter, is the other. The majority of the lipids in our diet are triacylglycerols. Surplus carbohydrate energy is also stored as triacylglycerols. Therefore, our focus here is on the metabolism of triacylglycerols, which are stored in fatty tissue and constitute our chief energy reserve. Storage of excess fat raises multiple health concerns.

Consider Malcolm, a middle-aged man who, while working at his desk, is suddenly struck with intense chest pain that radiates down his left arm. Rushed to an emergency room (ER), the ER staff physician orders an electrocardiogram, an enzyme blood panel including troponins, and a blood lipid panel and stabilizes Malcolm. A cardiologist arrives, notes that Malcolm is overweight, and questions him regarding his pain and personal habits such as exercise level, diet, smoking, drug and alcohol use as well as previous medical care. Because the initial test results show elevated lipids and elevated enzymes, a computed tomography (CT) cardiac scan is ordered. The results of this heart imaging will determine the next step in treatment. Throughout this chapter and in the Chemistry in Action "Fat Storage, Lipids, and Atherosclerosis" at the end of the chapter, we'll learn how this cardiac emergency could result from the regular metabolic processes of carbohydrate and fat metabolism.

24.1 Digestion of Triacylglycerols

Learning Objective:

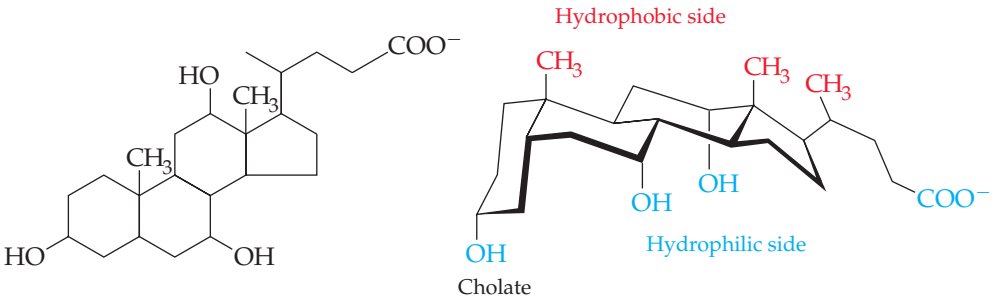
- List the steps in the digestion of dietary triacylglycerols and their transport into the bloodstream.

When eating, any triacylglycerols present pass through the mouth unchanged and enter the stomach (Figure 24.1). The heat and churning action of the stomach break triacylglycerols into small droplets, a process that takes longer than the physical breakdown and digestion of other food in the stomach. To ensure that there is time for this breakdown, the presence of triacylglycerols slows down the rate at which the mixture of partially digested food leaves the stomach (a reason foods containing lipids are a pleasing part of the diet is that the stomach feels full for a longer time after a fatty meal). No catabolism of triacylglycerols has taken place yet, only preparation for this step by breaking fats into microscopic droplets.

The pathway of dietary triacylglycerols from the mouth to their ultimate biochemical fate in the body is not as straightforward as that of carbohydrates. Complications arise because triacylglycerols are not water-soluble, but nevertheless must enter an aqueous environment. To be moved around within the body by the blood and lymph systems, they must be dispersed and surrounded by a water-soluble coating, a process that must happen more than once as triacylglycerols travel along their metabolic pathways. During these travels, they are packaged in various types of **lipoproteins,** which consist of droplets of hydrophobic lipids surrounded by phospholipids, proteins, and other molecules with their hydrophilic ends to the outside (Figure 24.2). Lipoproteins are special forms of micelles.

When partially digested food leaves the stomach, it enters the upper end of the small intestine (the *duodenum*), where its arrival triggers the release of *pancreatic lipases*—enzymes for the hydrolysis of lipids. The gallbladder simultaneously releases **bile,** a mixture that is manufactured in the liver and stored in the gallbladder until needed. Among other components, bile contains cholesterol and cholesterol-derived **bile acids,** both of which are sterols, and phospholipids.

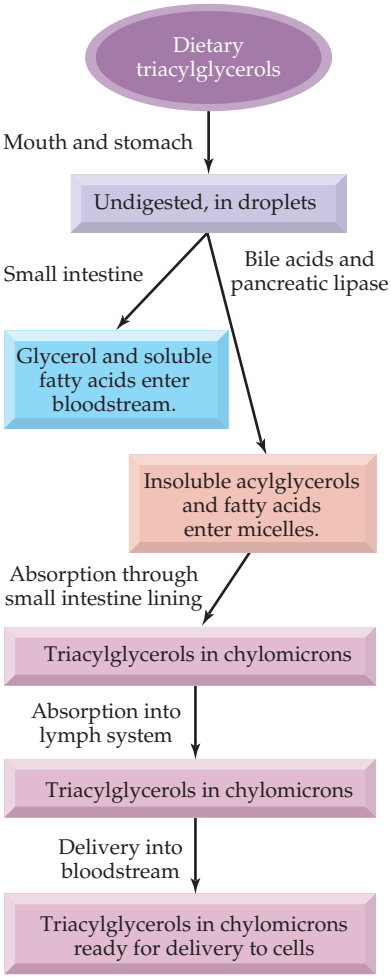
By the time dietary triacylglycerols enter the small intestine, they are dispersed as small, greasy, insoluble droplets, and for this reason enzymes in the small intestine cannot attack them. It is the job of the bile acids and phospholipids to emulsify the triacylglycerols by forming micelles similar to soap micelles (see Figure 23.3). The major bile acid is cholic acid, and the structure of its anion closely resembles soaps because it contains both hydrophilic and hydrophobic regions allowing it to act as an emulsifying agent.



Pancreatic lipase partially hydrolyzes the emulsified triacylglycerols, producing mono- and diacylglycerols plus "free" fatty acids and a small amount of glycerol.

CONCEPTS TO REVIEW

Recall that an *acyl* group is the R—C═O portion of an ester. The acyl groups from fatty acids have relatively long, R chain groups (Section 17.1).



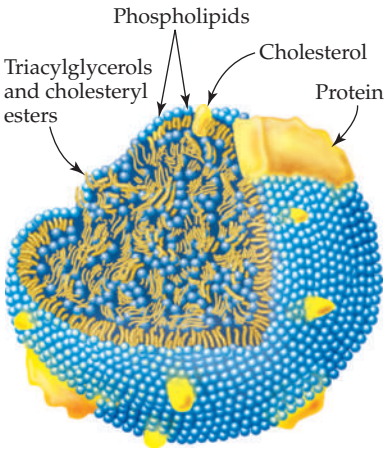
▲ **Figure 24.1**
Digestion of triacylglycerols.

Lipoprotein A lipid–protein complex that transports lipids.

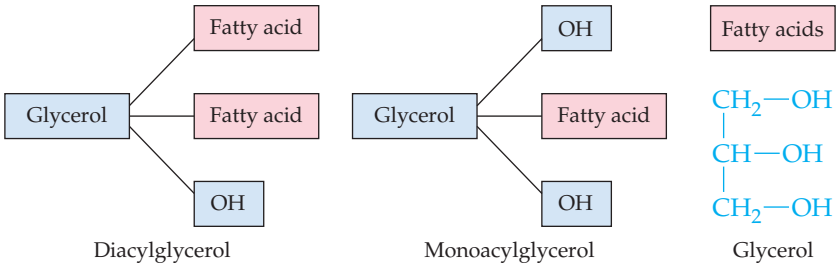
Bile Fluid secreted by the liver and released into the small intestine from the gallbladder during digestion; contains bile acids, cholesterol, phospholipids, hydrogen carbonate ions, and other electrolytes.

Bile acids Sterol acids derived from cholesterol that are secreted in bile.

Recall from Section 23.5 that polar phospholipids are the major component of cell membranes.



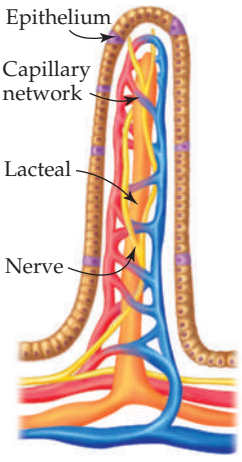
▲ **Figure 24.2**
A Lipoprotein.
A lipoprotein contains a core of neutral lipids, including triacylglycerols and cholesteryl esters. Surrounding the core is a layer of phospholipids in which varying proportions of proteins and cholesterol are embedded.



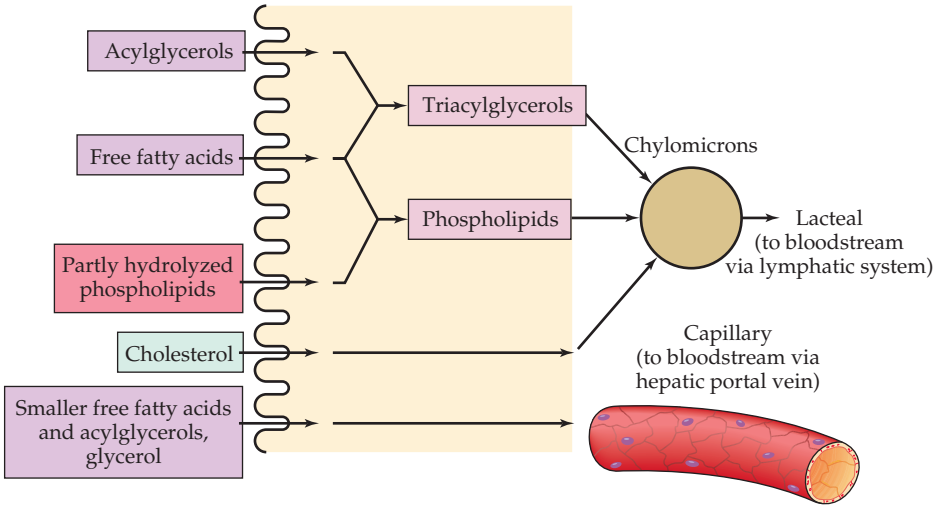
Small fatty acids and glycerol are water-soluble and are absorbed directly by simple diffusion through the surface of the villi that line the small intestine. Once they are inside the villi (Figure 24.3), these molecules diffuse into the capillaries and are carried by the blood to the liver (via the hepatic portal vein). Amino acids and simple sugars also move by simple diffusion into the villi and then the capillary network for transport to the liver by the bloodstream.

The water-insoluble acylglycerols and larger fatty acids are once again emulsified within the intestine. Then, at the intestinal lining they are released from the micelles and absorbed by the cells lining the intestine. Because these lipids, and also cholesterol and partially hydrolyzed phospholipids, must next enter the aqueous bloodstream for transport, they are once again packaged into water-soluble units—in this case, the lipoproteins known as *chylomicrons*. This elaborate process of hydrolysis, absorption, resynthesis, secretion, and transport is necessary for the triacylglycerol components to cross cell membranes and also for their travel through aqueous media. Remember, triacylglycerols and cholesterol must move from food particles in the intestinal system to the cytosol or mitochondria of liver cells and other cells for use in your body.

Chylomicrons are too large to enter the bloodstream through capillary walls. Instead, they are absorbed into the lymphatic system through lacteals, small vessels analogous to capillaries, within the villi (see Figure 24.3). Then, chylomicrons are carried to the thoracic duct (just below the collarbone), where the lymphatic system empties into the bloodstream. At this point, the lipids within these chylomicrons are ready to be used either for energy generation or to be put into storage; once leaving the thoracic duct the chylomicrons are carried directly to the liver, where hepatocytes use the lipid components depending on their own needs and the needs of other cells. The pathways of lipids through the villi and into the transport systems of the bloodstream and the lymphatic system are summarized in Figure 24.4.



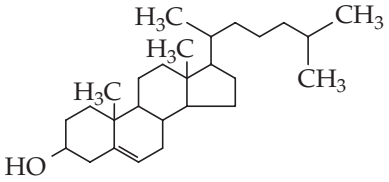
▲ **Figure 24.3**
A villus, site of absorption in the intestinal lining.
A huge number of villi provide the surface at which lipids and other nutrients are absorbed. Small molecules enter the capillary network, and larger lipids enter the lacteals, small vessels of the lymph system.



▲ **Figure 24.4**
Pathways of lipids through the villi.

KEY CONCEPT PROBLEM 24.1

Cholesterol (see structure in margin) and cholate (a bile acid anion, whose structure is shown on p. 765) are sterols with very similar structures. However, the roles they play in the body are different: Cholate is an emulsifier, whereas cholesterol plays an important role in membrane structure. Identify the small differences in their structures that make them well suited to their jobs in the body. Given their similar structures, can the roles of these molecules be reversed?



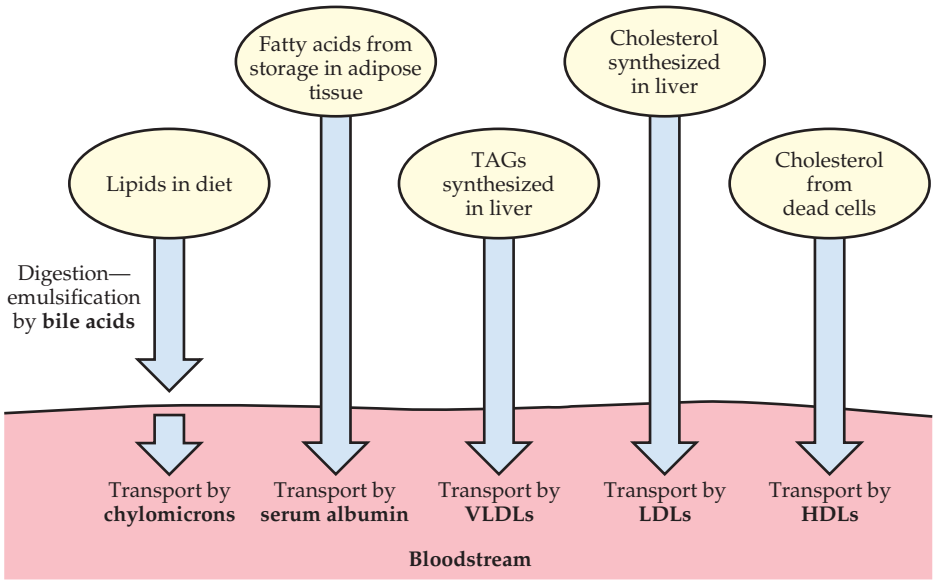
Cholesterol

24.2 Lipoproteins for Lipid Transport

Learning Objective:

- Name the major classes of lipoproteins, specify the nature and function of the lipids they transport, and identify their destinations.

The lipids used in the body's metabolic pathways have three sources: (1) from the digestive tract as food is broken down; (2) from adipose tissue, where excess lipids have been stored; and (3) from the liver, where lipids are synthesized. Whatever their source, these lipids must eventually be transported in blood, an aqueous medium, as summarized in Figure 24.5.



◂ **Figure 24.5**
Transport of lipids.
Fatty acids released from storage are carried by albumin, which is a large protein. All of the other lipids are carried packaged in various lipoproteins.

To become water-soluble, fatty acids released from adipose tissue associate with albumin, a protein found in blood plasma that binds up to 10 fatty acid molecules per protein molecule. All other lipids are carried by lipoproteins. (The role of lipoproteins in heart disease, where they are of great concern, is discussed in the Chemistry in Action "Fat Storage, Lipids, and Atherosclerosis" on p. 790.)

Because lipids are less dense than proteins, the density of lipoproteins depends on the ratio of lipid to protein. Therefore, lipoproteins are arbitrarily divided into five major types distinguishable by their composition and densities. Chylomicrons, which transport dietary lipids, carry triacylglycerols through the lymphatic system into the blood and thence to the liver for processing. These are the lowest-density lipoproteins (less than 0.95 g/cm^3) because they carry the highest ratio of lipid to protein. The four denser lipoprotein fractions have the following roles:

- *Very low-density lipoproteins (VLDLs)* (0.96–1.006 g/cm^3) carry triacylglycerols from the liver (where they are synthesized) to peripheral tissues for storage or energy generation.

- *Intermediate-density lipoproteins (IDLs)* ($1.007–1.019\ g/cm^3$) carry remnants of the VLDLs from peripheral tissues to the liver for use in synthesis.
- *Low-density lipoproteins (LDLs)* ($1.020–1.062\ g/cm^3$) transport cholesterol from the liver to peripheral tissues, where it is used in cell membranes or for steroid synthesis (and is also available for formation of arterial plaque).
- *High-density lipoproteins (HDLs)* ($1.063–1.210\ g/cm^3$) transport cholesterol *from* dead or dying cells to the liver, where it is converted to bile acids. The bile acids are then available for use in digestion or are excreted via the digestive tract when in excess.

Worked Example 24.1 Digesting and Transporting Fats

Describe how the fat in an ice cream cone gets from the ice cream to a liver cell.

ANALYSIS Dietary fat from animal sources (such as the whole milk often found in ice cream) is primarily triacylglycerols with a small amount of cholesterol present. Cholesterol is not degraded in the digestive system. Fat-digesting enzymes are secreted by the pancreas and delivered via the common duct to the small intestine, along with bile acids. As discussed earlier, only free fatty acids and mono- and diacylglycerols can cross the intestinal cell wall before being passed on to the bloodstream. Smaller molecules such as some free fatty acids and glycerol diffuse across the cell membrane to enter the bloodstream; larger molecules must be delivered there in special packaging, called lipoproteins.

SOLUTION

As the ice cream cone is eaten, it passes through the mouth to the stomach, where mixing occurs. This mixing action promotes the formation of triacylglycerols into small droplets. No enzymatic digestion of lipids occurs in the stomach. When the stomach contents move to the small intestine, bile acids and pancreatic lipases are secreted into the mixture. The bile acids help to emulsify the fat droplets into micelles. Once micelles have formed, lipases hydrolyze the triacylglycerols to mono- and diacylglycerols; the hydrolysis also produces fatty acids. These three hydrolysis products cross into the cells lining the small intestine, are resynthesized into triacylglycerides, and are secreted into the bloodstream in the form of chylomicrons. Chylomicrons travel to the liver and enter cells for processing. The small amount of cholesterol in the ice cream will be directly absorbed, packaged into chylomicrons as well, and sent to the liver.

24.3 Triacylglycerol Metabolism: An Overview

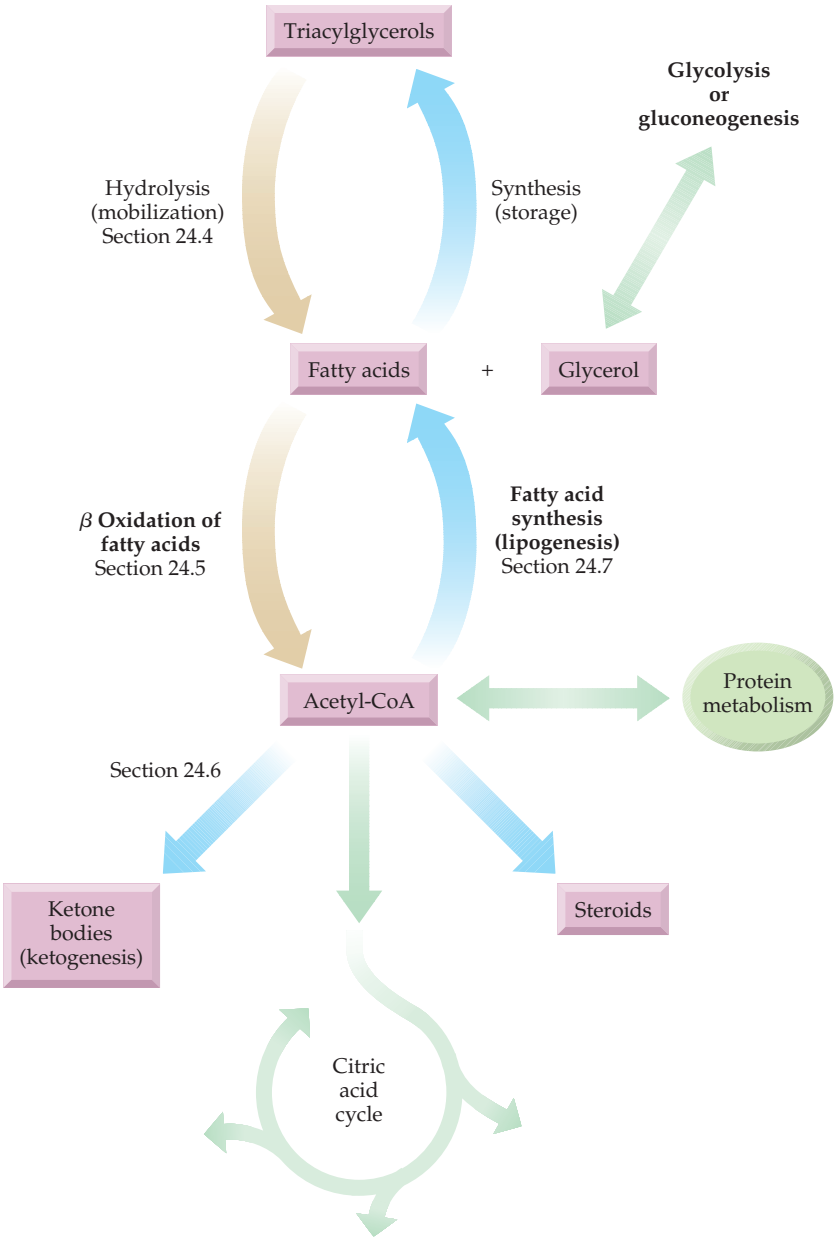
Learning Objective:

- Name the major pathways for the synthesis and breakdown of triacylglycerols and fatty acids, and identify their connections to other metabolic pathways.

Figure 24.6 summarizes the metabolic pathways for triacylglycerols. Triacylglcerols are essential for our well-being as long-term energy storage, insulation for our bodies, and cushioning for our internal organs. These essential molecules are made from any extra glucose or protein we eat as well as from dietary fat as you will see in the metabolic paths discussed here.

Dietary Triacylglycerols

Hydrolysis of dietary triacylglycerols occurs when chylomicrons in the bloodstream encounter lipoprotein lipase anchored in capillary walls as chylomicrons are moving to hepatocytes for processing. The resulting fatty acids then have two possible fates: (1) If energy is in good supply, they are converted back to triacylglycerols for storage in adipose tissue; (2) If cells need energy, the fatty acid carbon atoms are activated by conversion to fatty acyl-CoA and then oxidized to acetyl-CoA, shortening the fatty acyl-CoA molecule by two carbon atoms for each oxidation.



◀ **Figure 24.6**
Metabolism of triacylglycerols. Pathways that break down molecules (catabolism) are shown in light brown, and synthetic pathways (anabolism) are shown in blue. Connections to other pathways or intermediates of metabolism are shown in green.

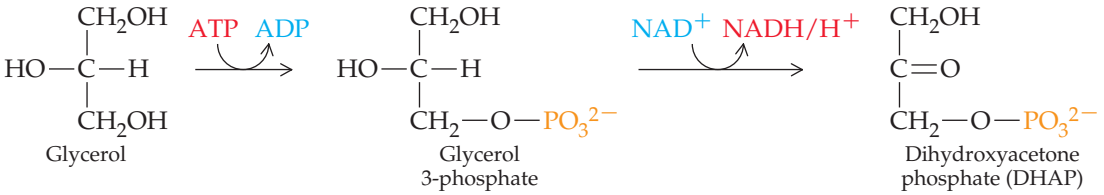
The primary metabolic fate of acetyl-CoA is the generation of energy via the citric acid cycle and oxidative phosphorylation (see Figure 21.4). Acetyl-CoA has several important roles in lipid metabolism as well. Acetyl-CoA serves as the starting material for the biosynthesis of fatty acids *(lipogenesis)* in the liver (Section 24.7). In addition, it enters the *ketogenesis* pathway for production of ketone bodies, a source of energy called on when glucose is in short supply (Section 24.6). Acetyl-CoA is also the starting material for the synthesis of cholesterol, from which all other steroids are made.

Triacylglycerols from Adipocytes

When stored triacylglycerols are needed as an energy source, lipases within fat cells are activated by hormone level variation (low insulin and high glucagon, Section 22.7). The stored triacylglycerols are hydrolyzed to fatty acids and glycerol, which are released into the bloodstream. These fatty acids travel in association with *albumins* (blood-plasma proteins) to cells (primarily muscle and liver cells), where they are converted to acetyl-CoA for energy generation.

Glycerol from Triacylglycerols

Glycerol produced from triacylglycerol hydrolysis is carried in the bloodstream to the liver or kidneys, where it is converted to glycerol 3-phosphate and dihydroxyacetone phosphate (DHAP):



DHAP can enter either the glycolysis or gluconeogenesis pathway (see Figure 22.3, step 5 and Figure 22.9, step 7) and is a link between carbohydrate metabolism and lipid metabolism.

The varied possible metabolic destinations of the fatty acids, glycerol, and acetyl-CoA from dietary triacylglycerols are summarized as follows:

Fate of Dietary Triacylglycerols

- *Triacylglycerols* undergo hydrolysis to fatty acids and glycerol.
- *Fatty acids* undergo
  - Resynthesis of triacylglycerols for storage
  - Conversion to acetyl-CoA
- *Glycerol* is converted to glyceraldehyde 3-phosphate and DHAP, which participate in
  - *Glycolysis*—energy generation (Section 22.3)
  - *Gluconeogenesis*—glucose formation (Section 22.9)
  - *Triacylglycerol synthesis*—energy storage (Section 24.4)
- *Acetyl-CoA* participates in
  - *Triacylglycerol synthesis* (Section 24.4)
  - Ketone body synthesis (*ketogenesis,* Section 24.6)
  - Synthesis of sterols and other lipids
  - *Citric acid cycle and oxidative phosphorylation* (Sections 21.7 and 21.8)

PROBLEM 24.2

Examine Figure 22.3 (pp. 728–729) and explain how DHAP can enter the glycolysis pathway and be converted to pyruvate.

PROBLEM 24.3

How are long-chain fatty acids released from triacylglycerides transported through the bloodstream?

24.4 Storage and Mobilization of Triacylglycerols

Learning Objective:

- Explain the reactions by which triacylglycerols are stored and mobilized, and how these reactions are regulated.

Although adipose tissue is the storage depot for triacylglycerols, triacylglycerols do not just sit unused until needed for energy production. The passage of fatty acids in and out of storage in adipose tissue is a continuous process essential to maintaining homeostasis (see the Chemistry in Action "Homeostasis," page 868).

Mobilization (of triacylglycerols)
Hydrolysis of triacylglycerols in adipose tissue and release of fatty acids into the bloodstream.

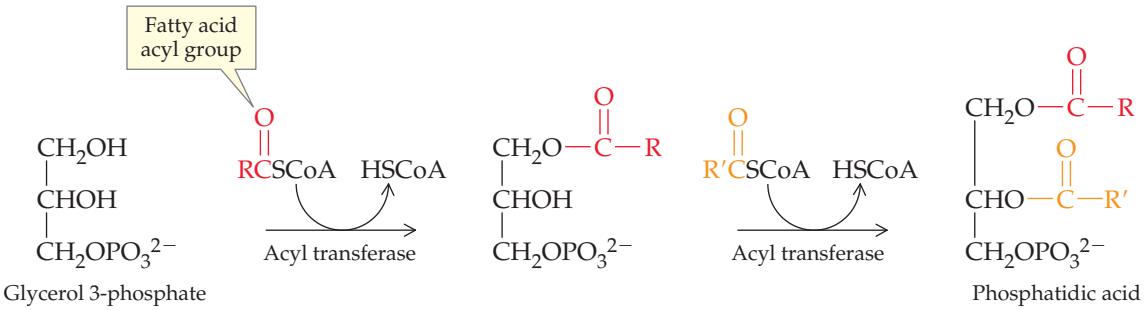
Triacylglycerol Synthesis

Our bodies regulate the storage and **mobilization** of triacylglycerols through the same hormones that regulate blood glucose concentration, insulin, and glucagon. After a

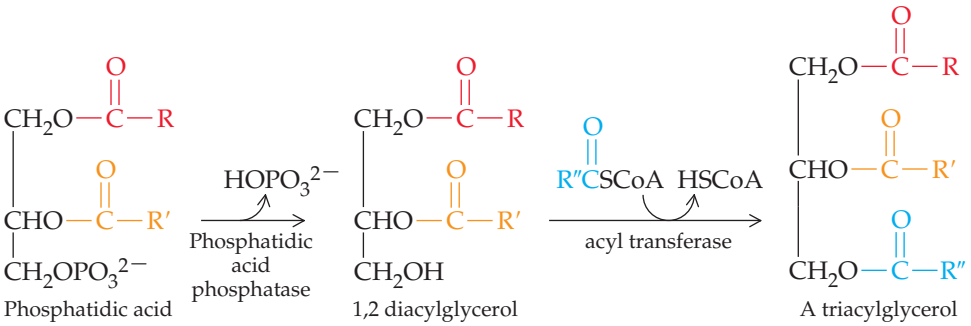
meal, blood glucose levels rise, and glucagon levels drop. Glucose enters cells, and the rate of glycolysis increases. Under these conditions, insulin activates the synthesis of triacylglycerols for storage.

Figure 22.6 shows the effects of insulin and glucagon hormones on metabolism.

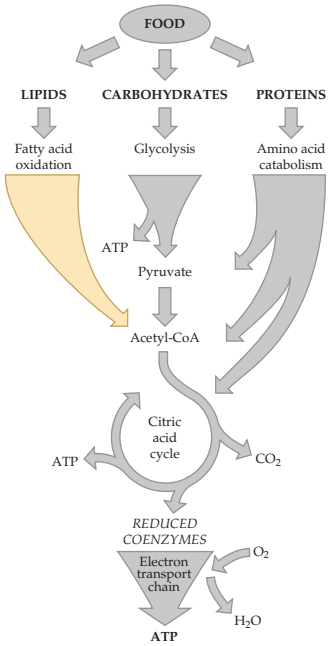
The reactants in triacylglycerol synthesis are glycerol 3-phosphate and fatty acid acyl groups carried by coenzyme A. Triacylglycerol synthesis proceeds by transfer of first one and then another fatty acid acyl group from coenzyme A to glycerol 3-phosphate. The reaction is catalyzed by acyl transferase, and the product is phosphatidic acid.



Next, the phosphate group is removed from phosphatidic acid by phosphatidic acid phosphatase to produce 1,2-diacylglycerol. In the presence of acyl transferase, the third fatty acid group is then added to give a triacylglycerol.



As the reaction on page 780 shows, glycerol is one source of glycerol phosphate. But adipocytes do not synthesize glycerol kinase, the enzyme needed to convert glycerol to glycerol 3-phosphate; thus they cannot synthesize glycerol 3-phosphate from glycerol. However, glycerol 3-phosphate can be synthesized from DHAP produced from glyceraldehyde 3-phosphate generated in gluconeogenesis (Figure 22.9). Thus, adipocytes can synthesize triacylglycerols as long as DHAP is available. In adipocytes, this pathway is called *glyceroneogenesis,* and it supplies the DHAP for conversion to glycerol 3-phosphate. Glyceroneogenesis is an abbreviated form of gluconeogenesis (see Figure 22.9), ending with the conversion of DHAP to glycerol 3-phosphate followed by triacylglycerol synthesis.



Triacylglycerol Mobilization

When digestion of a meal is finished, blood glucose levels return to normal; consequently, insulin levels drop and glucagon levels rise. The lower insulin level and higher glucagon level together activate *triacylglycerol lipase,* the enzyme within adipocytes that controls hydrolysis of stored triacylglycerols. If glycerol 3-phosphate is in short supply—an indication that glycolysis is not producing sufficient energy—the fatty acids and glycerol produced by hydrolysis of the stored triacylglycerols are released to the bloodstream for transport to energy-generating cells. Otherwise, the fatty acids and glycerol are cycled back into new triacylglycerides for storage. Dieters on special low-carbohydrate diets are trying to produce this metabolic state in order to "burn fat." An undesirable side effect of these diets is ketosis and the production of ketone bodies (Section 24.6).

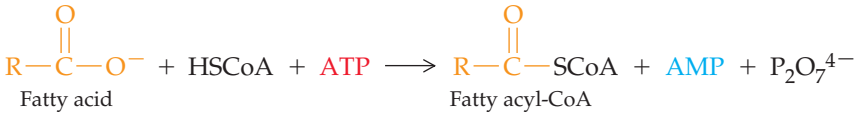
24.5 Oxidation of Fatty Acids

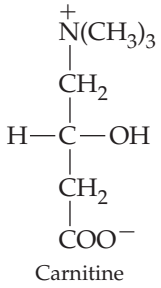
Learning Objectives:

- Describe fatty acid oxidation.
- Calculate the energy yield from fatty acid oxidation.

Once a fatty acid enters the cytosol of a cell that needs energy, three successive processes occur.

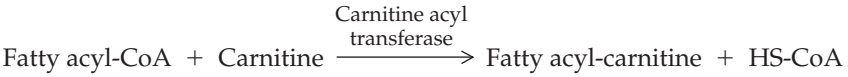
1. *Activation* The fatty acid is activated by conversion to fatty acyl-CoA. This activation, which occurs in the cytosol, serves the same purpose as the first few steps in oxidation of glucose by glycolysis. Initially, some energy from adenosine triphosphate (ATP) must be invested in converting the fatty acid to fatty acyl-CoA, a form that breaks down more easily. Since only one phosphate ester bond is broken in the reaction, the activation energy used is for one ATP only.





Carnitine

2. *Transport* The fatty acyl-CoA, which cannot cross the mitochondrial membrane by diffusion, is transported by carnitine from the cytosol into the mitochondrial matrix, where energy generation occurs. Carnitine, an amino-oxy acid, undergoes an ester-formation exchange reaction with the fatty acyl-CoA, resulting in a fatty acyl-carnitine ester that moves across the membrane into the mitochondria by facilitated diffusion. There, another ester-formation exchange reaction regenerates the fatty acyl-CoA and carnitine.

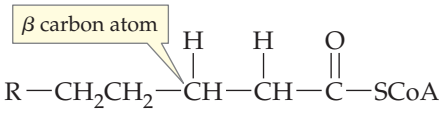


3. *Oxidation* The fatty acyl-CoA is oxidized by enzymes in the mitochondrial matrix to produce acetyl-CoA, nicotinamide adenine dinucleotide (NADH), and flavin adenine dinucleotide ($FADH_2$). The oxidation occurs by repeating the series of four reactions, which make up the ***β*-oxidation pathway.** Each repetition of these reactions cleaves a 2-carbon acetyl group from the end of a fatty acid acyl group and produces one acetyl-CoA. This pathway is a *spiral* because the shortened long-chain fatty acyl group must continue to return to the pathway until each pair of carbon atoms is removed.

***β*-Oxidation pathway** A repetitive series of biochemical reactions that degrades fatty acids to acetyl-CoA by removing carbon atoms two at a time.

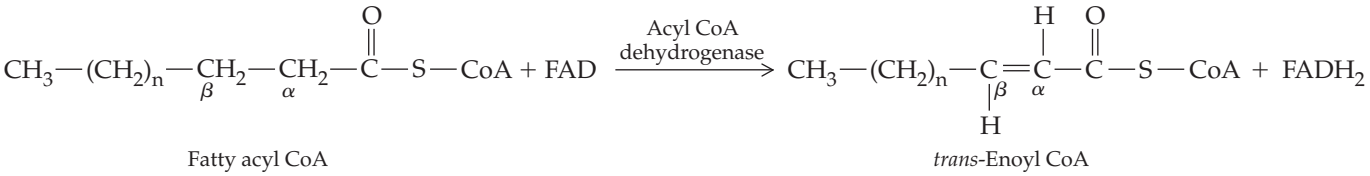
The *β*-Oxidation Pathway

The name β oxidation refers to the oxidation of the carbon atom β to the thioester linkage in two steps of the pathway.

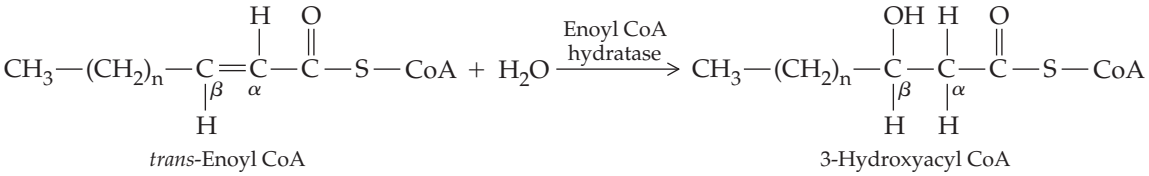


A fatty acyl-CoA

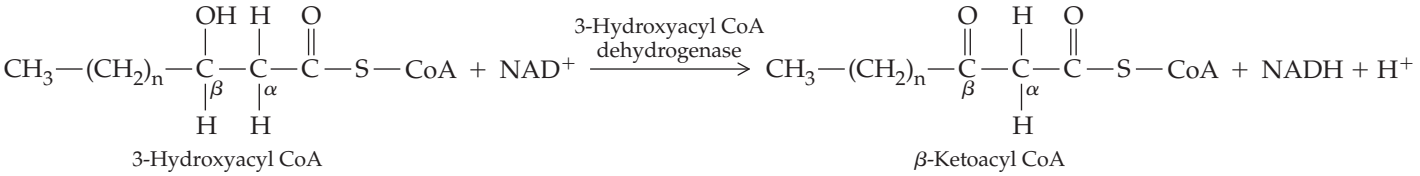
STEP 1: The first β oxidation *Acyl-CoA dehydrogenase* and its coenzyme FAD remove hydrogen atoms from the carbon atoms α and β to the carbonyl group in the fatty acyl-CoA, forming a carbon–carbon double bond. These hydrogen atoms and their electrons are passed directly from $FADH_2$ to coenzyme Q so that the electrons can enter the electron transport chain (Section 21.8).



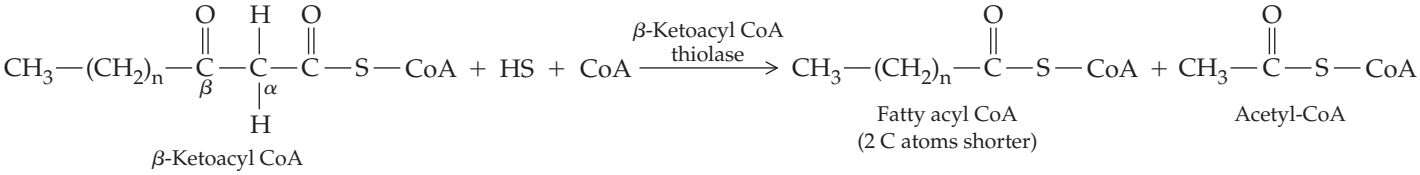
STEP 2: Hydration *Enoyl-CoA hydratase* adds a water molecule across the newly created double bond to give an alcohol with the —OH group on the β carbon.



STEP 3: The second β oxidation The coenzyme NAD^+ is the oxidizing agent for conversion of the β—OH group to a carbonyl group by β-hydroxyacyl-CoA dehydrogenase.



STEP 4: Cleavage to remove an acetyl group An acetyl group is split off by *thiolase (acyl-CoA acetyltransferase)* and attached to a new coenzyme A molecule, leaving behind an acyl-CoA that is two carbon atoms shorter.



If a fatty acid has an even number of carbon atoms, all of the carbons are transferred to acetyl-CoA molecules by an appropriate number of trips through the β-oxidation spiral. Additional steps are required to oxidize fatty acids with odd numbers of carbon atoms and those with double bonds. Ultimately, all fatty acid carbons are released for further oxidation in the citric acid cycle.

The total energy output from fatty acid catabolism, like that from glucose catabolism, is measured by the total number of ATP molecules produced. For fatty acids, this is the total number of ATP molecules from acetyl-CoA oxidation through the citric acid cycle, including those produced from the reduced coenzymes NADH and $FADH_2$ during oxidative phosphorylation, plus those produced by the reduced coenzymes (NADH and $FADH_2$) during fatty acid oxidation. The following worked examples show how to calculate the energy yield in ATP.

Worked Example 24.2 Spiraling through β Oxidation

How many times does stearic acid $(CH_3(CH_2)_{16}COOH)$ spiral through the β-oxidation pathway to produce acetyl-CoA?

ANALYSIS Each turn of the β-oxidation spiral pathway produces one acetyl-CoA. To determine the number of turns, divide the total number of carbon atoms in the fatty acid, 18 in this case, by two since an acetyl group contains two carbon atoms and they come from the fatty acid. Subtract one turn, since the last turn produces two acetyl-CoA molecules.

SOLUTION
Stearic acid contains 18 carbon atoms; the acetyl group contains two carbon atoms. Therefore, eight β-oxidation turns occur, and nine molecules of acetyl-CoA are produced.

▲ **Fat as a source of water.** A camel's hump is almost entirely fat, which serves as a source of energy and also water. As reduced coenzymes from fatty acid oxidation pass through electron transport to generate ATP, large amounts of water are formed (about one water molecule for each carbon atom in a fatty acid). This water sustains camels during long periods when no drinking water is available.

KEY CONCEPT PROBLEM 24.4

In β oxidation, (a) identify the steps that are oxidations and describe the changes that occur; (b) identify the oxidizing agents; (c) identify the reaction that is an addition; (d) identify the reaction that is a substitution.

PROBLEM 24.5

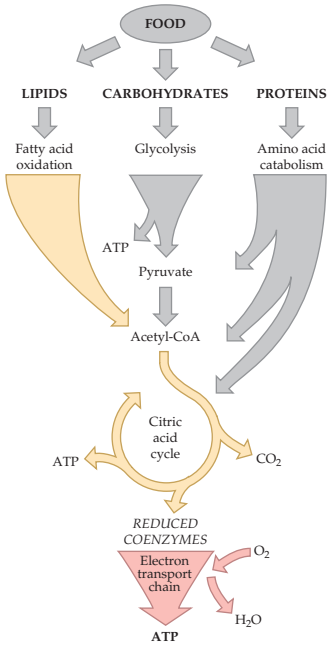
How many molecules of acetyl-CoA are produced by catabolism of the following fatty acids, and how many β oxidations are needed?

(a) Palmitic acid, $CH_3(CH_2)_{14}COOH$

(b) Lignoceric acid, $CH_3(CH_2)_{22}COOH$

PROBLEM 24.6

Look back at the reactions of the citric acid cycle (Figure 20.9) and identify the three reactions in that cycle that are similar to the first three reactions of the β oxidation of a fatty acid.



Worked Example 24.3 Calculating Energy Yield from β Oxidation

How much energy is released as ATP from the complete oxidation of lauric acid $(CH_3(CH_2)_{10}COOH)$?

ANALYSIS Complete oxidation of a molecule includes conversion of any energy released in oxidation pathways, as NADH or $FADH_2$ is also converted to ATP by passage through the electron transport system. To calculate the ATP yield from lauric acid:

- Determine the number of acetyl groups and number of turns of the β-oxidation spiral needed.
- Determine the ATP, NADH, and $FADH_2$ yield from one turn of the β-oxidation spiral.
- Determine the ATP, NADH, and $FADH_2$ yield from oxidation of acetyl-CoA in the citric acid cycle.
- Convert NADH and $FADH_2$ yields to ATP yields from oxidative phosphorylation.
- Adjust β-oxidation ATP yield for number of turns of the spiral.
- Adjust citric acid cycle ATP yield for number of acetyl-CoA molecules oxidized.
- Add the ATP yield and subtract 2 ATP molecules used to prime the start of β oxidation.

SOLUTION

From the citric acid cycle:

$$12 \text{ C atoms}/2 = 6 \text{ acetyl-CoA molecules}$$

$$\frac{12 \text{ ATP molecules}}{\text{acetyl-CoA molecule}} \times 6 \text{ acetyl-CoA molecules} = 72 \text{ ATP molecules}$$

Activation of the fatty acid: $= -2$ ATP molecules

From the 5 β oxidations:

$$\frac{5 \text{ ATP molecules}}{\beta \text{ oxidation}} \times 5\ \beta \text{ oxidations} = 25 \text{ ATP molecules}$$

Summation of the ATP used and produced:

$$\textit{Total} = (72 - 2 + 25) \text{ ATP molecules} = 95 \text{ ATP molecules}$$

Comparing the amount of ATP produced by fatty acid catabolism with the amount produced by glucose catabolism illustrates why our bodies use triacylglycerols rather than carbohydrates for long-term energy storage. We used lauric acid as our example because it has a molar mass close to that of glucose. Our best estimates show that 1 mol of glucose (180 g) generates 38 mol of ATP, whereas 1 mol of lauric acid (200 g) generates 95 mol of ATP. Thus, fatty acids yield nearly three times more energy per gram as carbohydrates. In terms of nutritional energy (i.e., kilojoules), carbohydrates yield 16.7 kJ/g, whereas fats and oils yield 37.7 kJ/g.

In addition, stored fats have a greater "energy density" than stored carbohydrates. Because glycogen—the storage form of carbohydrates—is hydrophilic, about 2 g of water are held with each gram of glycogen. The hydrophobic fats do not hold water in this manner.

PROBLEM 24.7

How much energy is released as ATP from the complete oxidation of stearic acid ($CH_3(CH_2)_{16}COOH$)?

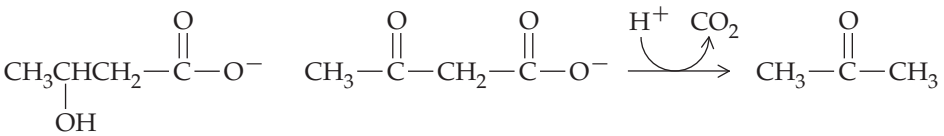
24.6 Ketone Bodies and Ketoacidosis

Learning Objective:

- Identify ketone bodies, describe their properties and synthesis, and explain their role in metabolism.

What happens if lipid catabolism produces more acetyl-CoA than the citric acid cycle can handle? This happens when β oxidation of the fatty acids from triacylglcerols produces acetyl-CoA faster than the citric acid cycle can process it. Not only does β oxidation produce several molecules of acetyl-CoA from each molecule of fatty acid, but the enzymes in the β-oxidation pathway catalyze reactions more rapidly than the enzymes in the citric acid cycle do. Consequently, the energy is preserved by conversion of excess acetyl-CoA in liver mitochondria to 3-hydroxybutyrate and acetoacetate. Because it is a β-keto acid and therefore somewhat unstable, acetoacetate undergoes spontaneous, nonenzymatic decomposition to acetone.

Ketone bodies



3-Hydroxybutyrate Acetoacetate Acetone

Ketone bodies Compounds produced in the liver that can be used as fuel by muscle and brain tissue; for example, 3-hydroxybutyrate, acetoacetate, and acetone.

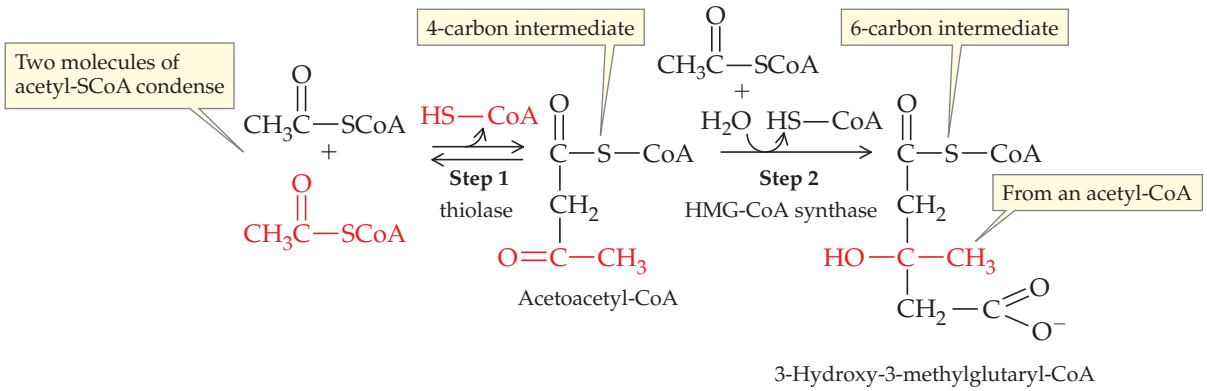
Ketogenesis The synthesis of ketone bodies from acetyl-CoA.

These compounds are traditionally known as **ketone bodies,** although one of them, 3-hydroxybutyrate, contains no ketone functional group. Because they are water-soluble, ketone bodies do not need protein carriers to travel in the bloodstream. Once formed, they become available to all tissues in the body.

The formation of the three ketone bodies, a process known as **ketogenesis,** occurs in four enzyme-catalyzed steps plus the spontaneous decomposition of acetoacetate.

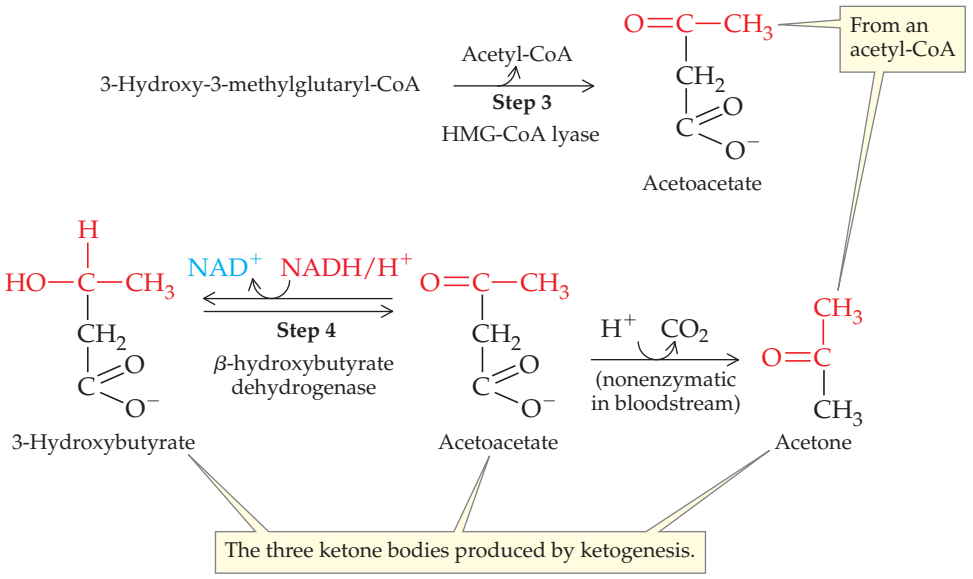
Ketogenesis

Steps 1 and 2 of Ketogenesis: Assembly of 6-Carbon Intermediate



In step 1, the reverse of the final step of β oxidation (step 4 in Figure 24.7), two acetyl-CoA molecules combine in a reaction catalyzed by *thiolase* to produce acetoacetyl-CoA. In step 2, a third acetyl-CoA and a water molecule react with acetoacetyl-CoA to give 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA). The enzyme for this step, *HMG-CoA synthase,* is found only in mitochondria and is specific only for the D isomer of the substrate. The enzyme for the β-oxidation pathway, also found in mitochondria, has the same name but is specific for the L form of HMG-CoA. The pathways are separated by the specificity of the enzymes for their respective substrates.

Steps 3 and 4 of Ketogenesis: Formation of the Ketone Bodies



In step 3, removal of acetyl-CoA from the product of Step 2 by *HMG-CoA lyase* produces the first of the ketone bodies, *acetoacetate.* Acetoacetate is the precursor of the other two ketone bodies produced by ketogenesis, 3-hydroxybutyrate and acetone. In step 4,

acetoacetate is reduced to 3-hydroxybutyrate by *3-hydroxybutyrate dehydrogenase*. (Note in the equation for step 4 that 3-hydroxybutyrate and acetoacetate are connected by a reversible reaction. In tissues that need energy, acetoacetate is produced by different enzymes than those used for ketogenesis. Acetyl-CoA can then be produced from the acetoacetate.) As acetoacetate and 3-hydroxybutyrate are synthesized by ketogenesis in liver mitochondria, they are released to the bloodstream. Decomposition of acetoacetate in the bloodstream forms acetone, which is excreted in urine and by exhalation.

CHEMISTRY IN ACTION

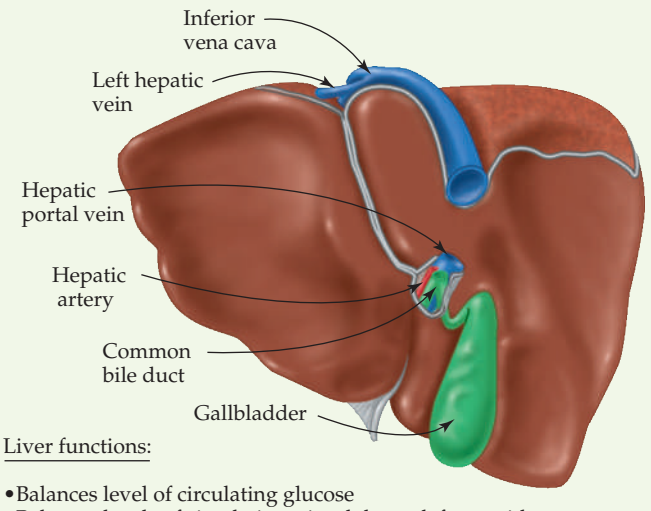
The Liver—Clearinghouse for Metabolism

The liver is the largest reservoir of blood in the body and also the largest internal organ, making up about 2.5% of the body's mass. Blood carrying the end products of digestion (glucose, other sugars, amino acids, and so forth) enters the liver through the hepatic portal vein before going into general circulation, so the liver is ideally situated to regulate the concentrations of nutrients and other substances in the blood. The liver is important as the gateway for entry of drugs into the circulation and also contains the enzymes needed to inactivate toxic substances as well.

The liver synthesizes glycogen from glucose, glucose from noncarbohydrate precursors, triacylglycerols from mono- and diacylglycerols, and fatty acids from acetyl-CoA. It also synthesizes cholesterol, bile acids, plasma proteins, and blood-clotting factors. In addition, liver cells catabolize glucose, fatty acids, and amino acids to yield carbon dioxide and energy stored in ATP. The *urea cycle,* which converts nitrogen to urea for excretion, takes place in the liver (Section 25.4).

The liver stores reserves of glycogen, certain lipids and amino acids, iron, and fat-soluble vitamins, in order to release them as needed to maintain homeostasis. In addition, only liver cells have the enzyme needed to convert glucose 6-phosphate from glycogenolysis and gluconeogenesis to glucose.

Given its central role in metabolism, the liver is subject to a number of pathological conditions based on excessive accumulation of various metabolites. For example *cirrhosis,* the development of fibrous tissue that is preceded by excessive triacylglycerol buildup is a serious medical condition. Cirrhosis occurs in alcoholism, uncontrolled diabetes, and metabolic conditions in which the synthesis of lipoproteins from triacylglycerols is blocked.



Liver functions:

- Balances level of circulating glucose
- Balances levels of circulating triacylglycerol, fatty acid, and cholesterol
- Removes excess amino acids from circulation; converts their nitrogen to urea for excretion
- Stores reserves of fat-soluble vitamins and iron
- Removes drugs from circulation and breaks them down

▲ Anatomy of the liver. Blood carries metabolites from the digestive system entering the liver through the hepatic portal vein. The gallbladder is the site for storage of bile.

CIA Problem 24.1 Give some reasons why the liver is so vital to proper metabolic function.

CIA Problem 24.2 What is cirrhosis of the liver, and what can trigger it?

CIA Problem 24.3 Why is the liver referred to as the clearinghouse for metabolism in your body?

Under normal conditions, acetoacetate supplies some of the daily energy needs for skeletal muscles, and heart muscles use it in preference to glucose when fatty acids are in short supply. But consider the situation when energy production from glucose is inadequate due to starvation or because glucose is not metabolized normally due to diabetes (Section 22.7). The body responds by providing other energy sources in what can become a precarious balancing act. Under these conditions, ketone body production accelerates because acetoacetate and 3-hydroxybutyrate are converted to acetyl-CoA for oxidation in the citric acid cycle.

During the early stages of starvation, heart and muscle tissues burn larger quantities of acetoacetate, thereby preserving glucose for use in the brain. In prolonged starvation, even the brain switches to ketone bodies to meet up to 75% of its energy needs.

The condition in which ketone bodies are produced faster than they are utilized *(ketosis)* occurs in diabetes. It is indicated by the characteristic odor of acetone (a highly volatile ketone) on the patient's breath and the presence of ketone bodies in the urine *(ketonuria)* and the blood *(ketonemia)*.

Ketoacidosis Lowered blood pH due to accumulation of ketone bodies.

Because two of the ketone bodies are carboxylic acids, continued ketosis such as might occur in untreated diabetes leads to the potentially serious condition known as **ketoacidosis**—acidosis resulting from increased concentrations of ketone bodies in the blood. The blood's buffers are overwhelmed and blood pH drops. An individual experiences dehydration due to increased urine flow, labored breathing because acidic blood is a poor oxygen carrier, and depression. Ultimately, if untreated, the condition leads to coma and death.

PROBLEM 24.8

Which of the following classifications apply to the formation of 3-hydroxybutyrate from acetoacetate?

(a) Condensation **(b)** Hydrolysis

(c) Oxidation **(d)** Reduction

PROBLEM 24.9

Consider the reactions of ketogenesis.

(a) What role does acetyl-CoA play?

(b) How many acetyl-CoA molecules are used in the production of the ketone bodies?

(c) What is the essential role of ketone bodies during prolonged starvation?

24.7 Biosynthesis of Fatty Acids

Learning Objective:

- Compare the pathways for fatty acid synthesis and oxidation, and describe the reactions of the synthesis pathway.

Lipogenesis The biochemical pathway for synthesis of fatty acids from acetyl-CoA.

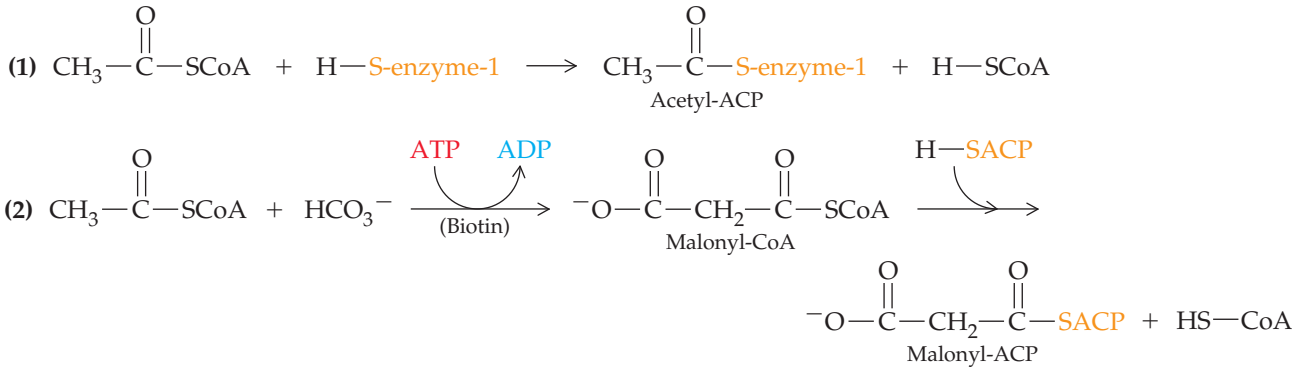
Fatty acid biosynthesis from acetyl-CoA, a process known as **lipogenesis,** provides a link between carbohydrate, lipid, and protein metabolism. Because acetyl-CoA is an end product of carbohydrate and amino acid catabolism, using it to make fatty acids allows the body to divert the energy of excess carbohydrates and amino acids into storage as triacylglycerols.

Fatty acid synthesis and catabolism are similar in that they both proceed two carbon atoms at a time and in that they are both recursive, spiral pathways. But, as is usually the case, the biochemical pathway in one direction is not the exact reverse of the pathway in the other direction because the reverse of an energetically favorable pathway is energetically unfavorable. This principle applies to β oxidation of fatty acids and its reverse, lipogenesis. Furthermore, catabolism of fatty acids occurs in the mitochondria and anabolism is located in the cytoplasm. The two pathways are compared in Table 24.1.

Table 24.1 Comparison of Fatty Acid Oxidation and Synthesis

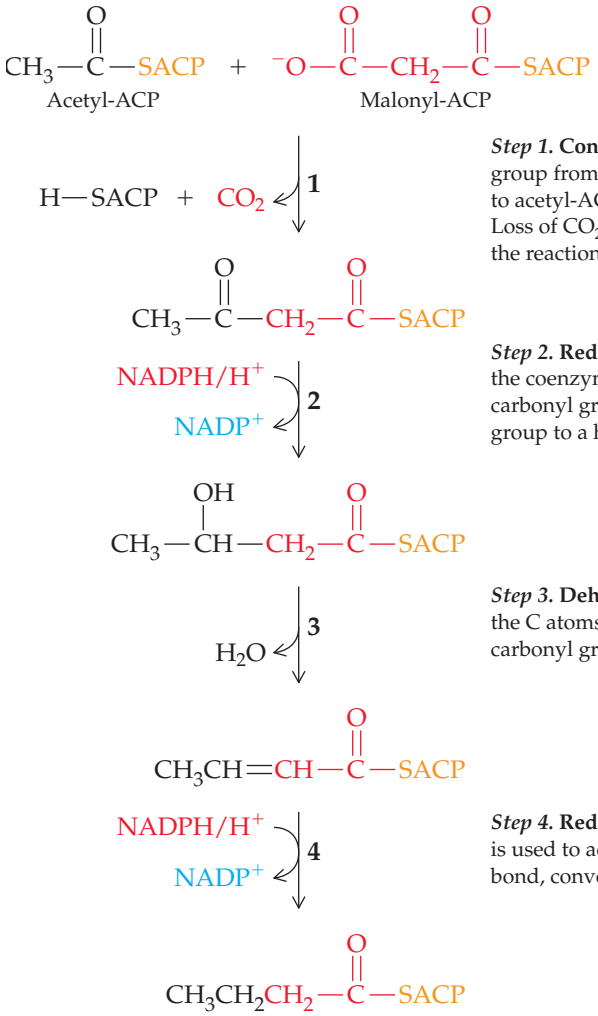
Oxidation	Synthesis
Occurs in mitochondria	Occurs in cytosol
Enzymes different from synthesis	Enzymes different from oxidation
Intermediates carried by coenzyme A	Intermediates carried by acyl carrier protein
Coenzymes: FAD and NAD^+	Coenzyme: NADPH
Carbon atoms removed two at a time	Carbon atoms added two at a time

The stage is set for lipogenesis by two separate reactions: (1) transfer of an acetyl group from acetyl-CoA to a carrier enzyme in the fatty acid synthase complex (S-enzyme-1) and (2) conversion of acetyl-CoA to malonyl-CoA in a reaction that requires the investment of energy from ATP, followed by transfer of the malonyl group to the acyl carrier protein (ACP) and regeneration of coenzyme A.



Fatty acid synthase is a multienzyme complex that contains all six of the enzymes needed for lipogenesis, with a protein called ACP anchored in the center of the complex. Enzyme-1 is also part of the complex. The malonyl group of reaction (2) carries the carbon atoms that will be incorporated two at a time into the fatty acid.

Once malonyl-ACP and the acetyl group on S-enzyme-1 have been readied, a series of four reactions, explained in Figure 24.7, lengthens the growing fatty acid chain by two carbon atoms with each repetition.



***Step 1.* Condensation** The malonyl group from malonyl-ACP transfers to acetyl-ACP with the loss of CO_2. Loss of CO_2 releases energy to drive the reaction.

***Step 2.* Reduction** This reaction uses the coenzyme NADPH to reduce the carbonyl group of the original acetyl group to a hydroxyl group.

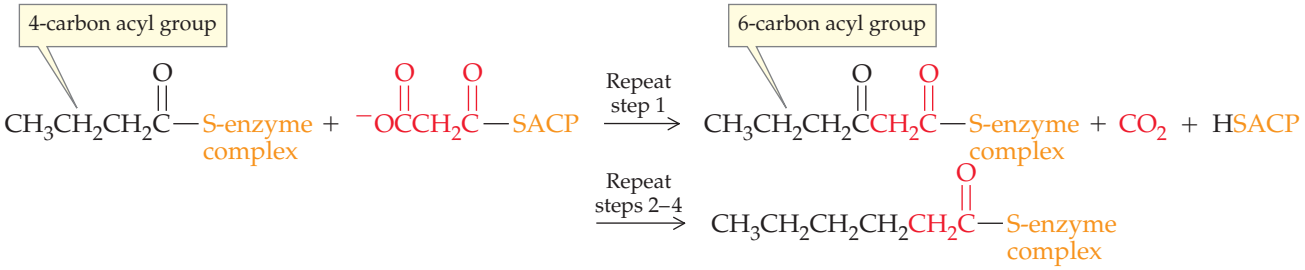
***Step 3.* Dehydration** Removal of H_2O at the C atoms α and β to the remaining carbonyl group introduces a double bond.

***Step 4.* Reduction** The coenzyme NADPH is used to add H atoms to the double bond, converting it to a single bond.

◂ Figure 24.7
Chain elongation in the biosynthesis of fatty acids.
The steps shown begin with acetyl-acyl carrier protein (acetyl-ACP), the reactant in the first spiral of palmitic acid synthesis. Each new pair of carbon atoms is carried into the next spiral by a new malonyl-ACP. The growing chain remains attached to the carrier protein from the original acetyl-ACP.

Chain Elongation of Fatty Acid

The result of the first cycle in fatty acid synthesis is the addition of two carbon atoms to an acetyl group to give a 4-carbon acyl group still attached to the carrier protein in fatty acid synthase. The next cycle then adds two more carbon atoms to give a 6-carbon acyl group by repeating the four steps of chain elongation shown here:



CHEMISTRY IN ACTION

Fat Storage, Lipids, and Atherosclerosis

Mammals store excess dietary calories as triacylglycerols in adipocytes (fat cells, found in adipose tissue). Some mammals, like bears and groundhogs, eat to store energy for use during hibernation; others, humans among them, seem simply to consume more sources of energy than necessary when given the opportunity. Your body can do several things with extra energy. It can burn fuel through exercise, use it to create heat, or store it for future use. Our bodies are very efficient at storing the extra energy against future need.

Excessive storage of triacylglycerols is a predictor of serious health problems and is associated with increased risk of developing Type II diabetes, colon cancer, heart disease, and fatty liver disease. For example, those with a body mass index (BMI) of 30 or greater (defined as obese) develop Type II diabetes at a higher rate than those with a normal BMI. The problem is even more acute in obese children. Not only do they risk developing serious health problems at an early age, but children have more fat cells than adults and can make new fat cells, allowing for storage of even more triacylglycerols.

Heart disease is the leading cause of death in many countries. Multiple long-term research projects provide consistent evidence for the connection between heart disease and diets high in saturated fats and cholesterol. Research has also provided strong evidence that high dietary fat is one risk factor for certain types of cancer. Several points are clear.

- A diet rich in saturated animal fats leads to an increase in blood-serum cholesterol.
- A diet lower in saturated fat and higher in unsaturated fat can lower the serum cholesterol level.

▲ These Emperor penguins will survive for months on the energy supplied by the catabolism of stored fat.

- High levels of serum cholesterol are correlated with *atherosclerosis,* a condition in which yellowish waxy deposits *(arterial plaque)* composed of cholesterol and other lipid-containing materials form within the larger arteries. The result of atherosclerosis is an increased risk of coronary artery disease and heart attack brought on by blockage of blood flow to heart muscles or an increased risk of stroke due to blockage of blood flow to the brain.

After seven trips through the elongation spiral, a 16-carbon palmitoyl group is produced and released from the fatty acid synthase. Larger fatty acids are synthesized from palmitoyl-CoA with the aid of specific enzymes in the endoplasmic reticulum.

PROBLEM 24.10

Starting with acetyl-S-enzyme-1 and malonyl-CoA, how many molecules of acetyl-CoA are needed to synthesize an 18-carbon fatty acid (C18:0)? How many molecules of CO_2 are released in this process?

HANDS-ON CHEMISTRY 24.1

The leading cause of death in the United States is cardiac disease. Use the Web to answer these questions.

- What is a heart attack?
- What are the symptoms of a heart attack in men? In women?
- Why is a heart attack dangerous?
- One treatment for heart problems is "bypass surgery." What is this and why is it done?

Other risk factors considered in an overall evaluation of an individual's risk of heart disease include high blood levels of cholesterol coupled with low levels of HDLs, cigarette smoking, high blood pressure, diabetes, obesity, a low level of physical activity, and a family history of early heart disease.

As discussed in Section 24.2, lipoproteins are complex assemblages of lipids and proteins that transport lipids throughout the body. If LDL delivers more cholesterol than is needed to peripheral tissues, and if insufficient HDL is present to remove it, the excess cholesterol is deposited in cells and arteries. Thus, the higher the HDL level, the less the likelihood of deposits and the lower the risk of heart disease. Also, LDL has the harmful potential to trigger inflammation and the buildup of plaque in artery walls. (Remember it this way—*low* LDL is good; *high* HDL is good.)

Many groups recommend that individuals strive for the following cholesterol levels in blood:

Total cholesterol	200 mg/dL or lower
LDL	100 mg/dL or lower
HDL	60 mg/dL or higher

Decreasing saturated fats and cholesterol in the diet, adopting an exercise program, and not smoking constitute the first line of defense for those at risk. For those at high risk or for whom the first-line defenses are inadequate, drugs are available that prevent or slow the progress of coronary artery disease by lowering serum cholesterol levels. Among the drugs are indigestible resins *(cholestyramine* and *colestipol)* that bind bile acids and accelerate their excretion, causing the liver to use up more cholesterol in bile acid synthesis. Another class of effective drugs is the statins (e.g., lovastatin), which inhibit an enzyme crucial to the synthesis of cholesterol.

Remember Malcom from the beginning of the chapter? His blood tests showed significantly elevated cholesterol and triacylglycerides as well as abnormal levels of HDL and LDL. Other tests revealed that he had a heart attack and needed bypass surgery due to large plaque deposits in the arteries leading to his heart. In addition to the heart surgery, Malcolm was given diet and exercise advice to improve his activity level and body mass and counseled on smoking cessation. He was prescribed a statin among other medications and given a follow-up appointment for a week after hospital discharge.

CIA Problem 24.4 What diseases are obese people at high risk of developing?

CIA Problem 24.5 What factors contribute to storage of excess energy as triacylglycerols?

CIA Problem 24.6 What are desirable goals for fasting levels of total cholesterol, HDL, and LDL values? What are the differences between the roles of LDL and HDL?

CIA Problem 24.7 What is atherosclerosis?

CIA Problem 24.8 What is arterial plaque? Why is it desirable to have a high HDL value and a relatively low LDL value?

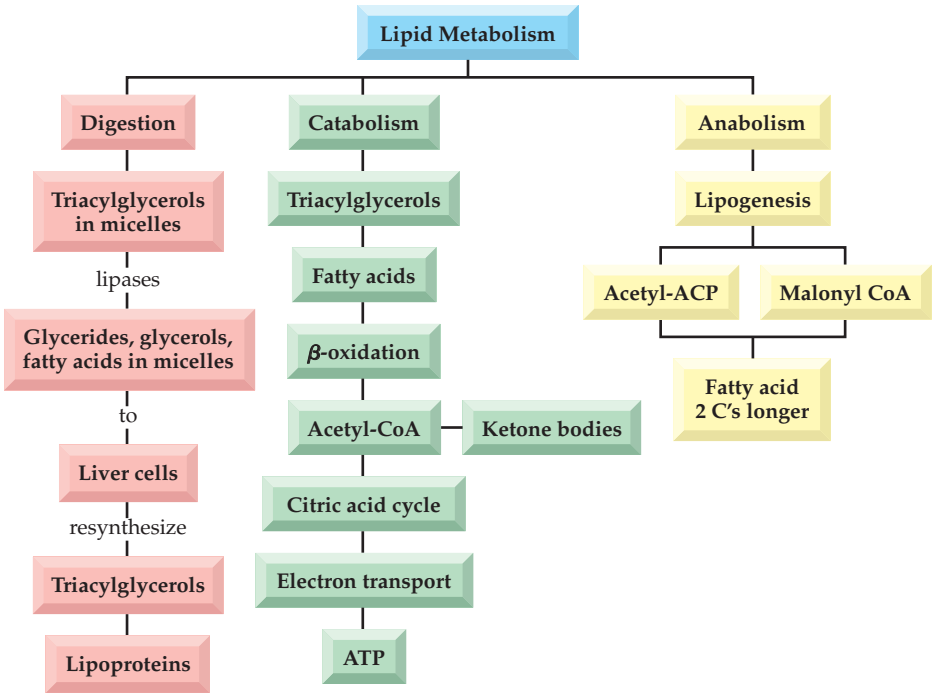
SUMMARY REVISITING THE CHAPTER GOALS

- **List the steps in the digestion of dietary triacylglycerols and their transport into the bloodstream.** *Triacylglycerols* from the diet are broken into droplets in the stomach and enter the small intestine, where they are emulsified by *bile acids* and form micelles. Pancreatic lipases partially hydrolyze the triacylglycerols in the micelles. Small fatty acids and glycerol from triacylglycerol hydrolysis are absorbed directly into the bloodstream at the intestinal surface. Insoluble hydrolysis products are carried to the lining in micelles, where they are absorbed and reassembled into triacylglycerols. These triacylglycerols are then assembled into *chylomicrons* (which are *lipoproteins*) and absorbed into the lymph system for transport to the bloodstream *(see Problems 19–24).*
- **Name the major classes of lipoproteins, specify the nature and function of the lipids they transport, and identify their destinations.** In addition to chylomicrons, which carry triacylglycerols from the diet into the bloodstream, there are VLDLs *(very low-density lipoproteins),* which carry triacylglycerols synthesized in the liver to peripheral tissues for energy generation or storage; LDLs *(low-density lipoproteins),* which transport cholesterol from the liver to peripheral tissues for cell membranes or steroid synthesis; and HDLs *(high-density lipoproteins),* which transport cholesterol from peripheral tissues back to the liver for conversion to bile acids that are used in digestion or excreted *(see Problems 12, 25–28, 68, 70, and 71).*
- **Name the major pathways for the synthesis and breakdown of triacylglycerols and fatty acids, and identify their connections to other metabolic pathways.** Dietary triacylglycerols carried by chylomicrons in the bloodstream undergo hydrolysis to fatty acids and glycerol by enzymes in capillary walls. Triacylglycerols in storage are similarly hydrolyzed within adipocytes. The fatty acids from either source undergo *β oxidation* to acetyl-CoA or resynthesis into triacylglycerols for storage. Acetyl-CoA can participate in resynthesis of fatty acids *(lipogenesis),* formation of *ketone bodies (ketogenesis),* steroid synthesis, or energy generation via the citric acid cycle and oxidative phosphorylation. Glycerol can participate in glycolysis, gluconeogenesis, or triacylglycerol synthesis *(see Problems 29, 64, 65, and 72).*
- **Explain the reactions by which triacylglycerols are stored and mobilized, and how these reactions are regulated.** Synthesis of triacylglycerols for storage is activated by insulin when blood glucose levels are high. The synthesis requires DHAP (from glycolysis or glycerol) for conversion to glycerol 3-phosphate, to which fatty acyl groups are added one at a time to yield triacylglycerols. Hydrolysis of triacylglycerols stored in adipocytes is activated by glucagon when glucose levels drop *(see Problems 13 and 31–34).*
- **Describe fatty acid oxidation.** Fatty acids are activated (in the cytosol) by conversion to fatty acyl coenzyme A, a reaction that requires the equivalent of two ATPs in the conversion of ATP to adenosine monophosphate (AMP). The fatty acyl-CoA molecules are transported into the mitochondrial matrix and are then oxidized two carbon atoms at a time to acetyl-CoA by repeated trips through the β-oxidation spiral *(see Problems 11, 14–16, 35–42, and 66).*
- **Calculate the energy yield from fatty acid oxidation.** Energy yield as ATP is calculated by summing the number of ATP molecules generated by β-oxidation freeing the acetyl-CoA groups, oxidation of acetyl-CoA in the citric acid cycle, and oxidative phosphorylation transformation of all NADH and $FADH_2$ molecules into ATP. Subtract the 2 ATP molecules used to prime the catabolism of the fatty acid *(see Problems 17, 43–50, and 69).*
- **Identify ketone bodies, describe their properties and synthesis, and explain their role in metabolism.** The ketone bodies are 3-hydroxybutyrate, acetoacetate, and acetone. They are produced from two acetyl-CoA molecules. Their production is increased when energy generation from the citric acid cycle cannot keep pace with the quantity of acetyl-CoA available. This occurs during the early stages of starvation and in unregulated diabetes. Ketone bodies are water-soluble and can travel unassisted in the bloodstream to tissues where acetyl-CoA is produced from acetoacetate and 3-hydroxybutyrate. In this way, acetyl-CoA is made available for energy generation when glucose is in short supply *(see Problems 51–55).*
- **Compare the pathways for fatty acid synthesis and oxidation, and describe the reactions of the synthesis pathway.** Fatty acid synthesis (lipogenesis), like β oxidation, proceeds two carbon atoms at a time in a four-step pathway. The pathways utilize different enzymes and coenzymes. In synthesis, the initial four carbons are transferred from acetyl-CoA to the malonyl carrier protein. Each additional pair of carbons is then added to the growing chain bonded to the carrier protein, with the final three steps of the four-step synthesis sequence the reverse of the first three steps in β oxidation *(see Problems 18 and 56–63).*

KEY WORDS

β-oxidation pathway, *p. 782*
Bile, *p. 775*
Bile acids, *p. 775*
Ketoacidosis, *p. 788*
Ketogenesis, *p. 786*
Ketone bodies, *p. 786*
Lipogenesis, *p. 788*
Lipoprotein, *p. 775*
Mobilization (of triacylglycerols), *p. 780*

CONCEPT MAP



▲ **Figure 24.8 Concept Map.** This map links the digestion and transport of lipids (especially triacylglycerides) to the catabolism products of triacylglycerides and energy yield and to the generation of fatty acids from other molecules.

UNDERSTANDING KEY CONCEPTS

24.11 Oxygen is not a reactant in the β oxidation of fatty acids. Can β oxidation occur under anaerobic conditions? Explain.

24.12 Identify each lipoprotein described here as either chylomicron, HDL, LDL, or VLDL.

(a) Which lipoprotein has the lowest density? Why?

(b) Which lipoprotein carries triacylglycerols from the diet?

(c) Which lipoprotein removes cholesterol from circulation?

(d) Which lipoprotein contains "bad cholesterol" from a vascular disease risk standpoint?

(e) Which lipoprotein has the highest ratio of protein to lipid?

(f) Which lipoprotein carries triacylglycerols from the liver to peripheral tissues? How are triacylglycerols used?

(g) Which lipoprotein transports cholesterol from the liver to peripheral tissues?

24.13 Lipid metabolism, especially triacylglycerol anabolism and catabolism, is closely associated with carbohydrate (glucose) metabolism. Insulin and glucagon levels in blood are regulated by the glucose levels in blood. Draw lines from the appropriate phrases in column A to appropriate phrases in columns B and C.

A	B	C
High blood glucose	High glucagon / low insulin	Fatty acid and triacylglycerol synthesis
Low blood glucose	High insulin / low glucagon	Triacylglycerol hydrolysis; fatty acid oxidation

24.14 One strategy used in many different biochemical pathways is an initial investment of energy early on and a large payoff in energy at the end of the pathway. How is this strategy utilized in the catabolism of fats?

24.15 When oxaloacetate in liver tissue is being used for gluconeogenesis, what impact does this have on the citric acid cycle? Explain.

24.16 Why is it more efficient to store energy as triacylglycerols rather than as glycogen?

24.17 Explain the rationale for the production of ketone bodies during starvation.

24.18 Compare the differences between β oxidation and fatty acid synthesis (lipogenesis). Are these pathways the reverse of each other?

ADDITIONAL PROBLEMS

DIGESTION OF LIPIDS (SECTION 24.1)

24.19 Why do lipids make you feel full for a long time after a meal?

24.20 Where does digestion of lipids occur?

24.21 What is the purpose of bile acids in lipid digestion?

24.22 Where are bile acids synthesized, and what is the starting molecule?

24.23 Write the equation for the hydrolysis of a triacylglycerol composed of stearic acid, oleic acid, and linoleic acid by pancreatic lipase.

24.24 Lipases break down triacylglycerols by catalyzing hydrolysis. What are the products of this hydrolysis?

LIPID TRANSPORT (SECTION 24.2)

24.25 What are chylomicrons, and how are they involved in lipid metabolism?

24.26 What is the origin of the triacylglycerols transported by very low-density lipoproteins?

24.27 How are the fatty acids from adipose tissue transported?

24.28 How is cholesterol transported around the body? When it leaves the liver, what is its destination and use?

OVERVIEW OF TRIACYLGYCERIDE STORAGE AND METABOLISM (SECTIONS 24.3 AND 24.4)

24.29 The glycerol derived from lipolysis of triacylglycerols is converted into glyceraldehyde 3-phosphate, which then enters into step 6 of the glycolysis pathway. What further transformations are necessary to convert glyceraldehyde 3-phosphate into pyruvate?

24.30 If the conversion of glycerol to glyceraldehyde 3-phosphate releases 1 molecule of ATP, how many molecules of ATP are released during the conversion of glycerol to pyruvate?

24.31 How many molecules of ATP are released in the overall catabolism of glycerol to acetyl-CoA? How many molecules of ATP are released in the complete catabolism of glycerol to CO_2 and H_2O? (Hint: Combine pathways of glycerol to DHAP with glycolysis from DHAP to pyruvate and pyruvate to acetyl-CoA. Remember to account for any NADH and $FADH_2$ produced.)

24.32 How many molecules of acetyl-CoA result from catabolism of 1 molecule of glyceryl trilaurate? (Hint: See Worked Example 24.3 and don't forget glycerol.)

24.33 What is an adipocyte?

24.34 What is the primary function of adipose tissues, and where in the body are they located?

OXIDATION OF FATTY ACIDS (SECTION 24.5)

24.35 Which tissues carry out fatty acid oxidation as their primary source of energy?

24.36 Where in the cell does β oxidation take place?

24.37 What initial chemical transformation takes place on a fatty acid to activate it for catabolism?

24.38 What must take place before an activated fatty acid undergoes β oxidation?

24.39 Why is the stepwise oxidation of fatty acids called β oxidation?

24.40 Why is the sequence of reactions that catabolize fatty acids described as a *spiral* rather than a *cycle*?

24.41 Which coenzymes are required for β oxidation?

24.42 Are these the same coenzymes necessary for fatty acid synthesis?

24.43 How many moles of ATP are produced by one cycle of β oxidation?

24.44 How many moles of ATP are produced by the complete oxidation of 1 mol of myristic acid?

24.45 Arrange these following four molecules in increasing order of their biological energy content (per mole):

(a) Sucrose

(b) Myristic acid, $CH_3(CH_2)_{12}COOH$

(c) Glucose

(d) Capric acid, $CH_3(CH_2)_8COOH$

24.46 Arrange these four molecules in increasing order of their biological energy content per mole:

(a) Mannose

(b) Stearic acid, $CH_3(CH_2)_{16}COOH$

(c) Fructose

(d) Palmitic acid, $CH_3(CH_2)_{14}COOH$

24.47 Show the products of each step in the fatty acid oxidation of hexanoic acid.

(a) $CH_3(CH_2)_4\overset{\overset{O}{\|}}{C}SCoA \xrightarrow[\text{Acetyl-CoA dehydrogenase}]{FAD \;\; FADH_2} \;?$

(b) Product of (a) $+ \; H_2O \xrightarrow[\text{hydratase}]{\text{Enoyl-CoA}} \;?$

(c) Product of (b) $\xrightarrow[\beta\text{-Hydroxyacyl-CoA dehydrogenase}]{NAD^+ \;\; NADH/H^+} \;?$

(d) Product of (c) $+ \; HSCoA \xrightarrow[\text{transferase}]{\text{Acetyl-CoA}} \;?$

24.48 Write the equation for the final step in the catabolism of any fatty acid with an even number of carbons.

24.49 How many molecules of acetyl-CoA result from complete catabolism of the following compounds?

(a) Myristic acid, $CH_3(CH_2)_{12}COOH$

(b) Caprylic acid, $CH_3(CH_2)_6COOH$

24.50 How many cycles of β oxidation are necessary to completely catabolize myristic and caprylic acids?

KETONE BODY PRODUCTION (SECTION 24.6)

24.51 What three compounds are classified as ketone bodies? Why are they so designated? What process in the body produces them? Why do they form?

24.52 What is ketosis? What condition results from prolonged ketosis? Why is it dangerous?

24.53 What causes acetone to be present in the breath of someone with uncontrolled diabetes?

24.54 Individuals suffering from ketoacidosis have acidic urine. What effect do you expect ketones to have on pH? Why is pH lowered when ketone bodies are present?

24.55 Diets that severely restrict carbohydrate intake often result in ketosis for the dieter. Explain why this occurs.

FATTY ACID ANABOLISM (SECTION 24.7)

24.56 Name the anabolic pathway that synthesizes fatty acids.

24.57 Explain why β oxidation cannot proceed backward to produce triacylglycerols.

24.58 Name the starting material for fatty acid synthesis.

24.59 Why are fatty acids generally composed of an even number of carbons?

24.60 How many rounds of the lipogenesis cycle are needed to synthesize stearic acid, $C_{17}H_{35}COOH$?

24.61 How many molecules of NADPH are needed to synthesize stearic acid, $C_{17}H_{35}COOH$?

24.62 How does the cell keep the processes of fatty acid synthesis and degradation separated?

24.63 Describe two differences in the reactions for fatty synthesis and the reactions for fatty acid degradation.

CONCEPTUAL PROBLEMS

24.64 Consuming too many carbohydrates causes deposition of fats in adipose tissue. How does this happen?

24.65 Why is extra energy consumed as carbohydrates stored as fat and not as glycogen?

24.66 Are any of the intermediates in the β-oxidation pathway chiral? Explain.

24.67 Compare fats and carbohydrates as energy sources in terms of the amount of energy released per mole, and account for the observed energy difference.

24.68 Lipoproteins that transport lipids from the diet are described as exogenous. Those that transport lipids produced in metabolic pathways are described as endogenous. Which of the following lipoproteins transports exogenous lipids and which transports endogenous lipids?

(a) Low-density lipoprotein (LDL)

(b) Chylomicrons

24.69 Behenic acid (C22:0) is present in peanut butter.

(a) How many molecules of acetyl-CoA are produced by β oxidation of behenic acid?

(b) How many molecules of ATP are produced in (a)?

(c) How many molecules of CO_2 are produced by complete oxidation of the acetyl-CoA produced in (a)?

(d) How many molecules of ATP are produced in (c)?

(e) How many total molecules of ATP are produced by the complete oxidation of behenic acid to CO_2?

GROUP PROBLEMS

24.70 High blood-cholesterol levels are dangerous because of their correlation with atherosclerosis and consequent heart attacks and strokes. Is it possible to eliminate all cholesterol from the bloodstream by having a diet that includes no cholesterol? Is it desirable to have no cholesterol at all in your body? Explain your answer.

24.71 In the synthesis of cholesterol, acetyl-CoA is converted to 2-methyl-1,3-butadiene. Molecules of 2-methyl-1,3-butadiene are then joined to give the carbon skeleton of cholesterol. Draw the condensed structure of 2-methyl-1,3-butadiene. How many carbon atoms does cholesterol contain? What minimum number of 2-methyl-1,3-butadiene molecules is required to make one molecule of cholesterol?

24.72 A low-fat diet of pasta, bread, beer, and soda can easily lead to an increase in body mass. The increase is stored triacylglycerols in adipocytes. Explain the increase in mass and why the excess carbohydrate is stored as fat.

25

Protein and Amino Acid Metabolism

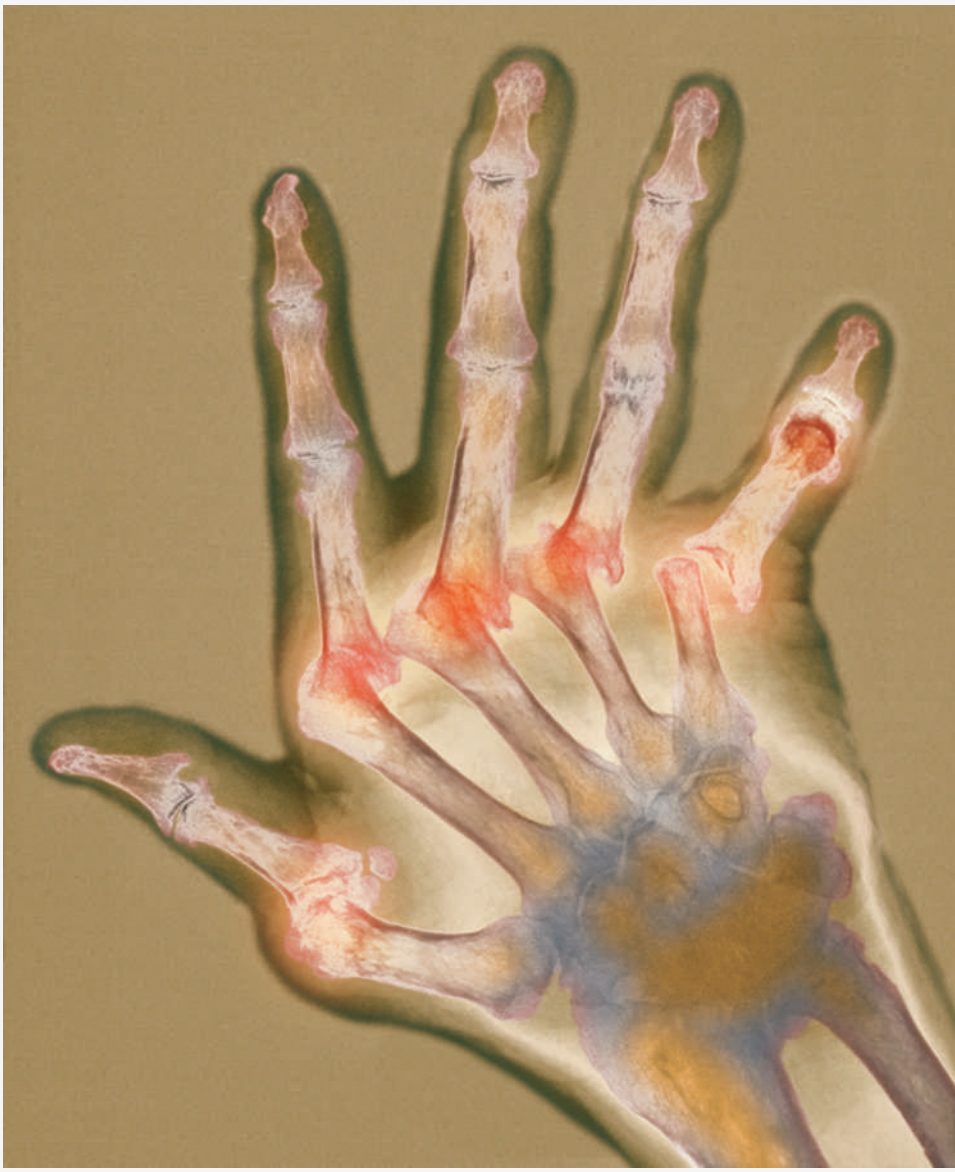
CONTENTS

CONCEPTS TO REVIEW

A. Amino Acids (Sections 18.3 and 18.4)

B. Primary Protein Structure (Section 18.7)

C. Overview of Metabolism (Section 21.3)



▲ Colored X ray of the deformed hand of a patient suffering from rheumatoid arthritis (RA). Joint damage (shown in red) has caused the fingers to bend abnormally. Decreased serum levels of the essential amino acid histidine is a specific metabolic marker for this disease

The number of extremely complex biomolecules our bodies can synthesize is astounding, yet there are some we need that we do not have the ability to make. These molecules, called essential nutrients, must be obtained daily from the foods we eat. Foremost among these are the nine essential amino acids, which must be obtained via the digestion of protein obtained from external sources. But what would happen if one or more of the essential amino acids was missing from our diet? In that case, any number of amino acid deficiency problems could arise, ranging from anemia and kidney disease to psychotic and schizophrenic behavior. For example, a dietary deficiency of histidine, one of the more debated essential amino acids, may play a role in rheumatoid arthritis (RA), one of the most debilitating diseases known and shown in the photo above. Indeed, decreased histidine levels in blood serum have been used as a specific metabolic

marker for RA. The role and additional consequences of deficiencies of the essential amino acids will be discussed in the Chemistry in Action "The Importance of Essential Amino Acids and Effects of Deficiencies" found at the end of this chapter.

We now turn to discuss the metabolic fate of proteins and ultimately the amino acids that they are constructed from. Although we have the biochemical machinery necessary to make almost all of the amino acids we need, the hydrolysis of dietary protein is still our major source for them. Before diving into the discussion of protein and amino acid metabolism, it will be helpful to review the structures of the amino acids and the proteins they form (Chapter 18) as well as the essential function of proteins as enzymes (Chapter 19). The actual biosynthesis of proteins will be examined in Chapter 26, and the examination of body fluids for the diagnosis of disease will be discussed in Chapter 29.

25.1 Digestion of Proteins

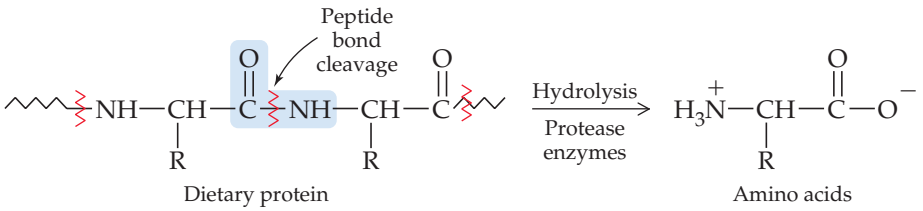
Learning Objective:

- List the steps of protein digestion.

Recall from Chapter 18 that proteins are polymers of individual amino acids linked together by connecting the $-NH_2$ group of one amino acid to the $-COOH$ of another, forming peptide bonds ($-CONH-$), which are nothing more than amide bonds. The end result of protein digestion is simple—the hydrolysis of all peptide bonds to produce a collection of amino acids.

CONCEPTS TO REVIEW
Hydrolysis of amide bonds was discussed in Section 17.6.

Hydrolysis of peptide bonds



For example,

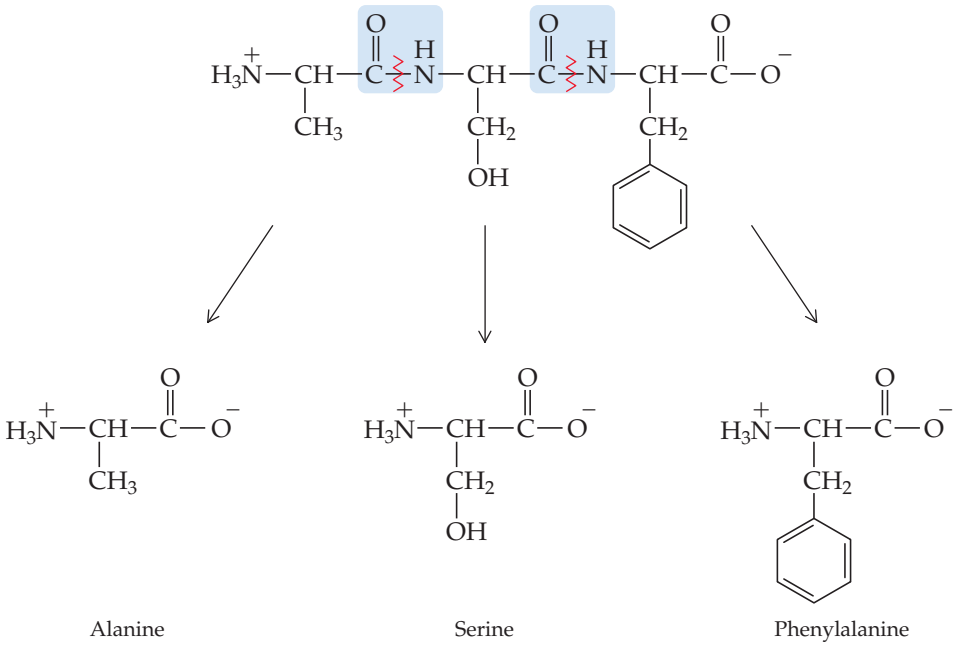
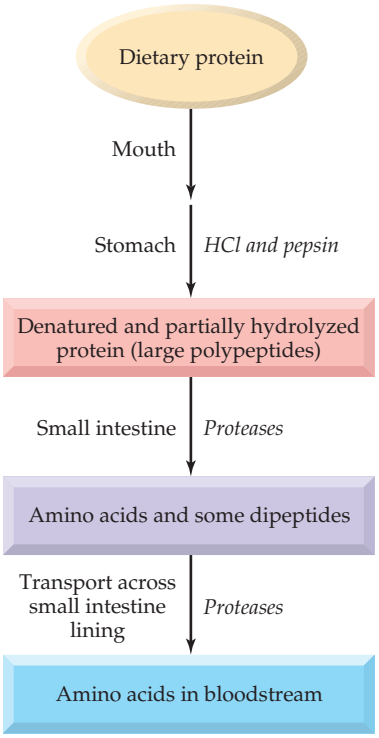


Figure 25.1 summarizes the digestive processes involved in the conversion of protein to amino acids. The breakdown of protein begins in the mouth, where large pieces of food are converted (by chewing) into smaller, more digestible portions. Although no



▲ **Figure 25.1**
Digestion of proteins.

Recall from Section 19.8 that a zymogen (or proenzyme) is a compound that becomes an active enzyme after undergoing a chemical change.

▲ Individual amino acids are promoted for a variety of unproven health benefits. Because amino acids are classified as foods, they need not undergo the stringent testing for purity, safety, and efficacy required for Food and Drug Administration (FDA) approval.

chemical digestion of the protein has begun, this step is necessary to increase the surface area of the food to be digested. The chemical digestion of dietary proteins begins with their denaturation in the strongly acidic environment of the stomach (pH 1–2), where the tertiary and secondary structures of consumed proteins begin to unfold. In addition to hydrochloric acid, gastric secretions include pepsinogen, a zymogen that is activated by acid to give the enzyme pepsin. Unlike most proteins, pepsin is stable and active at pH 1–2. Protein hydrolysis begins as pepsin breaks some of the peptide bonds in the denatured proteins, producing polypeptides.

The polypeptides produced by pepsin then enter the small intestine, where the pH is about 7–8. Pepsin is rendered inactive in this less acidic environment, and a group of pancreatic zymogens is secreted. These activated enzymes (proteases such as trypsin, chymotrypsin, and carboxypeptidase) then take over to further hydrolyze peptide bonds in the partially digested proteins.

The combined action of the pancreatic proteases in the small intestine and other proteases in the cells of the intestinal lining completes the conversion of dietary proteins into free amino acids. After active transport across cell membranes lining the intestine, the amino acids are absorbed directly into the bloodstream.

The active transport of amino acids into cells is managed by several transport systems devoted to different groups of amino acids. For this reason, an excess of one amino acid in the diet can dominate the transport and produce a deficiency of others. This condition usually arises only in individuals taking large quantities of a single amino acid dietary supplement, such as those often sold in health food stores.

HANDS-ON CHEMISTRY 25.1

Nutritional experts have established what are known as Recommended Daily Allowance (RDA) or Dietary Reference Intake (DRI) values for everything from vitamins to sugar. In this exercise you are going to calculate how much protein you should be taking in daily, and then examining some dietary scenarios and the consequences of them. You will need at least three days and an internet connection to fully carry out this activity.

a. Let's begin calculating how much protein you should be eating a day. Begin by getting an accurate body mass for yourself. Convert your mass from pounds to kilograms (this can be done by dividing your mass in pounds by 2.2). The DRI values for protein are 0.8 g of protein per kilogram of body mass for moderately active adults from 19 to 24 years old. Based on this number, calculate how much protein you should be consuming in a day.

b. The protein DRI value increases as a person's average daily activity levels increase. For example, if you are a runner your DRI for protein should be 1.2–1.4 g of protein per kilogram of body mass and up to 1.8 g of protein per kilogram of body mass if you are doing strength training. Let's assume that in an average day you are fairly active, either through walking, running, exercising, or playing sports. Assuming your DRI is 1.1 g of protein per kilogram of body mass, calculate how much protein you should be consuming in a day if this scenario were to describe you.

c. Now, using a journal, record exactly what you eat for breakfast, lunch, dinner, and snacks in between meals for three days. If you can, try and estimate how much of each item you ate. If you skip a meal, record that as well. Using the internet, see if you can find the grams of protein (if any) in each item you ate. Total that number up for each day and take the average for the three days you recorded. Are you eating too little, too much, or just enough protein based on the numbers in parts a and b?

d. Protein intake is not just about quantity, it is also about quality. As a final exercise, look up what "quality" means with respect to protein. Provide a list of foods that provide "quality protein." How can you personally change your diet to incorporate more quality protein in it?

25.2 Amino Acid Metabolism: An Overview

Learning Objectives:

- Define the amino acid pool and its metabolic role.
- Explain how amino acids are catabolized.

The entire collection of free amino acids throughout the body—the **amino acid pool**—occupies a central position in protein and amino acid metabolism (see the concept map at the end of the chapter; Figure 25.5). All tissues and biomolecules in the body are constantly being degraded, repaired, and replaced—a process known as **turnover.** A healthy adult turns over about 300 g of protein every day, meaning amino acids are continuously entering the pool, not only from digestion but also from the breakdown of old proteins, and are continuously being withdrawn for synthesis of new nitrogen-containing biomolecules.

Amino acid pool The entire collection of free amino acids in the body.

Turnover The continual renewal or replacement of biomolecules; for protein it is defined by the balance between protein synthesis and protein degradation.

Each of the 20 amino acids is degraded via its own unique pathway. The important point to remember is that the process is the same for each one.

General Process for Amino Acid Catabolism

- Removal of the amino group (Section 25.3)
- Use of the removed $-NH_2$ in the synthesis of new nitrogen compounds (Section 25.3)
- Passage of nitrogen into the urea cycle (Section 25.4)
- Incorporation of the carbon atoms into compounds that can enter the citric acid cycle (Section 25.5)

Recall from Section 21.3 that catabolism is the breakdown and anabolism is the synthesis of biomolecules.

Our bodies do not store nitrogen-containing compounds, and ammonia is toxic to cells. Therefore, the amino nitrogen from dietary protein has just two possible fates: It must either be incorporated into urea and excreted or be used in the synthesis of new nitrogen-containing compounds; these include the following:

- Nitric oxide (NO, a chemical messenger)
- Hormones
- Neurotransmitters
- Nicotinamide (in coenzymes NAD^+ and $NADP^+$)
- Heme (as part of hemoglobin in red blood cells)
- Purine and pyrimidine bases (for nucleic acids)

LOOKING AHEAD Hormones and neurotransmitters are chemical messengers discussed in Chapter 28; Figure 19.10 highlights the nicotinamide group on NAD^+; view the chemical structure of heme in Figure 21.10; purine and pyrimidines can be seen in Table 26.1.

Nitrogen monoxide (NO) is a particularly interesting molecule: Chemically, it has an odd number of electrons (a *free radical;* Section 13.7) and is therefore very reactive. Biologically, it lowers blood pressure, kills invading bacteria, and enhances memory. NO is synthesized in the linings of blood vessels and elsewhere from oxygen and the amino acid arginine. In blood vessels, NO activates reactions in smooth muscle cells that cause dilation and a resulting decrease in blood pressure. Drugs such as nitroglycerin release NO, which explains their usefulness in treating angina, the pain experienced during exertion by individuals with partially blocked blood vessels.

NO was discussed in Chapter 4's Chemistry in Action "CO and NO: Pollutants or Miracle Molecules?".

The carbon portion of the amino acid has a much more varied fate. The carbon atoms of amino acids are converted to compounds that can enter the citric acid cycle. They continue through the citric acid cycle (the body's main energy-generating pathway; Section 20.8) to give CO_2 and energy stored in adenosine triphosphate (ATP). About 10–20% of our energy is normally produced in this way from amino acids. If not needed immediately for energy, the carbon-carrying intermediates produced from amino acids enter storage as triacylglycerols (via lipogenesis) or glycogen (via gluconeogenesis and glycogen synthesis). They can also be converted to ketone bodies.

Lipogenesis and ketone body synthesis were discussed in Chapter 24. Review gluconeogenesis and glycogen synthesis in Chapter 22.

PROBLEM 25.1

Decide whether each of the following statements is true or false. If false, explain why.

(a) The amino acid pool is found mainly in the liver.
(b) Nitrogen-containing compounds can be stored in fatty tissue.
(c) Some hormones and neurotransmitters are synthesized from amino acids.

KEY CONCEPT PROBLEM 25.2

Serotonin is a monoamine neurotransmitter. It is formed in the body from the amino acid tryptophan (Figure 28.6, p. 870). What class of enzyme catalyzes each of the two steps that convert tryptophan to serotonin?

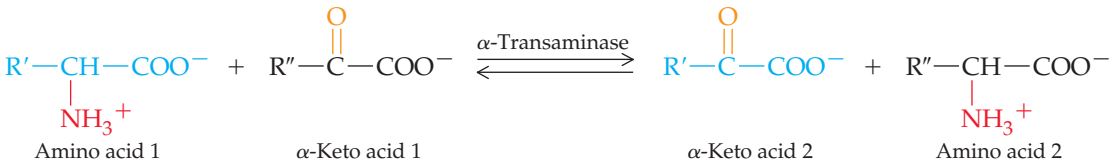
25.3 Amino Acid Catabolism: The Amino Group

Learning Objective:

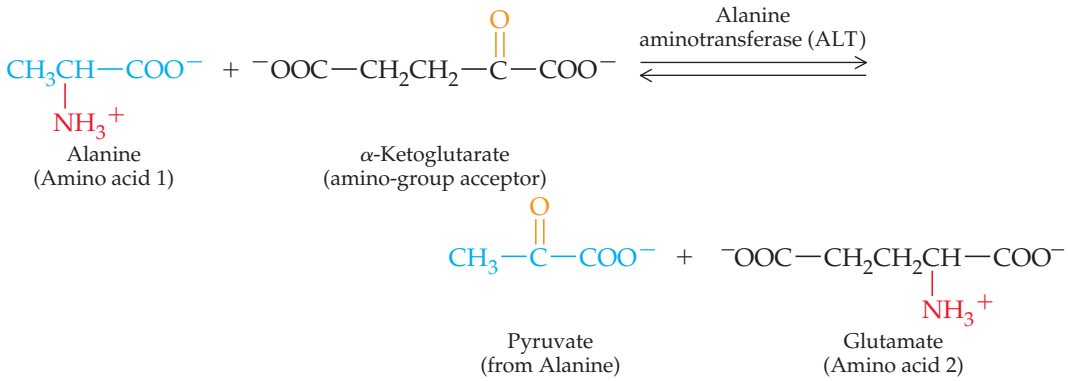
- Discuss the fate of the nitrogen of an amino acid.

Transamination The interchange of the amino group of an amino acid and the keto group of an α-keto acid.

The first step in amino acid catabolism is removal of the amino group and occurs primarily in the intracellular fluid (cytosol) of liver cells. In this process, known as **transamination,** the amino group of the amino acid and the keto group of an α-keto acid change places.



A number of transaminase enzymes are responsible for "transporting" (hence the prefix "trans") an amino group from one molecule to another. Most are specific for α-ketoglutarate as the amino-group acceptor and can remove the $-NH_2$ group (deaminate) from several different amino acids. The α-ketoglutarate is converted to glutamate, and the amino acid is converted to an α-keto acid. For example, alanine is converted to pyruvate by transamination.



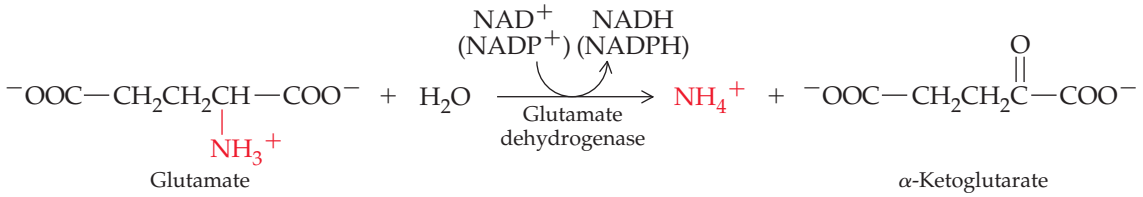
The enzyme for this conversion, alanine aminotransferase (ALT), is especially abundant in the liver, and above-normal ALT concentrations in the blood are taken as an indication of liver damage that has allowed ALT to leak into the bloodstream.

Transamination is a key reaction in many biochemical pathways, where amino acid amino groups and carbonyl groups are interconverted as necessary. This process is reversible and goes easily in either direction, depending on the concentrations of the reactants. In this way, amino acid concentrations are regulated by keeping synthesis and breakdown in balance. For example, the reaction of pyruvate with glutamate (the reverse of the preceding reaction) is the main synthetic route for alanine.

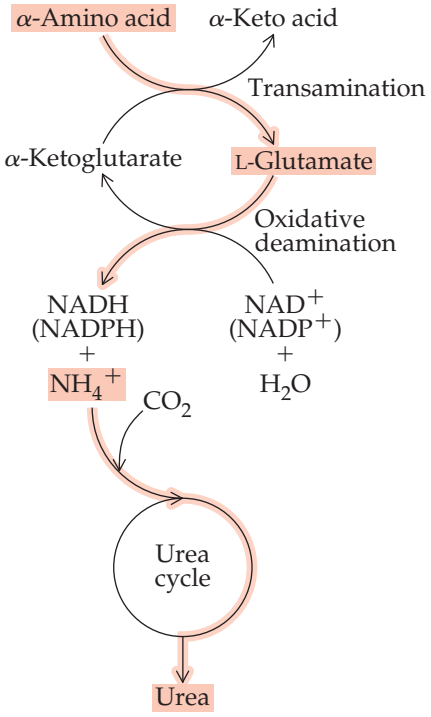
Glutamate from transamination serves as an amino-group carrier and can be used to provide amino groups for the synthesis of new amino acids. Most of the glutamate formed in this way, however, is recycled to regenerate α-ketoglutarate. This process,

which occurs in mitochondria, is known as **oxidative deamination.** Here, the glutamate amino group is oxidatively removed as ammonium ion to give back α-ketoglutarate.

Oxidative deamination Conversion of an amino acid —NH_2 group to an α-keto group, with removal of NH_4^+.



The ammonium ion formed in this reaction proceeds to the urea cycle where it is eliminated in the urine as urea. The pathway of nitrogen from an amino acid to urea is summarized in Figure 25.2, to the right.

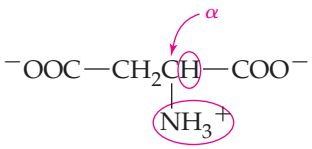


▲ **Figure 25.2**
Pathway of nitrogen from an amino acid to urea.
The nitrogen-bearing compounds and their pathway are highlighted in red.

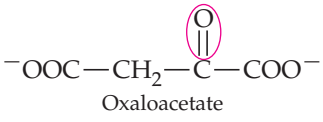
Worked Example 25.1 Predicting Transamination Products

The blood-serum concentration of the heart-muscle transaminase, aspartate aminotransferase (AST), is used in the diagnosis of heart disease because the enzyme escapes into the serum from damaged heart cells. AST catalyzes transamination of aspartate with α-ketoglutarate. What are the products of this reaction?

ANALYSIS The reaction is the interchange of an amino group from aspartate with the keto group from α-ketoglutarate. We know that α-ketoglutarate always gives glutamate in transamination, so one product is glutamate. The product from the amino acid will have a keto group instead of the amino group; we need to consider various amino acid structures to identify a candidate. Consulting Table 18.3 (which lists the structures of the 20 amino acids), we see that the structure of aspartate (aspartic acid) is as shown here.



Removing the $-NH_3^+$ and —H groups bonded to the α carbon and replacing them by a C=O gives the desired α-keto acid, which in this case happens to be oxaloacetate.



SOLUTION
The overall reaction is, therefore,

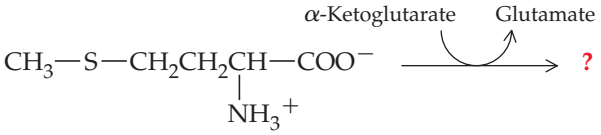
Aspartate + α-Ketoglutarate → Oxaloacetate + Glutamate

PROBLEM 25.3

What is the structure of the α-keto acid formed by transamination of the amino acid phenylalanine (Phe)? Refer to Table 18.3 for the structure of Phe.

PROBLEM 25.4

What is the structure of the α-keto acid formed in the following reaction?



PROBLEM 25.5

Explain how the conversion of alanine to pyruvic acid (pyruvate) can be identified as an oxidation reaction.

PROBLEM 25.6

Unlike most amino acids, branched-chain amino acids are broken down in tissues other than the liver. Using Table 18.3, identify the three amino acids with branched-chain R groups. For any one of these amino acids, write the equation for its transamination.

25.4 The Urea Cycle

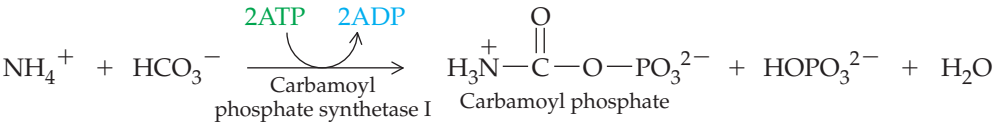
Learning Objective:

- Identify the major reactants and products of the urea cycle.

Ammonia (as well as the ammonium ion, NH_4^+) is highly toxic to living things and must be eliminated in a way that does no harm. Fish are able to excrete ammonia through their gills directly into their watery surroundings where it is immediately diluted and its toxic effects effectively neutralized. Since mammals do not live in an environment where this immediate dilution is possible, they must find other ways to get rid of ammonia. Direct excretion of ammonia in urine is not feasible for mammals, because the volume of water needed to accomplish this safely would cause dehydration. Mammals must first convert ammonia, in solution as ammonium ion, to nontoxic urea via the **urea cycle.**

Urea cycle The cyclic biochemical pathway that produces urea for excretion.

The conversion of ammonium ion to urea takes place in the liver. From there, the urea is transported to the kidneys and transferred to urine for excretion. Like many other biochemical pathways, urea formation begins with an energy investment. Ammonium ion (from oxidative deamination of amino acids), hydrogen carbonate ion (from carbon dioxide produced in the citric acid cycle), and ATP combine to form carbamoyl phosphate. This reaction takes place in the mitochondrial matrix. Two ATPs are invested and one phosphate is transferred to form the carbamoyl phosphate (an energy-rich phosphate ester, like ATP).



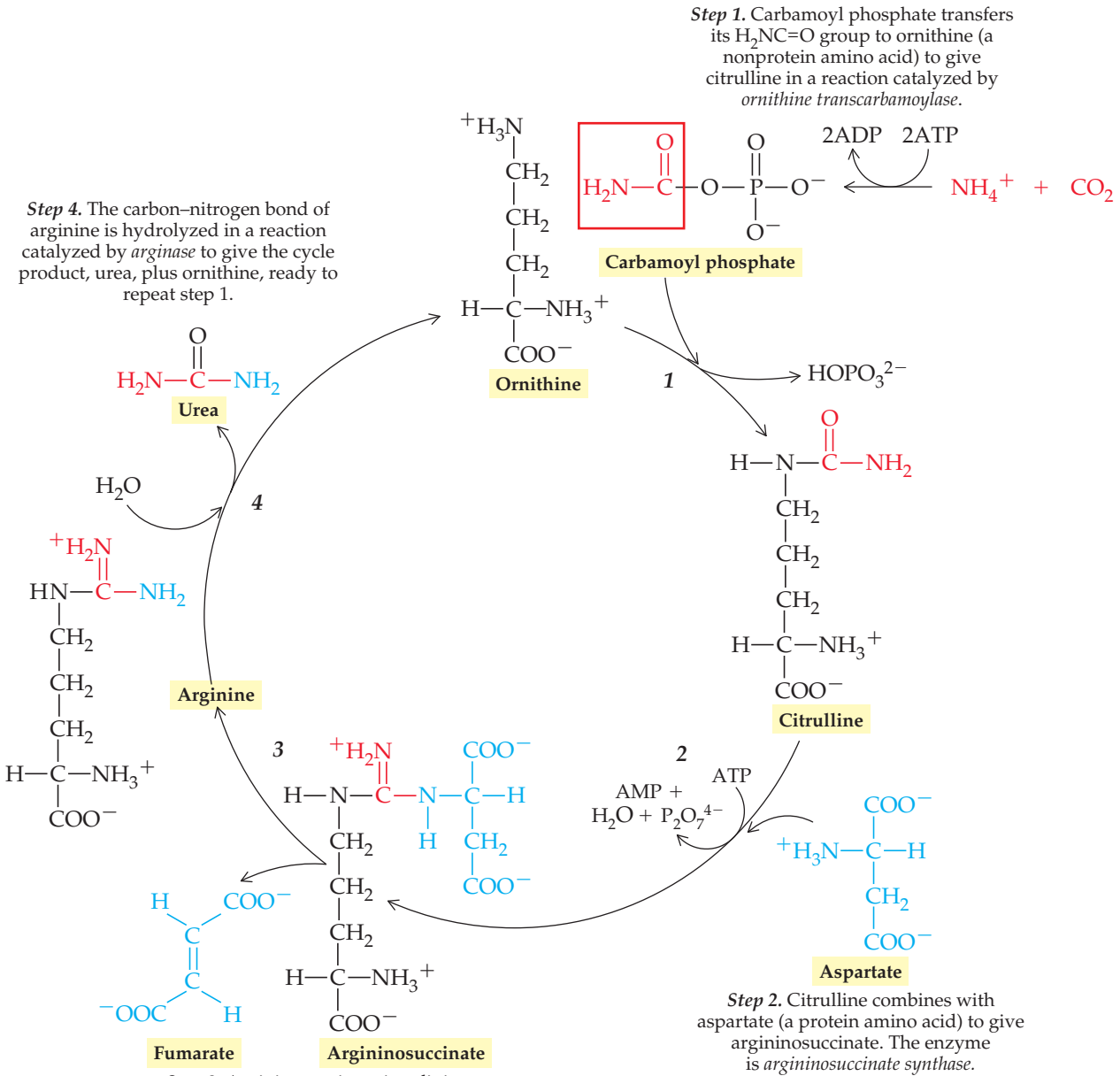
▲ Fish do not need to convert ammonia to urea for elimination because it is quickly diluted in the surrounding water; this is why the water in fish tanks must be constantly monitored to ensure that the ammonia concentration does not reach toxic levels.

Carbamoyl phosphate next reacts in the first step of the four-step urea cycle, shown in Figure 25.3.

STEPS 1 AND 2 OF THE UREA CYCLE: Building Up a Reactive Intermediate The first step of the urea cycle transfers the carbamoyl group, $H_2NC{=}O$, from carbamoyl phosphate to ornithine, an amino acid not found in proteins, to give citrulline, another nonprotein amino acid. This exergonic reaction introduces the first urea nitrogen into the urea cycle.

In Step 2, a molecule of aspartate combines with citrulline in a reaction driven by conversion of ATP to adenosine monophosphate (AMP) and pyrophosphate $(P_2O_7^{4-})$, followed by the additional exergonic hydrolysis of pyrophosphate. Both nitrogen atoms destined for elimination as urea are now bonded to the same carbon atom in argininosuccinate (red C atom in Figure 25.3).

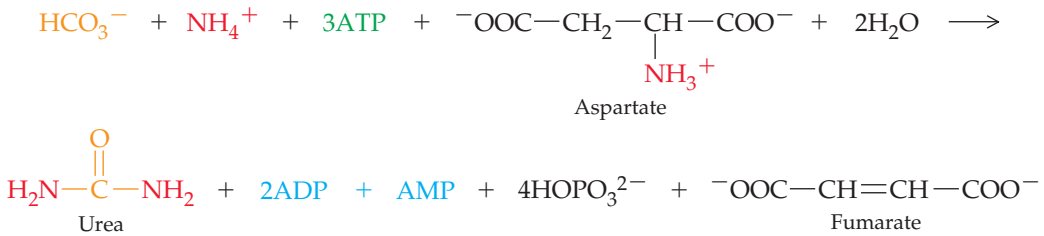
STEPS 3 AND 4 OF THE UREA CYCLE: Cleavage and Hydrolysis of the Step 2 Product Step 3 cleaves argininosuccinate into two pieces: arginine, an amino acid, and fumarate,



▲ **Figure 25.3**
The urea cycle.
The formation of carbamoyl phosphate and Step 1, the formation of citrulline, take place in the mitochondrial matrix. Steps 2–4 take place in the cytosol. The carbamoyl group is shown boxed in red at the top of the figure.

which you may recall is an intermediate in the citric acid cycle (Figure 21.8). Now all that remains, in step 4, is hydrolysis of arginine to give urea and regenerate the reactant in step 1 of the cycle, ornithine.

Net Result of the Urea Cycle

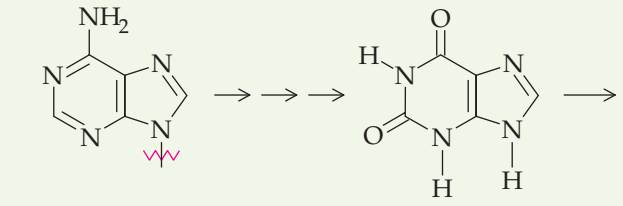


CHEMISTRY IN ACTION

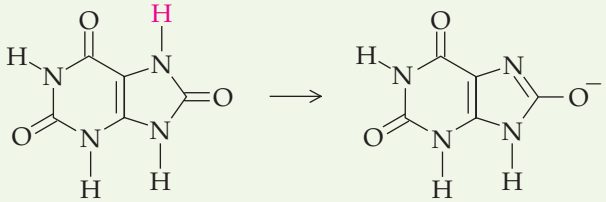
Gout: When Biochemistry Goes Awry

A small amount of our waste nitrogen is excreted in urine and feces as urate rather than urea. Because the urate salt is highly insoluble, any excess of the urate anion causes precipitation of sodium urate, which can lead to the severely painful condition known as gout. Gout has become more common in recent years; the increase is believed to be due to increasing risk factors in the population, such as longer life expectancy and changes in diet. The pain of gout results from a cascade of inflammatory responses to these crystals in the affected tissue. Even though it has been known for a very long time that the symptoms of gout are caused by urate crystals, understanding the many possible causes of the crystal formation is far from complete, even with modern medicine and all its sophisticated technology. Looking at a few of the pathways to gout illustrates some of the many ways that the delicate balance of our biochemistry can be disrupted.

Uric acid is an end product of the breakdown of purine nucleosides, and loss of its acidic H (in red) gives urate ion. Adenosine, for example, undergoes a number of enzymatic steps to produce xanthine, which is eventually converted to uric acid.



Adenosine Xanthine

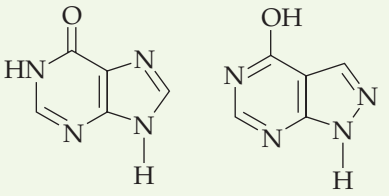


Uric acid Urate ion

Anything that increases the production of uric acid or inhibits its excretion in the urine is a possible cause of gout. For example, several known hereditary enzyme defects increase the quantity of purines and therefore of uric acid. Sometimes, gouty attacks follow injury or severe muscle exertion. Complicating matters is the observation that the presence of crystals in a joint is not always accompanied by inflammation and pain.

One significant cause of increased uric acid production is accelerated breakdown of ATP, ADP, or the production of AMP. For example, alcohol abuse generates acetaldehyde that must be metabolized in the kidney by a pathway that requires ATP and produces excess AMP. Inherited fructose intolerance, glycogen-storage diseases, and circulation of poorly oxygenated blood also accelerate uric acid production by this route. With low oxygen, ATP is not efficiently regenerated from ADP in mitochondria, leaving the ADP to be disposed of.

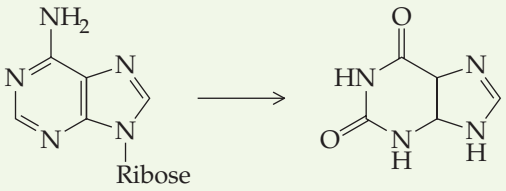
Conditions that diminish excretion of uric acid include kidney disease, dehydration, hypertension, lead poisoning, and competition for excretion from anions produced by ketoacidosis.



Hypoxanthine Allopurinol

One treatment for gout relies on allopurinol, a structural analog of hypoxanthine, which is a precursor of xanthine in the formation of urate. Allopurinol inhibits the enzyme for conversion of hypoxanthine and xanthine to urate. Since hypoxanthine and xanthine are more soluble than sodium urate, they are more easily eliminated.

CIA Problem 25.1 Adenosine is known to be converted to xanthine, the direct precursor to uric acid. Starting with adenosine, list all the chemical changes that occurred on its conversion to xanthine.



Adenosine Xanthine

CIA Problem 25.2 Your grandfather complains of pain in his swollen and inflamed big toe, and the doctor indicates that it is caused by gout.

(a) How would you explain to him what gout is and its biochemical cause?

(b) What can you suggest to him to prevent these gouty attacks?

CIA Problem 25.3 Compare the structure of allopurinol with the structures of hypoxanthine and xanthine. Where does allopurinol differ in structure from hypoxanthine?

We can summarize the results of the urea cycle as follows:

- Formation of urea from the carbon of CO_2, NH_4^+, and one nitrogen from the amino acid aspartate, followed by biological elimination through urine
- Breaking of four high-energy phosphate bonds to provide energy
- Production of the citric acid cycle intermediate, fumarate

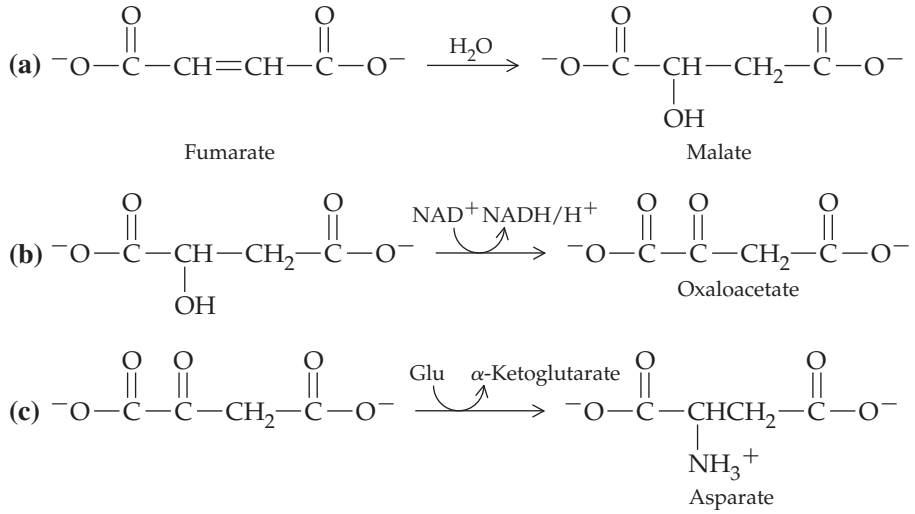
Hereditary diseases are associated with defects in the enzymes for each step in the urea cycle. The resulting abnormally high levels of ammonia in the blood *(hyperammonemia)* cause vomiting in infancy, lethargy, irregular muscle coordination *(ataxia),* and mental retardation. Immediate treatment consists of transfusions, blood dialysis *(hemodialysis),* and use of chemical agents to remove ammonia. Long-term treatment requires a low-protein diet and frequent small meals to avoid protein overload.

PROBLEM 25.7

As Figure 25.3 shows, arginine (a) is converted to ornithine (b) in the last step of the urea cycle. To ultimately enter the citric acid cycle, ornithine undergoes transamination at its terminal amino group to give an aldehyde (c), followed by oxidation to glutamate (d), and conversion to α-ketoglutarate (e). Write the structures of the five molecules (a–e) in the pathway beginning with arginine and ending with α-ketoglutarate. Circle the region of structural change in each.

KEY CONCEPT PROBLEM 25.8

Fumarate from step 3 of the urea cycle may be recycled into aspartate for use in step 2 of the cycle. The sequence of reactions for this process is



Classify each reaction as one of the following:

(1) Oxidation (2) Reduction (3) Transamination
(4) Elimination (5) Addition

25.5 Amino Acid Catabolism: The Carbon Atoms

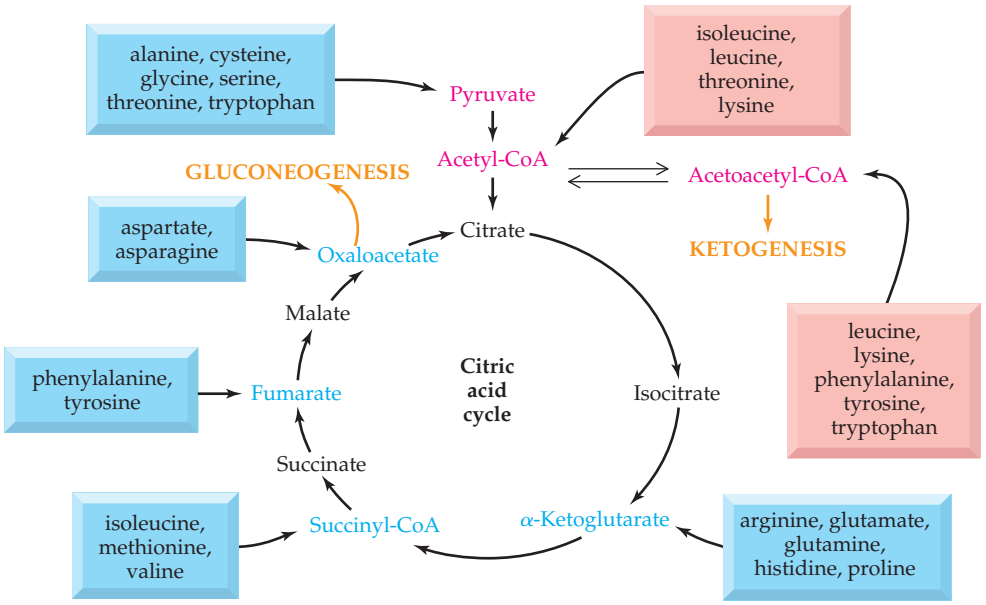
Learning Objective:

- Describe the metabolic fate of the carbon atoms in an amino acid.

The carbon atoms of each protein amino acid arrive, by distinctive pathways, at pyruvate, acetyl-CoA, or one of the citric acid cycle intermediates shown in blue type in Figure 25.4. Eventually, all of the amino acid carbon skeletons can be used to generate energy, either by passing through the citric acid cycle and into the gluconeogenesis pathway to form glucose or by entering the ketogenesis pathway to form ketone bodies.

Table 25.1 Glucogenic and Ketogenic Amino Acids

Glucogenic	
Alanine	Glycine
Arginine	Histidine
Aspartate	Methionine
Asparagine	Proline
Cysteine	Serine
Glutamate	Threonine
Glutamine	Valine
Glucogenic and Ketogenic	
Isoleucine	
Lysine	
Phenylalanine	
Tryptophan	
Tyrosine	
Ketogenic	
Leucine	



▲ **Figure 25.4**
Fate of amino acid carbon atoms.
The carbon atoms of the amino acids are converted to the seven compounds shown here in red and blue type, each of which is either an intermediate in the citric acid cycle or a precursor to citrate. The amino acids in the blue boxes are glucogenic—they can form glucose via the entry of oxaloacetate into gluconeogenesis. Those in the pink boxes are ketogenic—they are available for ketogenesis.

Those amino acids that are converted to acetoacetyl-CoA or acetyl-CoA then enter the ketogenesis pathway and are called *ketogenic amino acids.*

Those amino acids that proceed by way of oxaloacetate to the gluconeogenesis pathway (Section 22.9) are known as *glucogenic amino acids* (Table 25.1). Both ketogenic and glucogenic amino acids are able to enter fatty acid biosynthesis via acetyl-CoA (Section 24.7).

Nonessential amino acid One of 11 amino acids that are synthesized in the body and are therefore not necessary in the diet.

Essential amino acid An amino acid that cannot be synthesized by the body and thus must be obtained from the diet.

25.6 Biosynthesis of Nonessential Amino Acids

Learning Objective:

- Define essential and nonessential amino acids, and describe the general scheme of amino acid biosynthesis.

Table 25.2 Essential Amino Acids

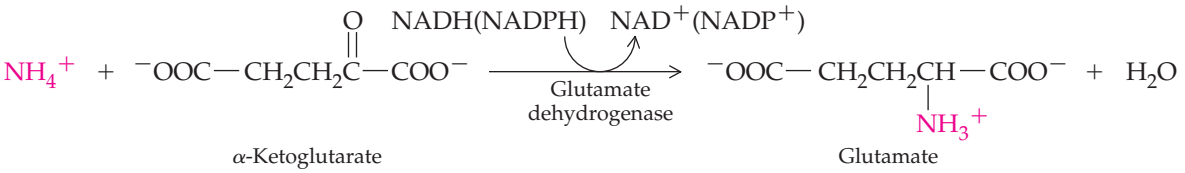
Amino Acids Essential for Adults		
Histidine	Lysine	Threonine
Isoleucine	Methionine	Tryptophan
Leucine	Phenylalanine	Valine
Some Foods with Incomplete Amino Acids		
Grains, nuts, and seeds: High in methionine, low in lysine		
Legumes: High in lysine, low in methionine		
Corn: High in methionine, low in lysine and tryptophan		
Some Examples of Complementary Sources of Protein		
Peanut butter on bread	Nuts and soybeans	
Rice and beans	Black-eyed peas and corn bread	
Beans and corn		

Humans are able to synthesize about half of the 20 amino acids found in proteins. These are known as the **nonessential amino acids** because they do not have to be supplied by our diet. The remaining amino acids—the **essential amino acids** (Table 25.2)—are synthesized only by plants and microorganisms. Humans must obtain the essential amino acids from food (see the Chemistry in Action "Proteins in the Diet" in Chapter 18). Meats contain all of the essential amino acids. The foods that do not have all of them are described as having *incomplete amino acids,* and dietary deficiencies of the essential amino acids can lead to a number of health problems (see the Chemistry in Action "The Importance of Essential Amino Acids and Effects of Deficiencies," p. 808). Food combinations that together contain all of the amino acids are *complementary* sources of protein. It is interesting to note that we synthesize the nonessential amino acids in pathways containing only one to three steps, whereas synthesis of the essential amino acids by other organisms is much more complicated, requiring many more steps and a substantial energy investment.

All of the nonessential amino acids derive their amino groups from glutamate. As you have previously seen, this is the molecule that picks up

ammonia in amino acid catabolism and carries it into the urea cycle. Glutamate can also be made from NH_4^+ and α-ketoglutarate by **reductive amination,** the reverse of oxidative deamination (Section 25.3). The same glutamate dehydrogenase enzyme carries out the reaction.

Reductive amination Conversion of an α-keto acid to an amino acid by reaction with NH_4^+.

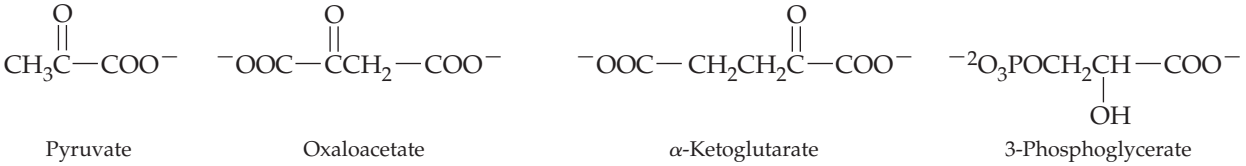


Glutamate also provides nitrogen for the synthesis of other nitrogen-containing compounds, including the purines and pyrimidines that are part of DNA.

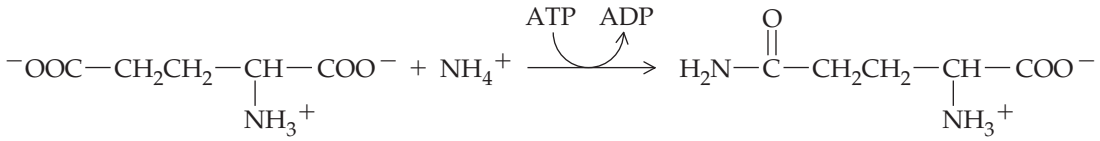
The following four common metabolic intermediates, which you have seen play many roles, are the precursors for synthesis of the nonessential amino acids.

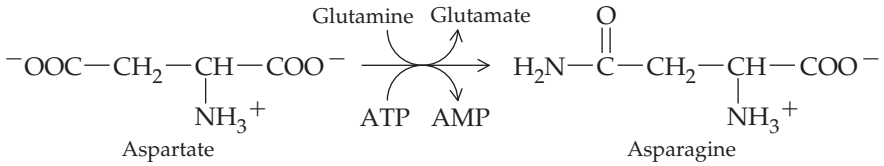
Recall that the structures and roles of NADH, NADPH, NAD^+, and $NADP^+$ were discussed in Chapter 21.

Precursors in synthesis of nonessential amino acids

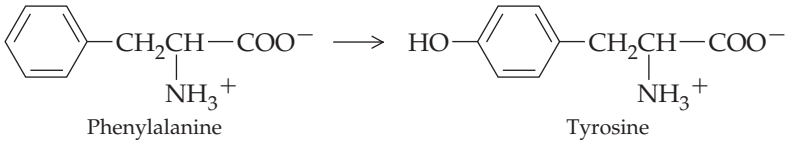


Glutamine is made from glutamate, and asparagine is made by reaction of glutamine with aspartate.





The amino acid tyrosine is classified as nonessential because we can synthesize it from phenylalanine, an essential amino acid.



Whatever the classification, we have a high nutritional requirement for phenylalanine, and several metabolic diseases are associated with defects in the enzymes needed to convert it to tyrosine and other metabolites. The best known of these diseases is phenylketonuria (PKU), the first inborn error of metabolism for which the biochemical cause was recognized. In 1947, it was found that failure to convert phenylalanine to tyrosine causes PKU.

PKU results in elevated blood-serum and urine concentrations of phenylalanine, phenylpyruvate, and several other metabolites produced when the body diverts

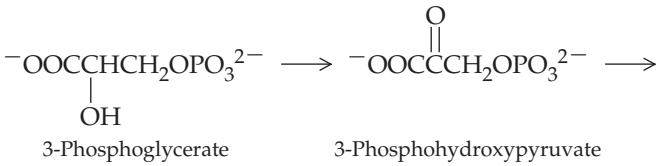
phenylalanine to metabolism by other pathways. Undetected PKU causes mental retardation by the second month of life. Estimates are that, prior to the 1960s, 1% of those institutionalized for mental retardation were PKU victims. Widespread screening of newborn infants is the only defense against PKU and similar treatable metabolic disorders that take their toll early in life. In the 1960s a test for PKU was introduced, and virtually all hospitals in the United States now routinely screen for it. Treatment consists of a diet low in phenylalanine, which is maintained in infants with special formulas and in older individuals by eliminating meat and using low-protein grain products. Individuals with PKU must be on alert for foods sweetened with aspartame (e.g., Nutrasweet), which is a derivative of phenylalanine.

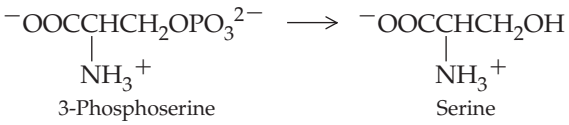
PROBLEM 25.9

Classify each of the essential amino acids as being either glucogenic, ketogenic, or both.

KEY CONCEPT PROBLEM 25.10

In the pathway for synthesis of serine,





identify which step of the reaction is a(n)

(a) transamination **(b)** hydrolysis **(c)** oxidation

CHEMISTRY IN ACTION

The Importance of Essential Amino Acids and Effects of Deficiencies

Regardless of the amazing numbers of biomolecules our bodies can synthesize, there are some we cannot make. These molecules, called "essential" nutrients, must be harvested daily from the foods we eat. Although there are no known essential carbohydrates, there are essential fatty acids and essential amino acids. The two essential fatty acids, linoleic and linolenic acid were discussed in Section 23.2. Let's now turn our attention to the amino acids.

The amino acids can nutritionally be placed into one of three groups: nonessential (Ala, Asn, Asp, and Glu), conditional (Arg, Cys, Gln, Tyr, Gly, Pro, and Ser), and essential (or indispensible) amino acids. Our bodies can make both the nonessential and conditional amino acids, even if we don't get them from the food we eat. Conditional amino acids are so named because in healthy individuals they are normally produced in sufficient quantities; however, in times of illness and physiological stress (like growth or tissue healing) dietary intake is necessary to achieve sufficient levels. The essential amino acids, on the other hand, cannot be prepared with the biochemical machinery we possess and must therefore be obtained through diet. Table 25.2 lists some dietary sources of these indispensible amino acids.

There are nine essential amino acids: histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. There is little discussion among scientists regarding the amino acids on this list; however, the classification of histidine as essential is argued by some biochemists, who wish to place it as a conditional amino acid. Although essential in growing children, histidine is generally considered

nonessential for healthy adults, who are quite capable of synthesizing enough to meet their normal biochemical requirements except under physiological requirements imposed by certain stress or disease situations.

Nutritional biochemists seek to understand what physiological fate will befall someone whose diet is deficient in one of the essential amino acids. This challenging research requires tight controls over the food given to the animal models under study. For example, to determine the effect of a valine deficiency on a mouse, researchers must ensure that its diet contains very little (if any) valine, while not lacking in any other nutrient. Studies like this, as well as observations in humans, have given rise to a number of conclusions concerning the functions of individual essential amino acids and the effects a deficiency may cause. For example, as we learned in the beginning of the chapter, low blood serum values of the amino acid histidine have been consistently found in people suffering from RA. While no direct cause and effect relationship has yet been established, it has given scientists new directions to explore in the possible prevention and treatment of this debilitating disease.

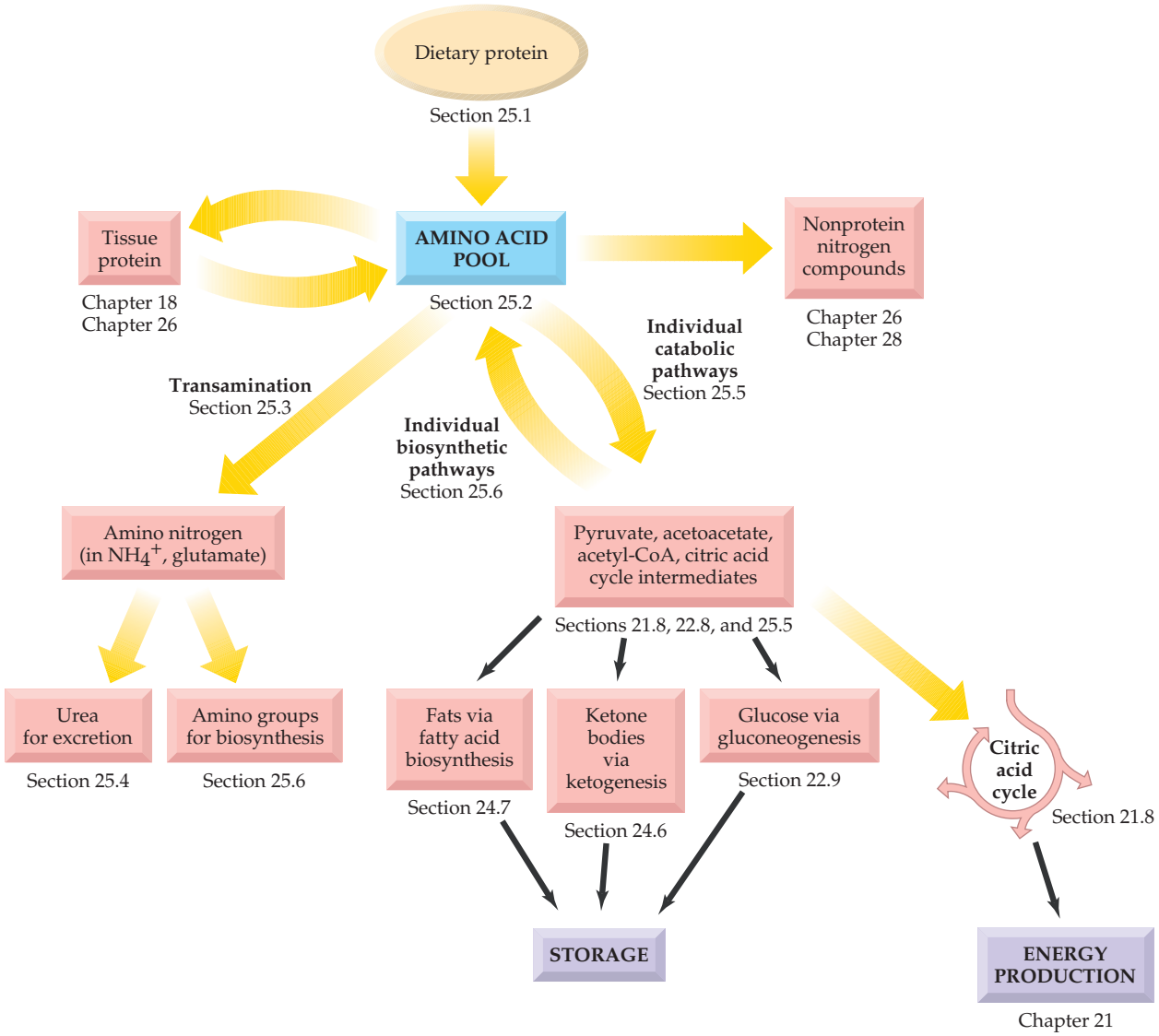
Amino Acid(s)	Role and Effect of Deficiency
Histidine	• Essential in growing children and repair of tissues. • Conditionally essential in adult diet during old age and in those suffering from degenerative diseases. • Deficiency can cause pain in bony joints and has been shown to lead to cataract formation in animals. • Deficiency also has a possible link to RA.
Isoleucine, Leucine, Valine	• All three essential for the production and maintenance of body proteins. • Difficult to assess the true effects of the deficiency of any of these three amino acids. • Leucine is especially important in controlling the net synthesis of protein. • Leucine deficiency may severely limit regeneration of protein and may affect healing after surgery. • Leucine and valine have been reported to increase mental alertness. • Valine deficiency has been reported to cause sensitivity to touch and sound.
Lysine	• Generally considered the most important of the essential amino acids. • Plays a role in absorption of calcium; formation of collagen for bones, cartilage, and connective tissues; and the production of antibodies, hormones, and enzymes. • Deficiency can lead to a poor appetite, reduction in body mass, anemia, and a reduced ability to concentrate. • Deficiency has also been associated with pneumonia, kidney disease (nephritis), and acidosis, as well as with malnutrition and rickets in children (due to the decreased calcium absorption).
Methionine	• Metabolically a primary source of sulfur. • Only necessary when cysteine intake is limited. • May play a role in lowering cholesterol and reducing liver fat, protecting kidneys, and promoting hair growth. • Deficiency may ultimately lead to chronic rheumatic fever in children, hardening of the liver (cirrhosis), and nephritis.
Phenylalanine	• The primary source of aromatic rings needed for a whole array of biomolecules, most notably the neurotransmitters (Section 28.4). • Deficiency can lead to behavioral changes such as psychotic and schizophrenic behavior (presumably due to its being needed for the synthesis of tyrosine, dopamine, and epinephrine).
Threonine	• Key in the formation of collagen, elastin, and tooth enamel. • Suggested to be essential in the prevention and treatment of mental illness. • Deficiency can result in irritability in children.
Tryptophan	• Considered to be a natural relaxant, it has been used to help relieve insomnia. • Often recommended for the treatment of migraines and mild depression (as it is the metabolic starting material for serotonin); sometimes called "nature's Prozac." • Deficiency can lead to serotonin deficiency syndrome, which in turn can lead to a broad array of emotional and behavioral problems such as depression, premenstrual syndrome (PMS), anxiety, alcoholism, insomnia, violence, aggression, and suicide.

CIA Problem 25.4 What is meant by a conditional amino acid?

CIA Problem 25.5 What medical conditions might arise if your diet was found to be low in methionine?

CIA Problem 25.6 What essential amino acid has been called "nature's Prozac"? What are some of the symptoms seen if deficiencies of it occur?

CONCEPT MAP: PROTEIN AND AMINO ACID METABOLISM



▲ **Figure 25.5 Concept Map.** This concept map shows how amino acids move in and out of the amino acid pool, and what their possible metabolic fates are.

SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **List the steps of protein digestion.** Protein digestion begins in the stomach and continues in the small intestine. The result is virtually complete hydrolysis to yield free amino acids. The active transport of amino acids into cells lining the intestine is managed by several transport systems devoted to different groups of amino acids. The amino acids enter the bloodstream after active transport where they enter the amino acid pool *(see Problems 11, 12, 17, 18, 47, 48, and 50).*
- **Define the amino acid pool and its metabolic role.** The amino acid pool represents the entire collection of free amino acids throughout the body. Amino acids are constantly entering the amino acid pool from dietary protein or broken-down body protein. The body does not store nitrogen compounds, using this pool for biosynthesis of nitrogen-containing biomolecules *(see Problems 17–20, 48, and 50).*
- **Explain how amino acids are catabolized.** Each amino acid is catabolized by a distinctive pathway, but the general sequence involves: (i) removal of the amino group; (ii) use of the removed $-NH_2$ in the synthesis of new nitrogen compounds or the ammonium ion; (iii) passage of nitrogen into the urea cycle; and

(iv) incorporation of the carbon atoms into compounds that can enter the citric acid cycle *(see Problems 21–30 and 51)*.

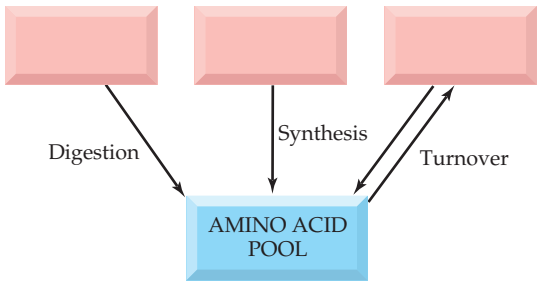
- **Discuss the fate of the nitrogen of an amino acid.** For almost all amino acids, the amino group is removed by *transamination* (the transfer of an amino group from an amino acid to a keto acid), usually to form glutamate. Then, the amino group of glutamate is removed as ammonium ion by *oxidative deamination*. The ammonium ion is destined for the *urea cycle*. The transamination process can also be used to synthesize new amino acids from appropriate keto acids *(see Problems 31, 33, 34, 36, and 43)*.
- **Identify the major reactants and products of the urea cycle.** Ammonium ion (from amino acid catabolism) and hydrogen carbonate ion (from carbon dioxide) react to produce carbamoyl phosphate, which enters the urea cycle. The first two steps of the urea cycle produce a reactive intermediate in which both of the nitrogens that will be part of the urea end product are bonded to the same carbon atom. Then arginine is formed and split by hydrolysis to yield urea, which will be excreted. The net result of the urea cycle is reaction of ammonium ion with aspartate to give urea and fumarate *(see Problems 31–34, 42, and 46)*.
- **Describe the metabolic fate of the carbon atoms in an amino acid.** The carbon atoms from amino acids are incorporated into compounds that can enter the *citric acid cycle*. Amino acids are classified as either glucogenic or ketogenic depending on how they enter the citric acid cycle. Ketogenic amino acids are those that are converted to acetoacetyl-CoA or acetyl-CoA; glucogenic amino acids are those that are eventually converted to oxaloacetate. These carbon compounds formed are then available for conversion to fatty acids or glycogen for storage or for synthesis of ketone bodies *(see Problems 14, 16, 29, 30, 44, 45, and 49)*.
- **Define essential and nonessential amino acids, and describe the general scheme of amino acid biosynthesis.** *Essential amino acids* must be obtained in the diet because our bodies do not synthesize them. They are made only by plants and microorganisms, and their synthetic pathways are complex. Our bodies do synthesize the so-called *nonessential amino acids*. Their synthetic pathways are quite simple and generally begin with pyruvate, oxaloacetate, α-ketoglutarate, or 3-phosphoglycerate. The nitrogen is commonly supplied by glutamate *(see Problems 35–41, 47, 51, and 53)*.

KEY WORDS

Amino acid pool, *p. 799*
Essential amino acid, *p. 806*
Nonessential amino acid, *p. 806*
Oxidative deamination, *p. 801*
Reductive amination, *p. 807*
Transamination, *p. 800*
Turnover, *p. 799*
Urea cycle, *p. 802*

UNDERSTANDING KEY CONCEPTS

25.11 In the diagram shown here, fill in the sources for the amino acid pool.



25.12 What are the fates of the carbon and nitrogen atoms in a catabolized amino acid?

25.13 A treatment for hyperammonemia (excess NH_4^+ in the blood) is to administer pyruvate. What two enzymes are necessary to detoxify the ammonium ion in the presence of pyruvate? What is the product?

25.14 Three metabolites that can result from the breakdown of the carbon skeleton of amino acids are ketone bodies, acetyl-CoA, and glucose. Briefly describe how each of these metabolites can be produced from amino acid catabolism.

25.15 Define what an "essential" nutrient is and explain how it differs from a "nonessential" nutrient.

25.16 In the liver, the relative activity of ornithine transcarbamylase is high, that of argininosuccinate synthetase is low, and that of arginase is high. Why is it important that ornithine transcarbamylase activity be high in the liver? What might be the consequence if arginase activity is low or defective?

ADDITIONAL PROBLEMS

AMINO ACID POOL (SECTIONS 25.1 AND 25.2)

25.17 Where is the body's amino acid pool?

25.18 In what part of the digestive tract does the digestion of proteins begin?

25.19 What glycolytic intermediates are precursors to amino acids?

25.20 What citric acid cycle intermediates are precursors to amino acids?

AMINO ACID CATABOLISM (SECTIONS 25.3 AND 25.5)

25.21 What is meant by transamination?

25.22 Pyruvate and oxaloacetate can be acceptors for the amino group in transamination. Write the structures for the products formed from transamination of these two compounds.

25.23 What is the structure of the α-keto acid formed from transamination of the following amino acids?

(a) Glutamic acid **(b)** Alanine

25.24 What is the structure of the α-keto acid formed from transamination of the following amino acids (Refer to Table 18.3)?

(a) Isoleucine **(b)** Valine

25.25 In general, how does oxidative deamination differ from transamination?

25.26 What coenzymes are associated with oxidative deamination?

25.27 Write the structure of the α-keto acid produced by oxidative deamination of the following amino acids (Refer to Table 18.3):

(a) Leucine **(b)** Tryptophan

25.28 What other product is formed in oxidative deamination besides an α-keto acid?

25.29 What is a ketogenic amino acid? Give three examples.

25.30 What is a glucogenic amino acid? Give three examples.

UREA CYCLE (SECTION 25.4)

25.31 Why does the body convert NH_4^+ to urea for excretion?

25.32 What is the source of carbon in the formation of urea?

25.33 From what two amino acids do the nitrogens in urea arise? (Hint: See Figure 25.3.)

25.34 Where does aspartate enter the urea cycle and what compound does it eventually leave as? What metabolic cycle does this compound then enter?

AMINO ACID BIOSYNTHESIS (SECTION 25.6)

25.35 How do essential and nonessential amino acids differ from each other in the number of steps required for their synthesis in organisms that synthesize both?

25.36 Which amino acid serves as the source of nitrogen for synthesis of the other amino acids?

25.37 If you were diagnosed as having a diet low in lysine, what foods might you include in your diet to alleviate this problem?

25.38 How is tyrosine biosynthesized in the body? What disease prevents this biosynthesis, thereby making tyrosine an essential amino acid for those who have this condition?

25.39 PKU is an abbreviation for what disorder? What are the symptoms of PKU? How can PKU be treated for a nearly normal life?

25.40 Diet soft drinks that are sweetened with aspartame carry a warning label for phenylketonurics. Why?

25.41 Which of the following biomolecules contain nitrogen?

(a) Glycogen (Chapter 22)

(b) Nitric oxide (Chapter 4)

(c) Collagen (Chapter 18)

(d) Epinephrine (Chapter 28)

(e) Stearic acid (Chapter 23)

(f) Fructose (Chapter 20)

CONCEPTUAL PROBLEMS

25.42 What energy source is used in the formation of urea?

25.43 Write the equation for the transamination reaction that occurs between phenylalanine and pyruvate.

25.44 **(a)** Name the four compounds within the citric acid cycle that the carbon skeletons of the glucogenic amino acid enter as.

(b) Which of these four compounds arise exclusively from aromatic amino acids?

25.45 Can an amino acid be both glucogenic and ketogenic? Explain why or why not.

25.46 Where in the body does the conversion of ammonium ion to urea occur? Where is the urea that is formed ultimately transported?

25.47 Considering all of the metabolic processes we have studied, why do we say that the biochemistry of the body is dynamic?

25.48 Two major differences between the amino acid pool and the fat and carbohydrate pools in the body center on storage and on energy. Discuss these major differences.

25.49 When some of the carbons of glutamate are converted to glycogen, what is the order of the following compounds in that pathway?

(a) Glucose **(b)** Glutamate

(c) Glycogen **(d)** Oxaloacetate

(e) α-Ketoglutarate **(f)** Phosphoenolpyruvate

25.50 The pancreatic proteases are synthesized and stored as zymogens. They are activated after the pancreatic juices enter the small intestine. Why is it essential that these enzymes be synthesized and stored in their inactive forms?

25.51 What is the general scheme by which amino acids are catabolized?

25.52 The net reaction for the urea cycle shows that three ATPs are hydrolyzed; however, the total energy "cost" is four ATPs. Explain why this is true.

25.53 Why might it be a bad idea to take large quantities of a single amino acid dietary supplement?

GROUP PROBLEMS

25.54 Write down what foods you had for lunch and dinner yesterday. Try and determine what essential amino acids were present in the foods you ate. Were there any that were missing?

25.55 Pretend that you were deficient in all of the essential amino acids. Have you and your group draw up with a diet plan for one day (breakfast, lunch, and dinner) that would ensure you were getting all of the essential amino acids over the course of that day.

25.56 Determine how many ATPs you would make if you consumed a tetrapeptide comprised of leucine, histidine, valine, and lysine. Have each member of your group take one of the four amino acids and determine the number of ATPs their amino acid would make and combine them to get the total.

26

Nucleic Acids and Protein Synthesis

CONTENTS

CONCEPTS TO REVIEW

A. Hydrogen Bonding (Section 8.2)
B. Phosphoric Acid Derivatives (Section 17.6)
C. Protein Structure (Sections 18.6–18.8)
D. Carbohydrate Structure (Section 20.3)

▲ Vaccinations educate the immune system so that it can rapidly kill disease-causing viruses such as influenza, measles, and many others preventing serious illnesses.

Flu is caused by the influenza virus, of which there are three major types—A, B, and C (all of which humans are susceptible to)—with many subtypes of each one. As you will learn in the Chemistry in Action "Influenza: Variations on a Theme" later in this chapter, influenza A and B are infectious. If enough people are affected, an epidemic can occur. Symptoms of a viral infection like the flu include fever, cough, sore throat, runny nose, headache,

tiredness, muscle or bone aches, or in more severe cases, vomiting, diarrhea, or stomach pain; however, humans can get a flu shot to prevent illness from types A and B influenza.

Viruses, just like humans, have either deoxyribonucleic acids (DNA) or ribonucleic acids (RNA), which use a host cell (our bodies) for replication. The influenza vaccine prevents the virus from replicating in our bodies by introducing inactivated strains of the influenza virus into the body. The flu shot provides the necessary molecules to strengthen our immune system to combat the effects of the influenza infection. In other words, the vaccine is engineered to provide immunity to influenza A and/or B, but because the nucleic acids that make up the DNA and RNA of the influenza virus change rapidly, annual flu shots are recommended.

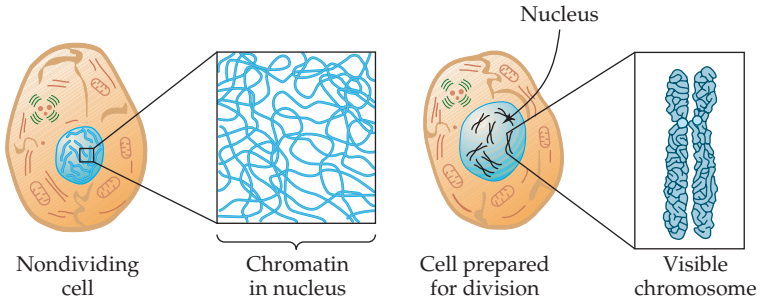
Nucleic acids are the basic molecular structures present in DNA and RNA, which ultimately form the blueprint for our genetic information. We will learn more about nucleic acids in this chapter and how our genetic information is duplicated, transferred, and expressed through protein synthesis. Protein synthesis also helps maintain all of our normal body functions, such as inhalation and exhalation of the lungs, food digestion, and energy generation.

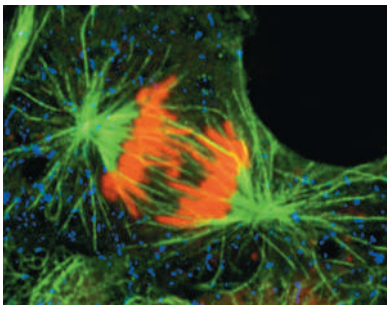
26.1 DNA, Chromosomes, and Genes

Learning Objective:

- Explain the role of chromosomes, genes, and DNA, and describe their basic function in the human body.

When a cell is not actively dividing, its nucleus is occupied by *chromatin,* which is a compact, orderly tangle of **deoxyribonucleic acid (DNA),** the carrier of genetic information, twisted around organizing proteins known as *histones.* During cell division, chromatin becomes even more compact and organizes itself into **chromosomes.** Each chromosome contains a different DNA molecule, and all of the DNA is duplicated so that each new cell receives a complete copy.





▲ Chromosomes (red) during cell division.

deoxyribonucleic acid (DNA) The nucleic acid that stores genetic information; a polymer of deoxyribonucleotides.

Chromosome A complex of proteins and DNA; visible during cell division.

Each DNA molecule, in turn, is composed of many **genes**—individual segments of the DNA molecule containing the instructions that direct the synthesis of a single polypeptide. Interestingly, not all genes coded for by an organism's DNA are expressed as protein. As we will see later in this chapter, some genes code for *functional RNA* molecules.

Interestingly, organisms differ widely in their numbers of chromosomes. A horse, for example, has 64 chromosomes (32 pairs), a cat has 38 chromosomes (19 pairs), a mosquito has 6 chromosomes (3 pairs), and a corn plant has 20 chromosomes (10 pairs). A human has 46 chromosomes (23 pairs).

Gene Segment of DNA that directs the synthesis of a single polypeptide.

LOOKING AHEAD The complete map of the genetic information passed along during cell division is now available for numerous organisms, including humans. This amazing development of the human genome will be further explored in Chapter 27.

26.2 Composition of Nucleic Acids

Learning Objective:

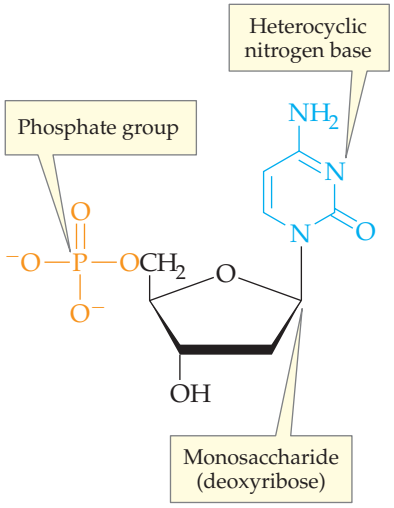
- Describe, identify, and draw the components of nucleosides and nucleotides.

Like proteins and carbohydrates, nucleic acids are polymers. Proteins are polypeptides, carbohydrates are polysaccharides, and **nucleic acids** are *polynucleotides*. Each **nucleotide** has three parts: a five-membered cyclic monosaccharide, a

Nucleic acid A polymer of nucleotides.

Nucleotide A five-carbon sugar bonded to a heterocyclic nitrogen base and a phosphate group; the monomer for nucleic acids.

A nucleotide



ribonucleic acid (RNA) Nucleic acids responsible for putting the genetic information to use in protein synthesis; a polymer of ribonucleotides. Includes messenger (mRNA), transfer (tRNA), and ribosomal RNA (rRNA).

Nucleoside A five-carbon sugar bonded to a heterocyclic nitrogenous base; like a nucleotide but with no phosphate group.

nitrogen-containing cyclic compound known as a *nitrogenous base,* and a phosphate group ($-OPO_3^{2-}$).

There are two classes of nucleic acids, DNA and **ribonucleic acid (RNA),** where several types of RNA exist. The function of one type of RNA is to put the information stored in DNA to use. Other types of RNA assist in the conversion of the message a specific RNA carries into protein. Before we discuss how the nucleic acids fulfill their functions, we need to understand how their component parts are joined together and how DNA and RNA differ from each other.

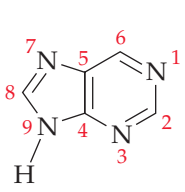
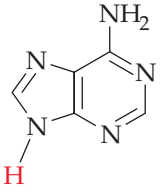
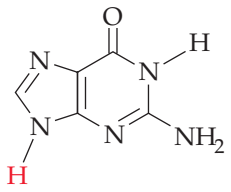
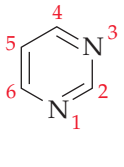
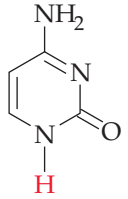
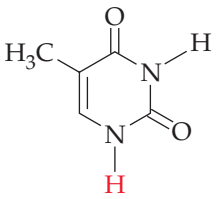
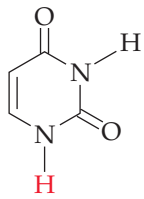
The Sugars

The difference between DNA and RNA is found in the sugar portion of the molecules. In RNA, the sugar is D-ribose, except hereafter simply referred to as ribose, as indicated by the name *ribonucleic acid*. In DNA, the sugar is 2-*deoxy*ribose, giving *deoxyribonucleic acid*. The prefix *2-deoxy-* means that an oxygen atom is missing from the C2 position of ribose.

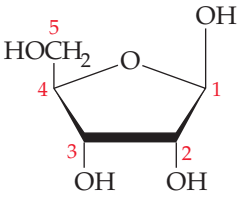
The Bases

There are five different kinds of nitrogenous bases found in DNA and RNA. They are all derived from two parent compounds, purine and pyrimidine, and each has its unique one-letter code (A, G, C, T, U). The five nitrogenous bases are shown in Table 26.1, along with the two parent bases; notice the functional groups in each. The nitrogenous bases that are purine derivatives, adenine and guanine, contain two fused nitrogen-containing rings. The bases that are pyrimidine derivatives—cytosine, thymine, and uracil—contain only one nitrogen-containing ring. Notice that adenine, guanine, and cytosine are in DNA and RNA, whereas thymine is present in DNA and uracil is present in RNA.

Table 26.1 Bases in DNA and RNA

Purine Bases in Nucleic Acids			Pyrimidine Bases in Nucleic Acids			
						
Purine (Parent)	Adenine (A) (DNA, RNA)	Guanine (G) (DNA, RNA)	Pyrimidine (Parent)	Cytosine (C) (DNA, RNA)	Thymine* (T) (DNA)	Uracil (U) (RNA)

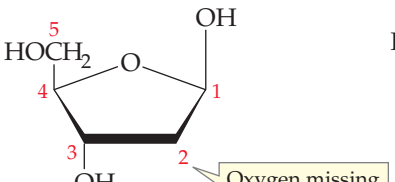
**Thymine occurs in a few cases of RNA.*



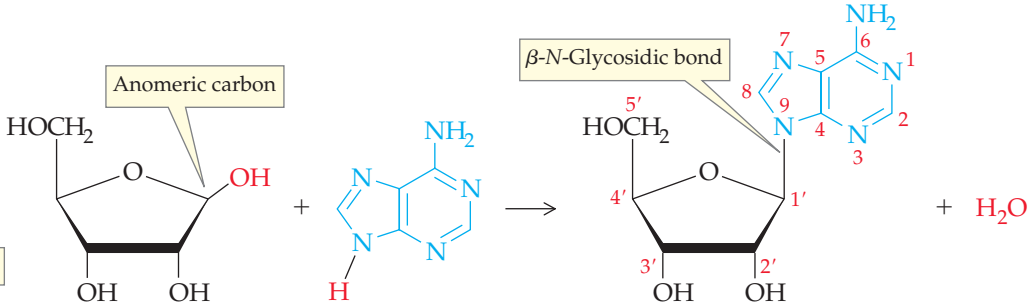
D-Ribose (in RNA)

Sugar + Base = Nucleoside

A molecule composed of either ribose or deoxyribose and one of the five nitrogenous bases found in DNA and/or RNA is called a **nucleoside.** The combination of ribose and adenine, for example, gives the nucleoside known as adenosine, which you should recognize as the parent molecule of adenosine triphosphate (ATP) (Section 21.4, p. 701).



2-Deoxy-D-ribose (in DNA)



The sugar and base are connected by a bond between one of the nitrogen atoms in the base and the anomeric carbon atom (the one bonded to two oxygen atoms) of the sugar. This bond is a β-*N*-glycosidic bond. Notice that this linkage (the 1′ position of the sugar to the nine-position nitrogen atom of the adenine) is closely related to an acetal (Section 15.7).

In each of the nucleic acid bases in Table 26.1, the hydrogen atom lost in nucleoside formation is shown in red.

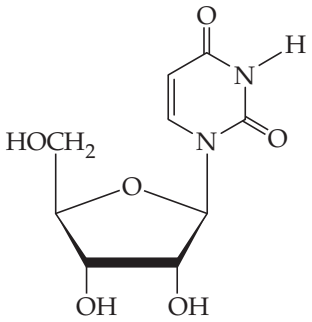
Nucleoside names are the nitrogenous base name modified by the suffix *-osine* for the purine bases (as we just saw for adenosine) and the suffix *-idine* for the pyrimidine bases. No prefix is used for nucleosides containing ribose, but the prefix *deoxy-* is added for those that contain deoxyribose. Therefore the four nucleosides found in RNA are named adenosine, guanosine, cytidine, and uridine, and the four found in DNA are named deoxyadenosine, deoxyguanosine, deoxycytidine, and deoxythymidine.

To distinguish between atoms in the sugar ring of a nucleoside and atoms in the base ring (or rings), numbers without primes are used for atoms in the base ring (or rings), and numbers with primes are used for atoms in the sugar ring.

CONCEPTS TO REVIEW Recall from Chapter 20 that a glycosidic bond is the bond between the anomeric carbon atom of a sugar and an —OR or —NR group. β Bonds point above the sugar ring, and α bonds point below it.

Worked Example 26.1 Naming a Nucleic Acid Component from Its Structure

Is the compound shown here a nucleoside or a nucleotide? Identify its sugar and base components, and name the compound.



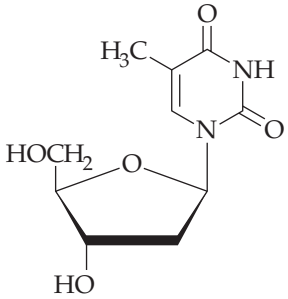
ANALYSIS The compound contains a sugar, recognizable by the oxygen atom in the ring and the —OH groups. It also contains a nitrogenous base, recognizable by the nitrogen-containing ring. The sugar has an —OH in the 2′ position and is therefore ribose (if it were missing the —OH in the 2′ position, it would be a *deoxy*ribose). Checking the base structures in Table 26.1 shows that this is uracil, a pyrimidine base, requiring its name to end in *-idine*.

SOLUTION

The compound is a nucleoside, and its name is uridine.

KEY CONCEPT PROBLEM 26.1

Name the nucleoside shown here. Copy the structure, and number the C and N atoms (refer to Table 26.1).

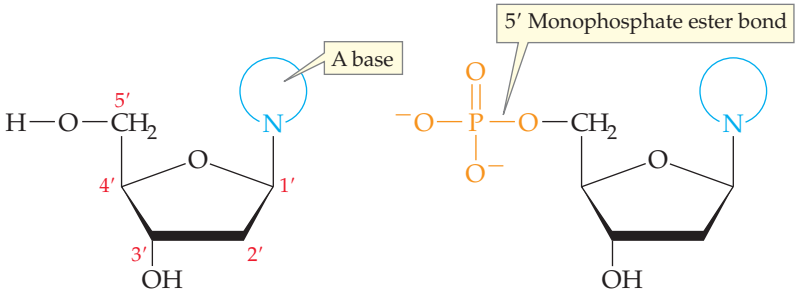


PROBLEM 26.2

Write the molecular formulas for the sugars D-ribose and 2-deoxy-D-ribose. Exactly how do they differ in composition? Can you think of one chemical property that might differ slightly between the two?

Nucleoside + Phosphate = Nucleotide

Nucleotides are the building blocks of nucleic acids; they are the monomers of the DNA and RNA polymers. Each nucleotide is a 5′-monophosphate ester of a nucleoside.

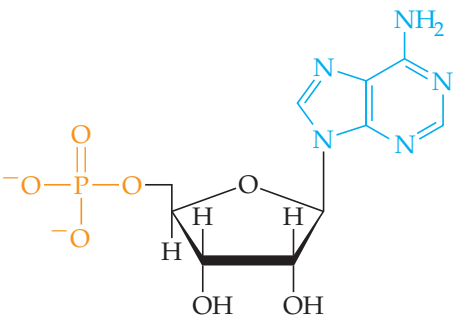


A deoxyribonucleoside — A deoxyribonucleotide

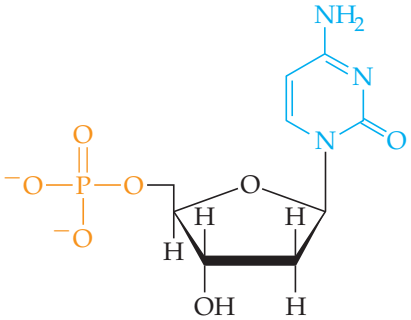
Nucleotides are named by adding 5′-*monophosphate* at the end of the name of the nucleoside. The nucleotides corresponding, for example, to adenosine and deoxycytidine are thus adenosine 5′-monophosphate (AMP) and deoxycytidine 5′-monophosphate (dCMP). Nucleotides that contain ribose are classified as **ribonucleotides** and those that contain 2-deoxy-D-ribose are known as **deoxyribonucleotides** (and are designated by leading their abbreviations with a lower case "d"). For example,

Ribonucleotide A nucleotide that contains D-ribose—monophosphate examples are AMP, uridine monophosphate (UMP), cytidine monophosphate (CMP), and guanosine monophosphate (GMP).

Deoxyribonucleotide A nucleotide that contains 2-deoxy-D-ribose (monophosphate examples are dAMP, dTMP, dCMP, and dGMP).

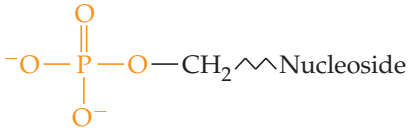


Adenosine 5′-monophosphate (AMP) (a ribonucleotide)

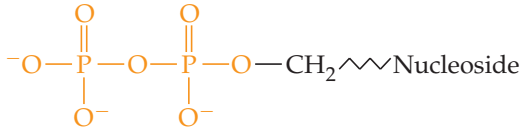


Deoxycytidine 5′-monophosphate (dCMP) (a deoxyribonucleotide)

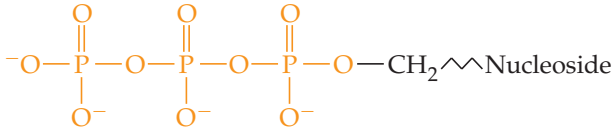
Phosphate groups can be added to any of the nucleotides to form diphosphate or triphosphate esters. As illustrated by *ATP,* these esters are named with the nucleoside name plus *diphosphate* or *triphosphate.* In preceding chapters, you learned that the biochemical energy from the conversion of ATP to adenosine diphosphate (ADP) can be coupled to another less favorable reaction (Section 21.5).



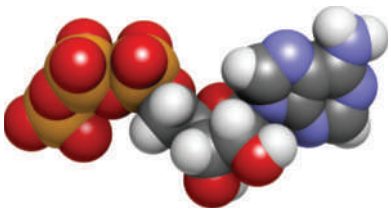
Nucleoside monophosphate



Nucleoside diphosphate



Nucleoside triphosphate



▲ ATP is the triphosphate of the adenosine nucleotide; brown is phosphorus, red is oxygen, and blue is nitrogen.

Summary—Nucleoside, Nucleotide, and Nucleic Acid Composition

Nucleoside
- A sugar and a base

Nucleotide
- A sugar, a base, and a phosphate group ($-OPO_3^{2-}$)

DNA
- A polymer of deoxyribonucleotides
- The sugar is 2-deoxy-D-ribose
- The bases are A, G, C, and *T*

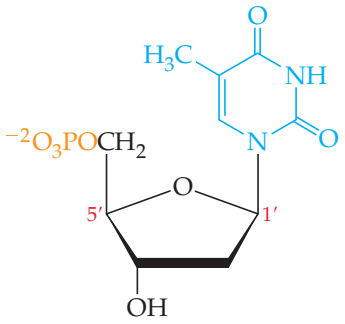
RNA
- A polymer of ribonucleotides
- The sugar is D-ribose
- The bases are A, G, C, and *U*

Worked Example 26.2 Drawing a Nucleic Acid Component from Its Name

Draw the structure of the nucleotide represented by dTMP.

ANALYSIS Referencing Table 26.1 the "T" in dTMP is thymine, "M" is for mono- and "P" is for phosphate. The prefix "d" stands for *deoxy-* on the ribose sugar 2′ carbon. Since nitrogen base in this nucleotide is thymine, whose structure is shown in Table 26.1. This base must be bonded (by replacing the H that is red in Table 26.1) to the 1′ position of the deoxyribose. Lastly, there must be a phosphate group in the 5′ position of the deoxyribose.

SOLUTION
The structure is



KEY CONCEPT PROBLEM 26.3

Draw the structure of 2′-deoxyadenosine 5′-monophosphate, dAMP, and use the primed-unprimed format to number all the atoms in the rings.

PROBLEM 26.4

Draw the structure of the triphosphate of guanosine, a triphosphate that, like ATP, provides energy for certain reactions (see reaction 5 of the citric acid cycle in Section 21.7).

PROBLEM 26.5

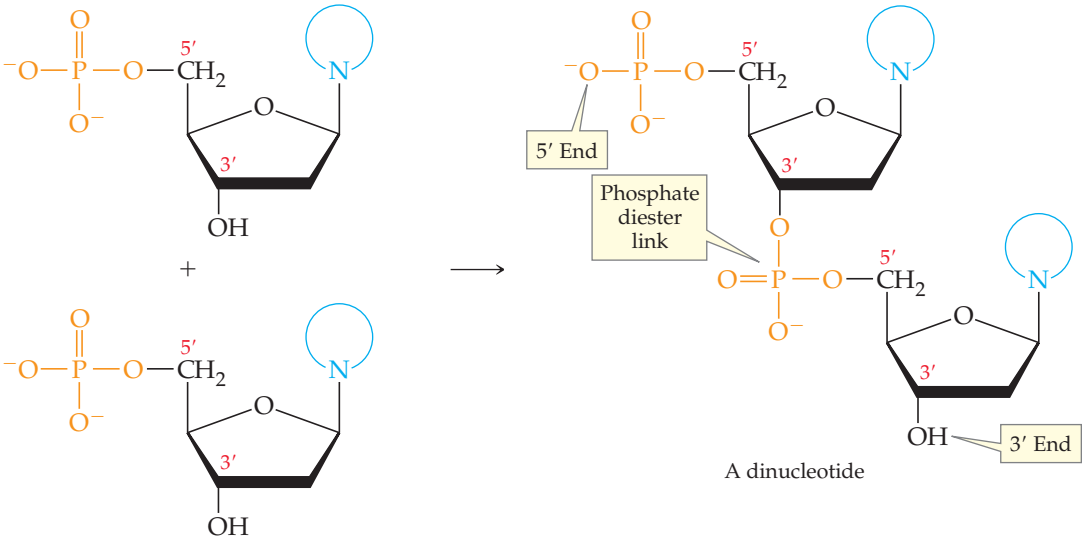
Write the full names of dUMP, UMP, CDP, AMP, and ATP.

26.3 The Structure of Nucleic Acid Chains

Learning Objective:

- Describe and identify nucleic acid chains in DNA and RNA.

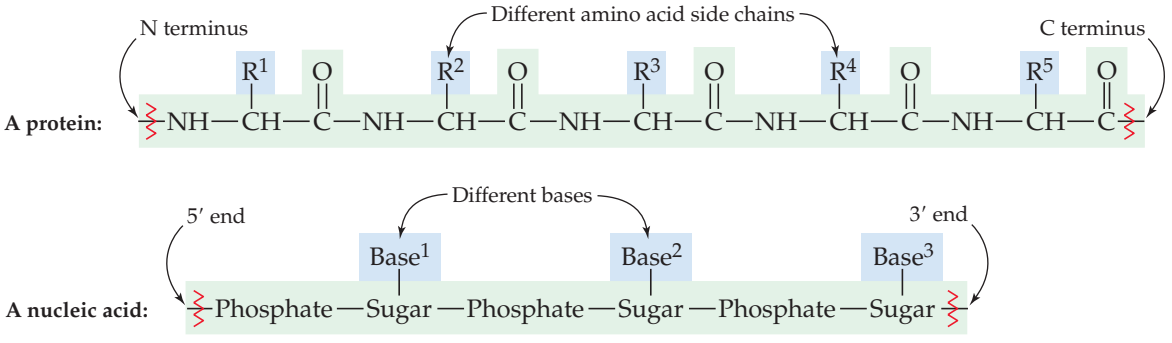
Keep in mind that nucleic acids are polymers of nucleotides. The nucleotides in DNA and RNA are connected by phosphate diester linkages between the —OH group on C3′ of the sugar ring of one nucleotide and the phosphate group on C5′ of the next nucleotide.

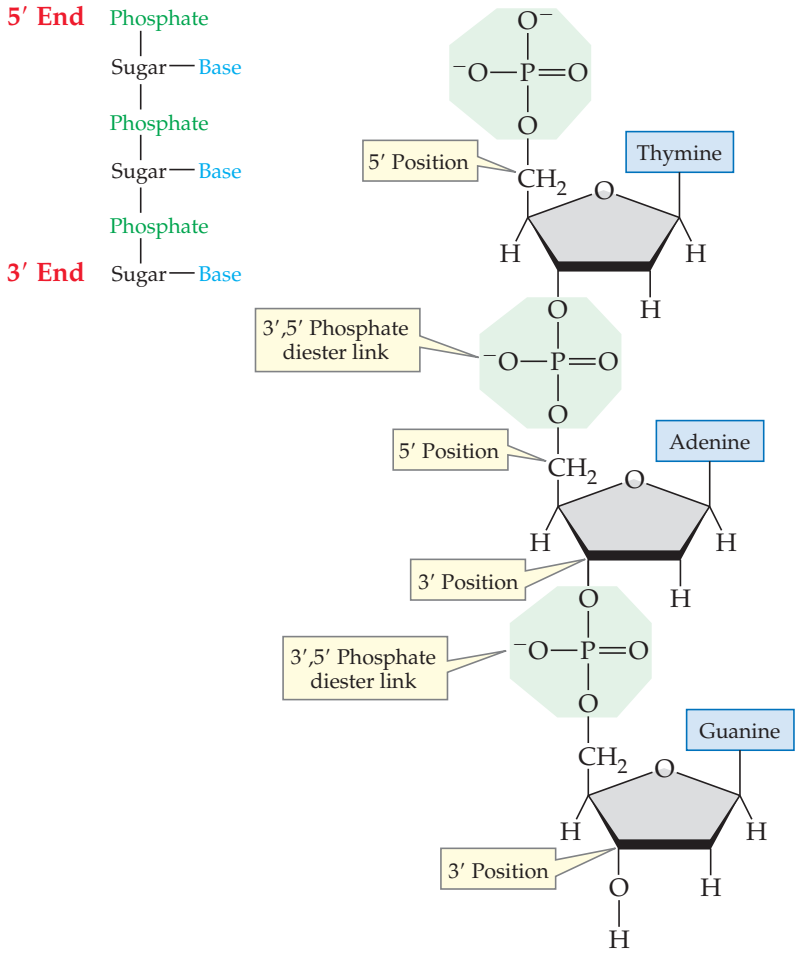


A nucleotide chain commonly has a free phosphate group on a 5′ carbon at one end (known as the 5′*end*) and a free —OH group on a 3′ carbon at the other end (the 3′ *end*), as illustrated in the dinucleotide just above and in the trinucleotide in Figure 26.1. Additional nucleotides join by forming additional phosphate diester linkages between these groups until the polynucleotide chain of a DNA molecule is formed.

Just as the structure and function of a protein depend on the sequence in which the amino acids are connected (see Section 18.7), the structure and function of a nucleic acid depend on the sequence in which the nucleotides are connected. With a nucleic acid, however, we have a second detail to consider: Structure and function both depend on the *direction* in which the nucleic acid is read by enzymes involved in making gene products. Like proteins, nucleic acids have backbones that do not vary in composition. The differences between different proteins and between different nucleic acids result from the *order* of the groups bonded to the backbone—amino acid side chains in proteins and bases in nucleic acids.

Comparison of protein and nucleic acid backbones and side chains





◀ **Figure 26.1**
A deoxytrinucleotide.
In all polynucleotides, as shown here, there is a phosphate group at the 5′ end; there is a sugar —OH group at the 3′ end; and the nucleotides are connected by 3′, 5′-phosphate diester links.

The sequence of nucleotides in a nucleic acid chain is read by starting at the 5′ end and identifying the bases in the order of occurrence. Rather than writing the full name of each nucleotide or each base, one-letter abbreviations of the bases are commonly used to designate the order in which they are attached to the sugar–phosphate backbone: A for adenine, G for guanine, C for cytosine, T for thymine, and U for uracil in RNA. The trinucleotide in Figure 26.1, for example, would be represented by T-A-G or TAG.

PROBLEM 26.6

Name the bases in the pentanucleotide with the sequence G-A-U-C-A. Does this come from RNA or DNA? Explain.

PROBLEM 26.7

Draw the full structure of the DNA dinucleotide C-T. Identify the 5′ and 3′ ends of this dinucleotide.

26.4 Base Pairing in DNA: The Watson–Crick Model

Learning Objective:

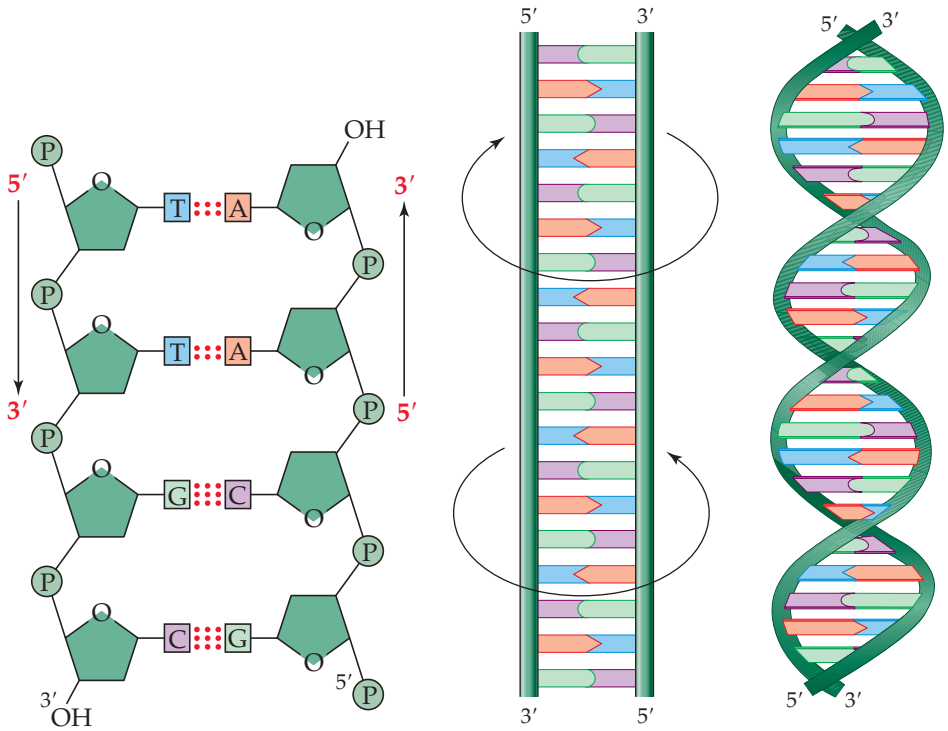
- Interpret the structure of DNA, and write complementary sequences.

Analysis of the nitrogenous bases in many DNA samples from many different species revealed that in any given species, the amounts of adenine and thymine were always equal, and the amounts of cytosine and guanine were always equal (A = T and G = C). It was also found that the proportions of each (A/T:G/C) vary from one species to another. For example, human DNA contains 30% each of adenine and thymine and 20% each of

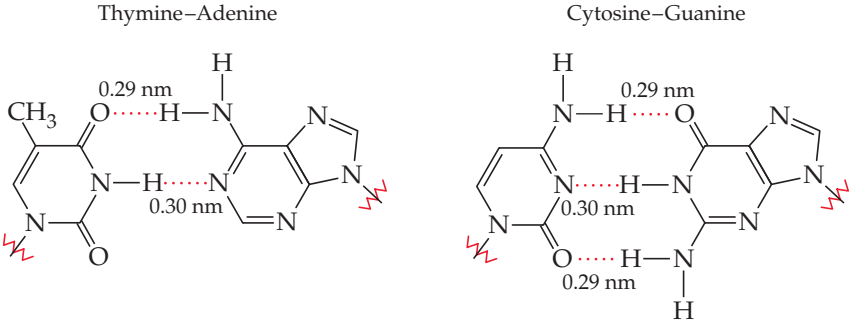
guanine and cytosine, whereas the bacterium *Escherichia coli* contains 24% each of adenine and thymine and 26% each of guanine and cytosine. Note that in both cases, A and T are present in equal amounts and G and C are present in equal amounts. This observation, known as Chargaff's rule (named for Erwin Chargaff, who discovered these base ratios in 1950), suggests that the bases occur in discrete pairs. Why should this be?

In 1953, James Watson and Francis Crick proposed a structure for DNA that not only accounts for the pairing of bases but also accounts for the storage and transfer of genetic information. According to the Watson–Crick model, a DNA molecule consists of *two* polynucleotide strands coiled around each other in a helical, screw-like fashion. The sugar–phosphate backbone is on the *outside* of this right-handed **double helix,** and the heterocyclic bases are on the *inside,* so that a base on one strand points directly toward a base on the second strand. The double helix resembles a twisted ladder, with the sugar–phosphate backbone making up the sides and the paired bases, the rungs.

Double helix Two strands coiled around each other in a screw-like fashion; in most organisms the two polynucleotides of DNA form a double helix.



The two strands of the DNA double helix run in opposite directions—one in the 5′ to 3′ direction, the other in the 3′ to 5′ direction (the strands are said to be *antiparallel* to each other). The stacking of the hydrophobic bases in the interior and the alignment of the hydrophilic sugars and phosphate groups on the exterior provide stability to the structure. Hydrogen bonding also enhances DNA stability. Each pair of bases in the center of the double helix is connected by hydrogen bonding. As shown in Figure 26.2, adenine and thymine (A-T) form two hydrogen bonds to each other, and cytosine and guanine (C-G) form three hydrogen bonds to each other. Although individual hydrogen bonds are not especially strong, the thousands upon thousands along a DNA chain collectively contribute to stability of the double helix.

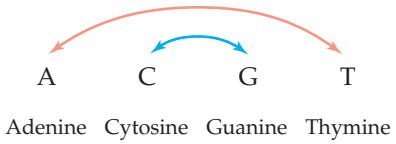


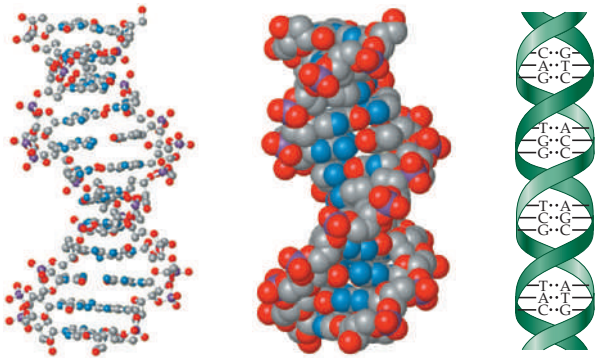
▶ Figure 26.2
Base pairing in DNA.
Hydrogen bonds (red dots) of similar lengths connect the pairs of bases; thymine with adenine and cytosine with guanine.

The pairing of the bases linearly ordered along the two polynucleotide strands of the DNA double helix is described as *complementary*. Wherever a thymine occurs in one strand, an adenine falls opposite it in the other strand; wherever a cytosine occurs in one strand, a guanine falls opposite it on the other strand. This **base pairing** explains why A and T occur in equal amounts in double-stranded DNA, as do C and G.

The DNA double helix is shown in Figure 26.3. Both its strength and its shape depend on the fit and hydrogen bonding of the bases. As you will see, base pairing is also the key to understanding how DNA functions.

Base pairing The pairing of bases connected by hydrogen bonding (G-C and A-T), as in the DNA double helix.





◀ **Figure 26.3**
A segment of DNA.
(a) In this model, notice that the base pairs are nearly perpendicular to the sugar–phosphate backbones. (b) A space-filling model of the same DNA segment. (c) An abstract representation of the DNA double helix and base pairing.

Worked Example 26.3 Writing Complementary Nucleic Acid Sequences

What sequence of bases on one strand of DNA (reading in the 3′ to 5′ direction) is complementary to the sequence 5′ T-A-T-G-C-A-G 3′ on the other strand?

ANALYSIS Remembering that A always bonds to T and C always bonds to G, go through the original 5′ to 3′ sequence, replacing each A by T, each T by A, each C by G, and each G by C. Keep in mind that when a 5′ to 3′ strand is matched in this manner to its complementary strand, the complementary strand will be oriented 3′ to 5′ when read from left to right. (If the direction in which a base sequence is written is not specified, you can assume it follows the customary 5′ to 3′ direction when read left to right.)

SOLUTION

Original strand	5′ T-A-T-G-C-A-G 3′
Complementary strand	3′ A-T-A-C-G-T-C 5′

PROBLEM 26.8

Write the complementary sequence of bases for each DNA strand shown next.

(a) 5′T-A-T-A-C-T-G 3′ **(b)** 5′G-A-T-C-G-C-T-C-T 3′

PROBLEM 26.9

Draw the structures of adenine and uracil (which replaces thymine in RNA), and show the hydrogen bonding that occurs between them.

PROBLEM 26.10

Is a DNA molecule neutral, negatively charged, or positively charged? Explain.

KEY CONCEPT PROBLEM 26.11

(a) DNA and RNA, like proteins, can be denatured to produce unfolded or uncoiled strands. Heating DNA to what is referred to as its "melting temperature" denatures it (the two strands of the double helix become separated). Why does a longer strand of DNA have a higher melting temperature than a shorter one? (b) The DNA melting temperature also varies with base composition. Would you expect a DNA with a high percentage of G-C base pairs to have a higher or lower melting point than one with a high percentage of A-T base pairs? How do you account for your choice?

26.5 Nucleic Acids and Heredity

Learning Objective:

- Describe how genetic information is duplicated, transferred, and expressed.

Your heredity is determined by the DNA in the fertilized egg from which you grew. A sperm cell carrying DNA from your father united with an egg cell carrying DNA from your mother. Their combination produced the full complement of chromosomes and genes that you carry through life. Each of your 23 pairs of chromosomes contains one DNA molecule copied from that of your father and one DNA molecule copied from that of your mother. Most cells in your body contain copies of these originals. (The exceptions are red blood cells, which have no nuclei and no DNA, and egg or sperm cells, which have 23 single DNA molecules, rather than pairs.)

Cell division is an ongoing process—no single cell has a life span equal to that of the organism in which it is found. Therefore, every time a cell divides, its DNA must be copied. The double helix of DNA and complementary base pairing make this duplication possible. Because of how bases pair, each strand of the double helix is a blueprint for the other strand. However, there are two remaining questions: How do nucleic acids carry the information that determines our inherited traits, and, how is stored information interpreted and put into action?

Genetic information is conveyed not just in the numbers and kinds of bases in DNA, but in the *sequence* of bases along the DNA strands; any mistakes in either copying or reading a given DNA sequence can lead to changes in the DNA code (called mutations), which may have disastrous consequences for the resulting daughter cells. Every time a cell divides, the information is passed along to the daughter cells, which ultimately pass this genetic information to their daughter cells. Within cells, the genetic information encoded in the DNA directs the synthesis of proteins, a process known as the *expression* of genes.

The duplication, transfer, and expression of genetic information occur as the result of three fundamental processes: *replication, transcription,* and *translation*.

Replication The process by which copies of DNA are made when a cell divides.

Transcription The process by which the information in DNA is read and used to synthesize RNA.

Translation The process by which RNA directs protein synthesis.

- **Replication** (Section 26.6) is the process by which a replica, or identical copy, of DNA is made when a cell divides, so that each of the two daughter cells has the same DNA (Figure 26.4).
- **Transcription** (Section 26.8) is the process by which the genetic messages contained in DNA are read and copied. The products of transcription are specific RNAs, which carry the instructions stored by DNA out of the nucleus and to the sites of protein synthesis.
- **Translation** (Section 26.10) is the process by which the genetic messages carried by RNA are decoded and used to build proteins.

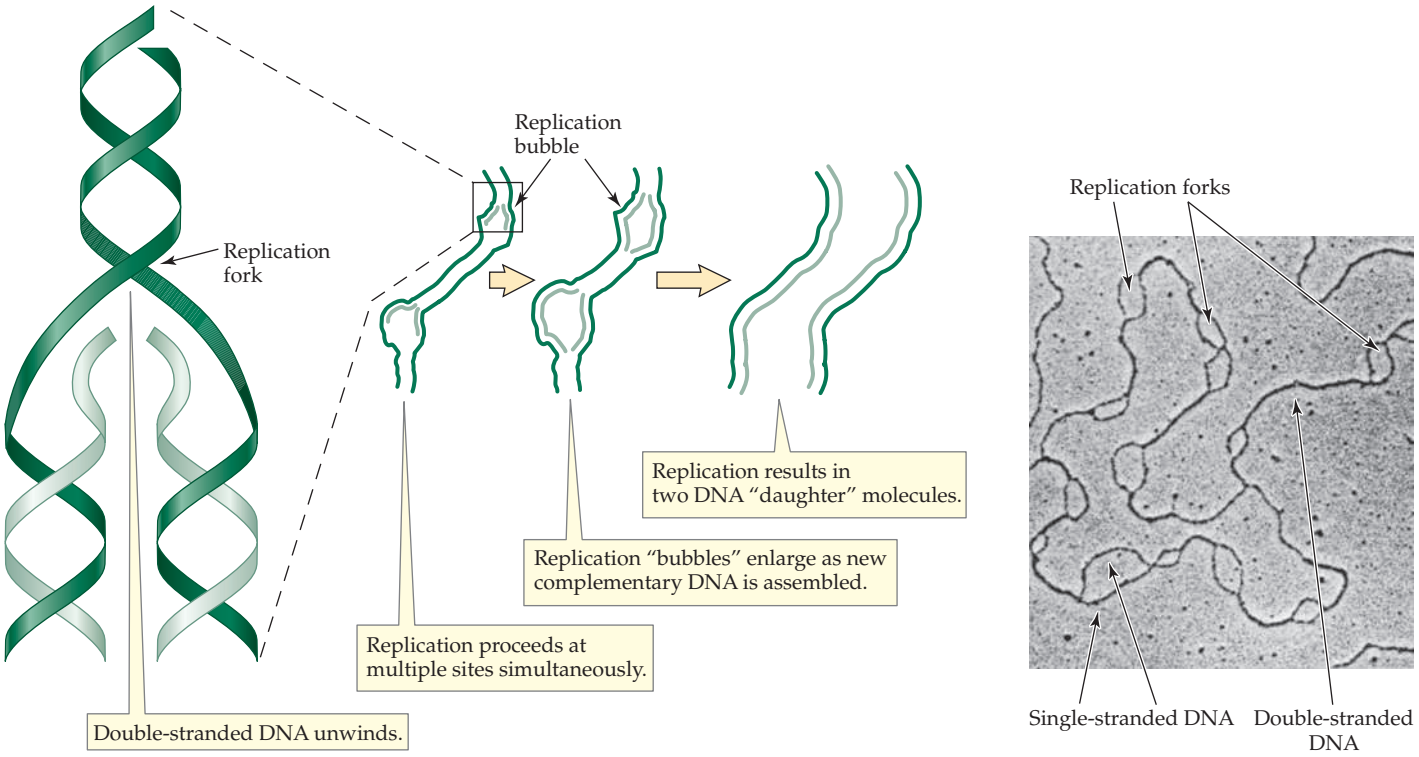
In the following sections, we will look at these important processes. Replication, transcription, and translation must proceed with great accuracy and require participation by many auxiliary molecules to ensure the integrity (or fidelity) of the genetic information. Many enzymes working in harmony with one another, coupled with energy-supplying nucleoside triphosphates (NTPs), play essential roles. Our next goal in this chapter is to present a simple overview of how the genetic information is duplicated and put to work, as the full elucidation of these processes is still in progress.

26.6 Replication of DNA

Learning Objective:

- Explain the process of DNA replication.

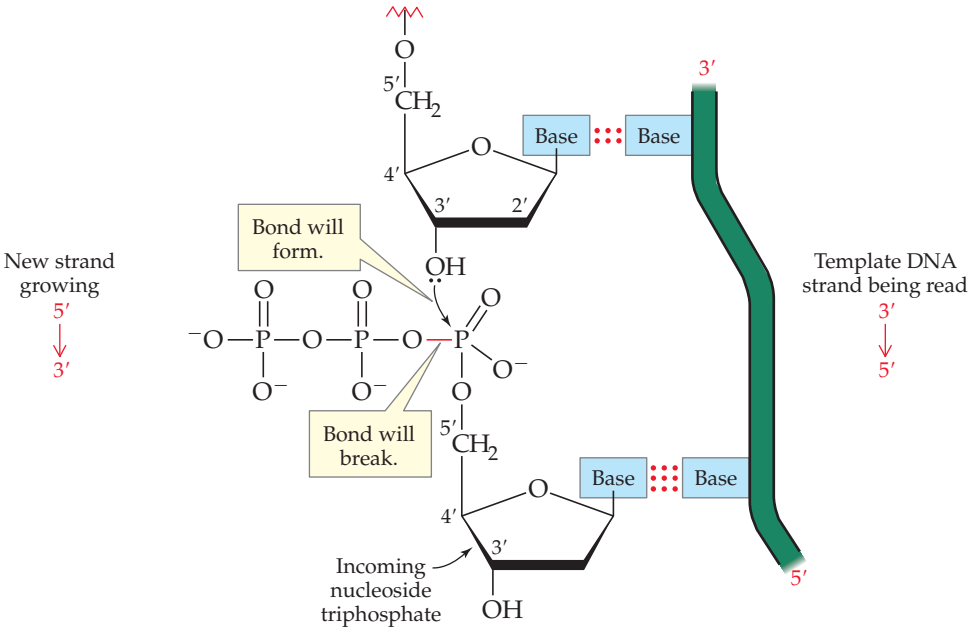
DNA replication begins in the nucleus with partial unwinding of the double helix; this process involves enzymes known as *helicases.* The unwinding occurs simultaneously in many specific locations known as *origins of replication* (Figure 26.4). The DNA strands separate, exposing the bases and effectively forming a "bubble" in which the replication process can begin. At either end of the bubble, where double-stranded DNA and single-stranded DNA meet, are branch points known as *replication forks.* A set of multisubunit enzymes called DNA polymerases move into position on the separated strands—their

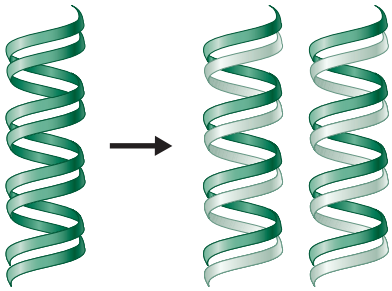


▲ Figure 26.4
DNA replication sites.
(a) Replication initiates at sites where the DNA unwinds, exposing single strands. This occurs in multiple locations simultaneously. (For simplicity, only one replication fork is shown.) (b) Electron micrograph of DNA. As DNA unwinds at multiple sites, single-stranded DNA is exposed and replication forks form at the junctions between single- and double-stranded DNA.

function is to facilitate transcription of the exposed single-stranded DNA. The NTPs carrying each of the four bases are available in the vicinity. One by one, the triphosphates move into place by forming hydrogen bonds with the bases exposed on the DNA template strand. A can only form hydrogen bonds with T, and G can only form hydrogen bonds with C. DNA polymerase then catalyzes covalent bond formation between the 5′ phosphate group of the arriving NTP and the 3′—OH at the end of the growing polynucleotide strand, as the two extra phosphate groups are removed.

Bond formation in DNA replication



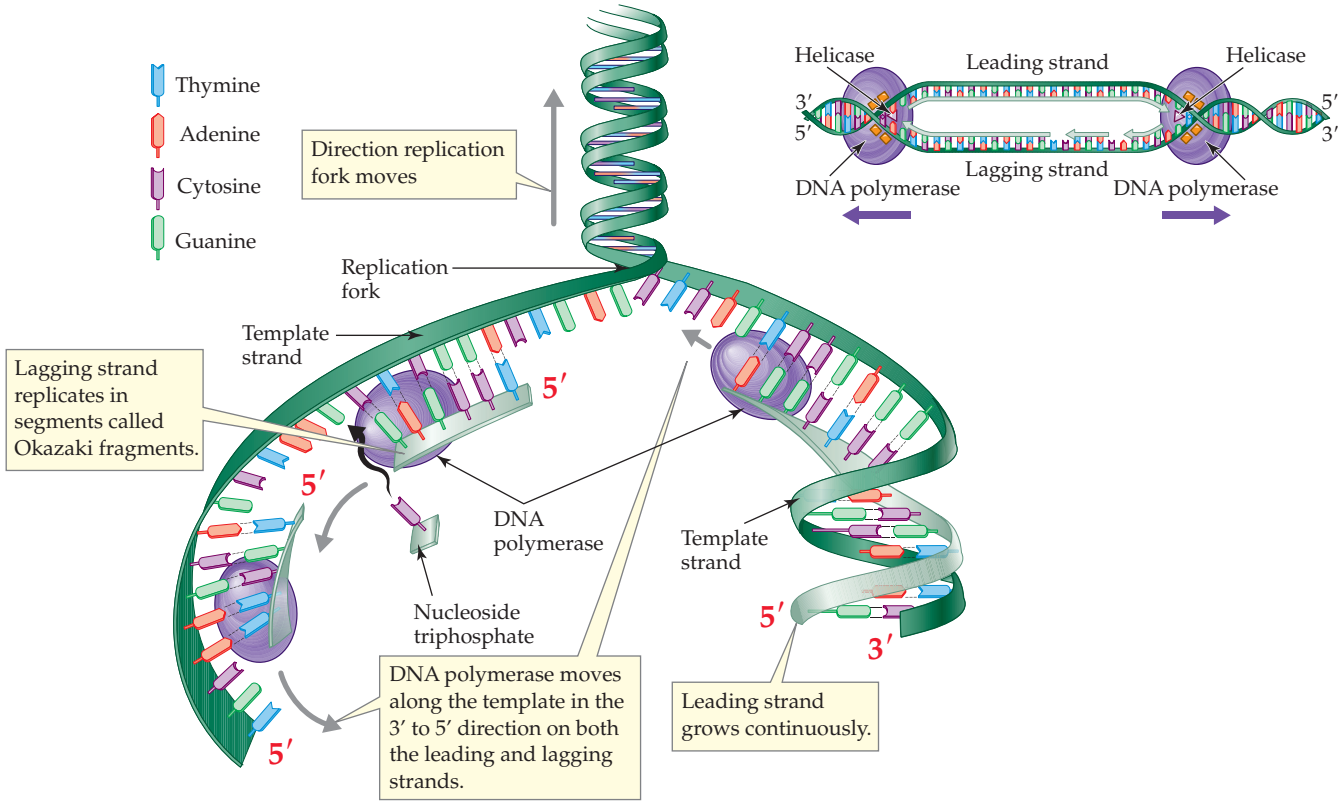


▲ Semiconservative replication produces a pair of DNA double helixes in which one strand (dark green) is the original strand and the other (light green) is the strand that has been copied from the original.

DNA polymerase catalyzes the reaction between the 5′ phosphate on an incoming nucleotide and the free 3′—OH on the growing DNA strand. Therefore, the template strand can only be read in the 3′ to 5′ direction, and the new DNA strand can grow only in the 5′ to 3′ direction.

Since each new strand is complementary to its template strand, two identical copies of the DNA double helix are produced during replication. In each new double helix, one strand is the template and the other is the newly synthesized strand. We describe the result as *semiconservative* replication (one of the two parent strands is conserved in each of the two new DNA molecules).

Note in Figure 26.5 that the incoming NTP is added to the 3′ end of the new strand. In other words, new DNA is synthesized in the 5′ to 3′ direction as the polymerase travels along the template strand in the 3′ to 5′ direction. Because the original DNA strands are antiparallel, only one new strand, known as the *leading strand,* is able to grow continuously as the point of replication (the *replication fork*) moves along. For the leading strand the DNA polymerase, traveling along the template in the 3′ to 5′ direction, is moving in the *same* direction as the replication fork. On the other strand, movement of the DNA polymerase along the template strand in the 3′ to 5′ direction means that the DNA polymerase is moving in the *opposite direction* as the replication fork. As a consequence, this other strand, called the *lagging strand,* is replicated in short segments called *Okazaki fragments* (after the Japanese scientist who discovered them). The directions of growth are shown in Figure 26.5, where the leading strand is the continuously growing strand of the new DNA and the lagging strand is the one composed of the short Okazaki fragments. To form the lagging strand from the Okazaki fragments, these short DNA segments are joined together by the action of an enzyme known as *DNA ligase.*



▲ **Figure 26.5**
DNA replication.
(a) Because the new polynucleotide chain must grow in the 5′ to 3′ direction, the leading strand (shown at the right, in light green) grows continuously toward the replication fork while the lagging strand (at the left in light green) grows in segments as the fork moves. The segments are later joined by a DNA ligase enzyme. (b) DNA polymerases at each replication fork travel along the DNA as more and more of it unwinds. The DNA polymerases are responsible for copying of the single-stranded DNA, generating new strands that grow in the 5′ to 3′ direction. One single strand, the leading strand, is copied continuously; the other single strand, called the lagging strand, is copied in segments.

The total number of base pairs in a human cell—the human **genome**—is 3 *billion* base pairs. The complete copying process in human cells takes several hours. To replicate a huge molecule such as human DNA at this speed requires not one, but many replication forks, producing many segments of DNA strands that are ultimately joined to produce a faithful copy of the original.

Genome All of the genetic material in the chromosomes of an organism; its size is given as the number of base pairs.

PROBLEM 26.12

What are Okazaki fragments? What role do they serve in DNA replication?

PROBLEM 26.13

What is the difference between DNA polymerase and DNA ligase?

26.7 Structure and Function of RNA

Learning Objective:

- List the types of RNA, their locations in the cell, and their functions.

RNA is similar to DNA—both are sugar–phosphate polymers and both have nitrogen-containing bases attached—but there are important differences (Table 26.2). We have already seen that RNA and DNA differ in composition (Section 26.2): The sugar in RNA is ribose rather than deoxyribose, and the base uracil in RNA pairs up with adenine rather than with thymine. RNA and DNA also differ in size and structure—RNA strands are not as long as DNA molecules. The RNAs are almost always single-stranded molecules (as distinct from DNA, which is almost always double-stranded); RNA molecules also often have complex folds, sometimes folding back on themselves to form double helices in some regions.

Table 26.2 Comparison of DNA and RNA

	Sugar	Bases	Shape and Size	Function
DNA	Deoxyribose	Adenine Guanine Cytosine Thymine	Paired strands in double helix; 50 million or more nucleotides per strand	Stores genetic information
RNA	Ribose	Adenine Guanine Cytosine Uracil	Single-stranded with folded regions; <100 to about 50,000 nucleotides per RNA	*mRNA*—Encodes a copy of genetic information ("blueprints" for protein synthesis) *tRNA*—Carries amino acids for incorporation into protein *rRNA*—Component of ribosomes (sites of protein synthesis)

There are also different kinds of RNA, each type with its own unique function in the flow of genetic information, whereas DNA has only one function—storing genetic information. Working together, the three types of RNA make it possible for the encoded information carried by DNA to be put to use in the synthesis of proteins.

- **Ribosomal RNAs** Outside the nucleus but within the cytoplasm of a cell are the **ribosomes**—small granular organelles where protein synthesis takes place. (Their location in the cell is shown in Figure 21.2, p. 697.) Each ribosome is a complex consisting of about 60% **ribosomal RNA (rRNA)** and 40% protein, with a total molecular mass of approximately 5,000,000 amu.
- **Messenger RNAs** The **messenger RNAs (mRNA)** carry information transcribed from DNA. They are formed in the cell nucleus and transported out to the ribosomes, where proteins will be synthesized. They are polynucleotides of varying length that carry the same code for proteins as does the DNA.
- **Transfer RNAs** The **transfer RNAs (tRNA)** are smaller RNAs that deliver amino acids one by one to protein chains growing at ribosomes. Each tRNA carries only one amino acid.

Ribosome The structure in the cell where protein synthesis occurs; composed of protein and rRNA.

Ribosomal RNA (rRNA) The RNA that is complexed with proteins in ribosomes.

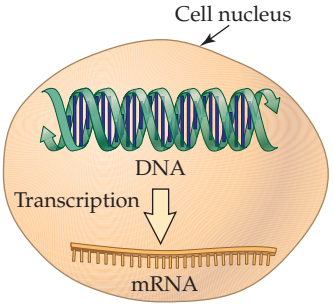
Messenger RNAs (mRNA) The RNA that carries code transcribed from DNA and directs protein synthesis.

Transfer RNA (tRNA) The RNA that transports amino acids into position for protein synthesis.

26.8 Transcription: RNA Synthesis

Learning Objective:

- Explain the process of transcription, and write complementary strands through mRNA.

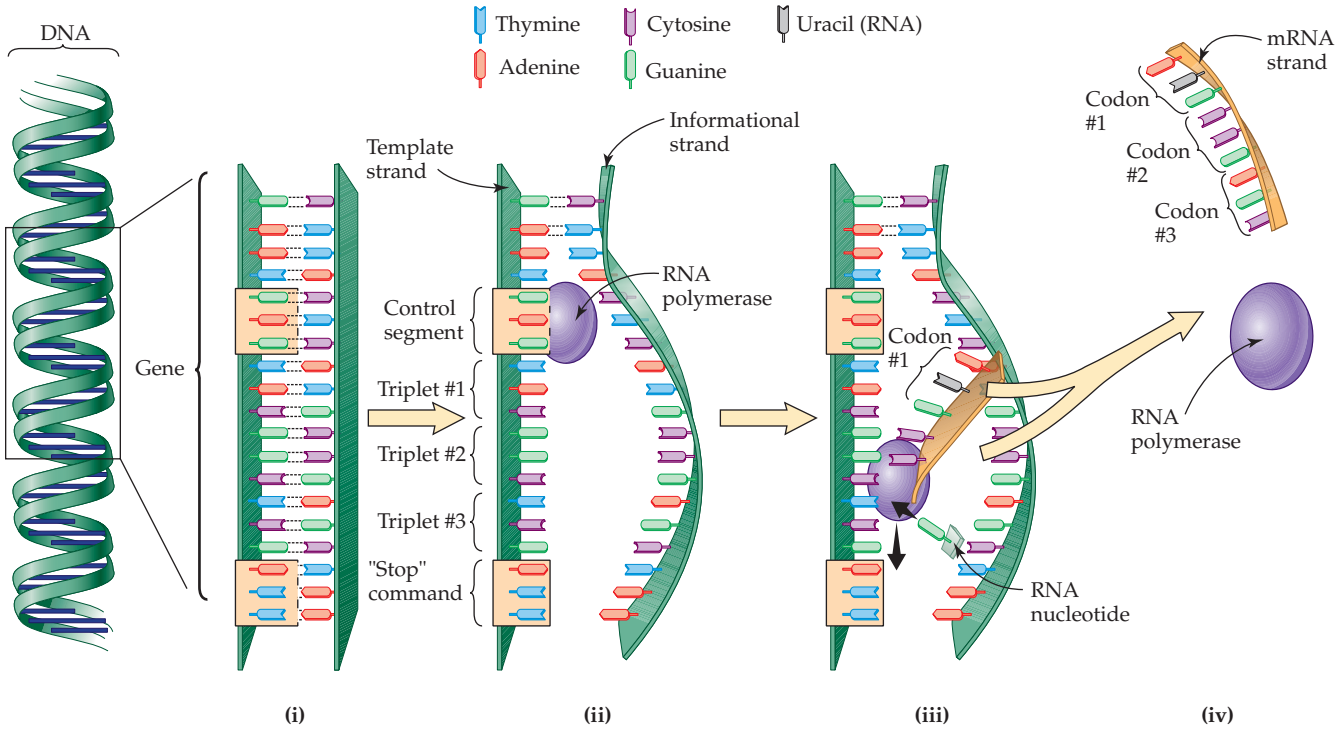


RNAs are synthesized in the cell nucleus. Before leaving the nucleus, all types of RNA molecules are modified in various ways that enable them to perform their different functions. We focus here on mRNA (in eukaryotes) because its synthesis (transcription) is the first step in transferring the information carried by DNA into protein synthesis.

In transcription, as in replication, a small section of the DNA double helix unwinds, the bases on the two strands are exposed, and one by one the complementary nucleotides are attached. rRNA, tRNA, and mRNA are all synthesized in essentially the same manner. Only one of the two DNA strands is transcribed during RNA synthesis. The DNA strand that is transcribed is the *template strand;* its complement in the original helix is the *informational strand.* The mRNA molecule is complementary to the template strand, which makes it an exact RNA duplicate of the DNA informational strand, with the exception that a U replaces each T in the DNA strand. The relationships are illustrated by the following short DNA and mRNA segments:

DNA informational strand	5′ ATG CCA GTA GGC CAC TTG TCA 3′
DNA template strand	3′ TAC GGT CAT CCG GTG AAC AGT 5′
mRNA	5′ AUG CCA GUA GGC CAC UUG UCA 3′

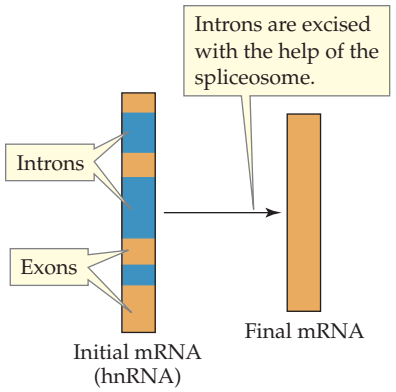
The transcription process, shown in Figure 26.6, begins when RNA polymerase, an enzyme that synthesizes RNA, recognizes a control segment in DNA that precedes the nucleotides to be transcribed. *The genetic code,* which we will discuss in Section 26.9, consists of triplets of consecutive bases known as *codons.* The nucleotide triplets carried by mRNA code for amino acids to be assembled into proteins (Section 26.10). The sequence of nucleic



▲ **Figure 26.6**
Transcription of DNA to produce mRNA.
The transcription shown here produces a hypothetical three-codon mRNA. From left to right, (i) the DNA unwinds; (ii) the RNA polymerase connects with the control, or start, segment on the template strand; (iii) the mRNA is assembled as the polymerase moves along the template strand; and (iv) transcription ends when the polymerase reaches the stop command, releasing both the new mRNA strand and RNA polymerase.

acid code that corresponds to a complete protein is known as a *gene*. RNA polymerase moves down the DNA segment to be transcribed, adding complementary nucleotides one by one to the growing RNA strand as it goes. Transcription ends when the RNA polymerase reaches a termination sequence that signals the end of the sequence to be copied.

At the end of transcription, the mRNA molecule contains a matching base for every base that was on the informational DNA strand, from the site of transcription initiation to the site of transcription termination. The code for a gene is contained in one or more small sections of DNA called an **exon** (exons carry code that is *ex*pressed). The code for a given gene may be interrupted by a sequence of bases called an **intron** (a section that *in*tervenes or *in*terrupts) and then resumed farther down the chain in another exon. Introns are sections of DNA that do not code for any part of the protein to be synthesized. The initial mRNA strand (the "primary transcript"), like the DNA from which it was synthesized, contains both exons and introns and is known as **heterogeneous nuclear RNA (hnRNA).** In the final mRNA molecule released from the nucleus, the intron sections have been cut out and the remaining pieces (consisting of the exons) are spliced together through the action of a structure known as a *spliceosome*.



Exon A nucleotide sequence in a gene that codes for part of a protein.

Intron A nucleotide sequence in mRNA that does not code for part of a protein; removed before mRNA proceeds to protein synthesis.

Heterogeneous nuclear RNA (hnRNA) The initially synthesized mRNA strand containing both introns and exons.

Worked Example 26.4 Writing Complementary DNA and RNA Strands from Informational DNA Strands

The nucleotide sequence in a segment of a DNA informational strand is given here. What is the nucleotide sequence in the complementary DNA template strand? What is the sequence transcribed from the template strand into mRNA?

5′AAC GTT CCA ACT GTC 3′

ANALYSIS Recall:

1. In the informational and template strands of DNA, the base pairs are A-T and C-G.
2. Matching base pairs along the informational strand gives the template strand written in the 3′ to 5′ direction.
3. The mRNA strand is identical to the DNA informational strand except that it has a U wherever the informational strand has a T.
4. Matching base pairs along the template strand produces the mRNA strand written in the 5′ to 3′ direction.

SOLUTION

Applying these principles gives

DNA informational strand	5′AAC GTT CAA ACT GTC 3′
DNA template strand	3′TTG CAA GTT TGA CAG 5′
mRNA	5′AAC GUU CAA ACU GUC 3′

PROBLEM 26.14

What is the function of the spliceosome in hnRNA?

PROBLEM 26.15

What mRNA base sequences are complementary to the following DNA template sequences? Be sure to label the 5′ and 3′ ends of the complementary sequences.

(a) 5′CAT GCT CTA CAG 3′ **(b)** 3′TAT TAG CGA CCG 5′

26.9 The Genetic Code

Learning Objective:

- Interpret mRNA codons from the genetic code, and write the primary sequence of a protein.

Codon A sequence of three ribonucleotides in the mRNA chain that codes for a specific amino acid; also a three-nucleotide sequence that is a stop codon and stops translation.

Genetic code The sequence of nucleotides, coded in triplets (codons) in mRNA, that determines the sequence of amino acids in protein synthesis.

The ribonucleotide sequence in an mRNA chain is like a coded sentence that spells out the order in which amino acid residues should be joined to form a protein. Each "word" consists of a triplet of ribonucleotides, or **codon,** in the mRNA sentence, which in turn corresponds to a specific amino acid. That is, a series of codons spells out a sequence of amino acids. For example, the series uracil-uracil-guanine (UUG) on an mRNA transcript is a codon directing incorporation of the amino acid leucine into a growing protein chain. Similarly, the sequence guanine-adenine-uracil (GAU) codes for aspartate.

Of the 64 possible three-base combinations in RNA, 61 code for specific amino acids and 3 code for chain termination (the *stop codons*). The "meaning" of each codon—the **genetic code** universal to all but a few living organisms—is given in Table 26.3. Note that most amino acids are specified by more than one codon and that codons are always written in the 5′ to 3′ direction.

Table 26.3 Codon Assignments of Base Triplets in mRNA

First Base (5′ end)	Second Base	Third Base (3′ end) U	C	A	G
U	U	Phe	Phe	Leu	Leu
	C	Ser	Ser	Ser	Ser
	A	Tyr	Tyr	*Stop*	*Stop*
	G	Cys	Cys	*Stop*	Trp
C	U	Leu	Leu	Leu	Leu
	C	Pro	Pro	Pro	Pro
	A	His	His	Gln	Gln
	G	Arg	Arg	Arg	Arg
A	U	Ile	Ile	Ile	Met
	C	Thr	Thr	Thr	Thr
	A	Asn	Asn	Lys	Lys
	G	Ser	Ser	Arg	Arg
G	U	Val	Val	Val	Val
	C	Ala	Ala	Ala	Ala
	A	Asp	Asp	Glu	Glu
	G	Gly	Gly	Gly	Gly

The relationship between the DNA informational and template strand segments illustrated earlier is repeated here along with the protein segment for which they code.

DNA informational strand	5′ATG CCA GTA GGC CAC TTG TCA 3′
DNA template strand	3′TAC GGT CAT CCG GTG AAC AGT 5′
mRNA	5′AUG CCA GUA GGC CAC UUG UCA 3′
Protein	Met Pro Val Gly His Leu Ser

Notice that the 5′ end of the mRNA strand codes for the *N*-terminal amino acid, whereas the 3′ end of the mRNA strand codes for the *C*-terminal amino acid. (Remember, proteins are written *N*-terminal to *C*-terminal, reading left to right.)

Worked Example 26.5 Translating RNA into Protein

In Worked Example 26.4, we derived the mRNA sequence of nucleotides shown. What is the sequence of amino acids coded for by the mRNA sequence?

5′AAC GUU CAA ACU GUC 3′

ANALYSIS The codons must be identified by consulting Table 26.3. They are

5′AAC	GUU	CAA	ACU	GUC	3′
Asn	Val	Gln	Thr	Val	

SOLUTION

Written out in full, the protein sequence is

asparagine-valine-glutamine-threonine-valine

HANDS-ON CHEMISTRY 26.1

In this activity, you will assemble an unwound section of DNA and then build a complementary section of mRNA (see Figure 26.6). Then, by using Table 26.3, you will determine the amino acids for the primary structure of a tripeptide (very small protein).

In this exercise, you will use colored drinking straws to represent nucleotides. If possible, select a package of drinking straws with five colors. If only four colors are possible, then one end of a color can be marked with a pen.

1. Cut each straw into four pieces. Follow the color code in Figure 26.6: T = blue, A = red, C = purple, G = green, and U = gray by matching the straw colors if possible. (If matching the Figure 26.6 colors is not possible, just assign each straw color a nucleoside; T, A, C, G, and for U use the color for T but mark it with a pen).
2. Look at Figure 26.6, part i. The template strand is on the left and the informational strand is on the right. In part ii, the control segment and stop command are highlighted. You will assemble the DNA from the control segment to the stop command. The template strand will begin with GAGTACGGCTCGATT. Remember, the mRNA complementary sequence is the same as the informational strand but uracil is present in mRNA and thymine is present in DNA. Take the pieces of straws (the nucleotides), and put them in the order of the template strand in Figure 26.6, part i.
3. Next, put the pieces of straw that are complementary to the template strand to make the informational strand. Then, squeeze and fold one piece of the straw and connect it to its complementary base. This will represent the hydrogen bonding between the bases for the DNA template and informational strands.
4. Next, you must put the mRNA sequence in order. Since mRNA carries the codons needed for proteins, determine which straws are needed for the mRNA sequence from the template strand. Then, using Table 26.3, write down the amino acids you need from the codons in the mRNA. Do the straw colors for the mRNA matchup with the mRNA in Figure 26.6, part iv? How many amino acids do you need for the protein that is encoded in the DNA? Notice that in the mRNA the control segment and stop command are not represented.
5. Refer back to Problem 26.15. Assemble the template and informational strands for each part of Problem 26.15. Determine which colored straws are needed for the mRNA and determine which amino acids will be synthesized into a protein.

CHEMISTRY IN ACTION

Influenza: Variations on a Theme

Flu is caused by the influenza virus, where influenza A and B viruses cause human flu epidemics almost every winter. In the United States, these seasonal epidemics can cause illness in 10–20% of the human population and are associated with an average of 36,000 deaths and 114,000 hospitalizations per year.

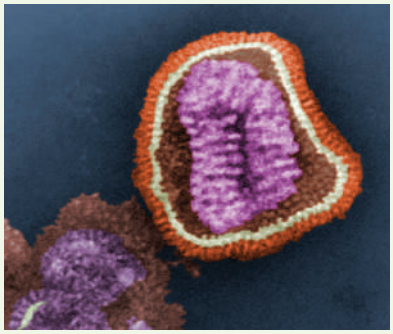
Viruses are submicroscopic infectious agents that can replicate only inside living cells. Thousands of viruses are known, each of which can infect a particular plant or animal cell. Virus particles consist of only a few biomolecules: some nucleic acid (either DNA or RNA, which can be either single-stranded or double-stranded) and a protein coating (capsid) made of just a few proteins. Some viral classes also have a lipid coating over the capsid. How can something so small and with so few components cause the flu?

A virus particle cannot make copies of itself without a host cell providing the necessary cellular machinery. Once a virus enters a living cell, it takes over the host cell and forces it to produce virus copies, which then leave the host and spread the infection to other cells causing symptoms of the flu. To prevent illnesses from types A and B influenza, we can get a flu shot. The other influenza infection called type C causes a mild respiratory illness and is not thought to cause epidemics. Flu shots do not protect against type C influenza. Unfortunately, one shot does not protect you from influenza for life; you have to be re-immunized yearly because the influenza virus mutates rapidly, especially the protein coat. Since influenza viruses are ubiquitous, flu can cause either an epidemic or a pandemic. A disease that quickly and severely affects a large number of people and then subsides is an epidemic. A pandemic is a widespread epidemic that may affect entire continents or even the world. Both have occurred.

Can animals get the flu? The answer is yes. Many subtypes of influenza A viruses are also found in a variety of animals, including ducks, chickens, pigs, whales, horses, and seals. Birds are susceptible to all known subtypes of the influenza A virus and serve as reservoirs.

Influenza viruses that infect birds are called avian influenza viruses; first identified in Italy more than 100 years ago, these viruses occur naturally among birds worldwide. Wild birds, most notably migratory waterfowl such as wild ducks, carry the viruses in their intestines. Avian influenza is very contagious among birds. If infection does occur, domesticated birds, such as chickens, ducks, and turkeys, are particularly susceptible to infection, which either makes them very sick or kills them.

Humans also are susceptible to influenza A viruses, but avian influenza viruses do not usually infect humans due to subtype differences. However, several cases of human infection with avian influenza viruses have occurred since 1997. These viruses may be transmitted to humans directly from birds, from an environment contaminated by avian virus, or through an intermediate host, such as a pig. Because pigs are susceptible to infection by both avian and human viruses, they can serve as a "mixing vessel" for the scrambling of genetic material from human and avian viruses, resulting in the emergence of a novel viral subtype. For example, if a pig is infected with a human influenza virus and an avian influenza virus at the same time, the viruses can re-assort genes and produce a new virus that has most of the genes from the human virus but surface proteins from the avian virus. This process is known as an antigenic shift. This is how a new virus is formed—a virus against which humans will have little or no immunity and that may result in sustained human-to-human transmission and ultimately an influenza epidemic. Conditions favorable for the emergence of antigenic shift have long been thought to involve humans living in close proximity to domestic poultry and pigs. However, recent events suggest humans themselves can serve as the "mixing vessel." This scenario has frightening consequences; so frightening that the Centers for Disease Control and Prevention (CDC) considers the control of avian influenza to be a top priority. Luckily, the bird flu outbreak in 2006 was limited, although serious, and the swine flu pandemic of 2009 was not as virulent a strain as was first thought. That particular influenza A virus mixed genes from human, avian, and swine viruses, resulting in a novel virus to which humans had no immunity. The 2009 viral strain has some genetic similarities to an older influenza virus that had an alarmingly high mortality rate.



▲ A transmission electron micrograph of negatively stained influenza A virus particles.

Scientists continue to monitor viral sub-strain shifts and drug companies prepare seasonal influenza vaccine based on predictions of what the next season's predominant viral strains will be. Work is also moving forward on a universal vaccine so that you can avoid the yearly shot and be immunized against influenza like you are against other common viral diseases such as measles.

CIA Problem 26.1 How do viruses differ from living organisms?

CIA Problem 26.2 What symptoms might a person have when infected with influenza A? influenza B? influenza C?

CIA Problem 26.3 Using a variety of sources, research which influenza types and strains are being incorporated into the flu shot?

CIA Problem 26.4 Why is it difficult to develop a universal influenza vaccine?

PROBLEM 26.16

List possible codon sequences for the following amino acids.

(a) Val **(b)** Phe **(c)** Asn **(d)** Gly **(e)** Met

PROBLEM 26.17

Identify the amino acid for which the codon GAG codes, and what other codon could encode for this same amino acid?

PROBLEM 26.18

What amino acids do the following sequences code for?

(a) AUC **(b)** GCU **(c)** CGA **(d)** AAG

PROBLEM 26.19

A hypothetical tripeptide Leu-Leu-Leu could be synthesized by the cell. What three different base triplets in mRNA could be combined to code for this tripeptide?

26.10 Translation: tRNA and Protein Synthesis

Learning Objective:

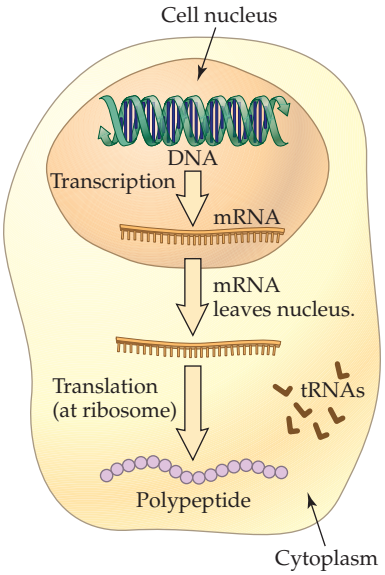
- Identify the initiation, elongation, and termination steps in translation for protein synthesis.

How are the messages carried by mRNA translated and how does the translation process result in the synthesis of proteins? Protein synthesis occurs at ribosomes, which are located outside the nucleus in the cytoplasm of cells. First, mRNA binds to the ribosome; then, amino acids, which are available in the cytosol, are delivered one by one by tRNA molecules to be joined into a specific protein by the ribosomal "machinery." All of the RNA molecules required for translation were synthesized from DNA by transcription in the nucleus and moved to the cytosol for translation.

Every cell contains more than 20 different tRNAs, each designed to carry a specific amino acid, even though they are all similar in overall structure. A tRNA molecule is a single polynucleotide chain held together by regions of base pairing in a partially helical structure something like a cloverleaf (Figure 26.7a). In three dimensions, a tRNA molecule is L-shaped, as shown in Figure 26.7b.

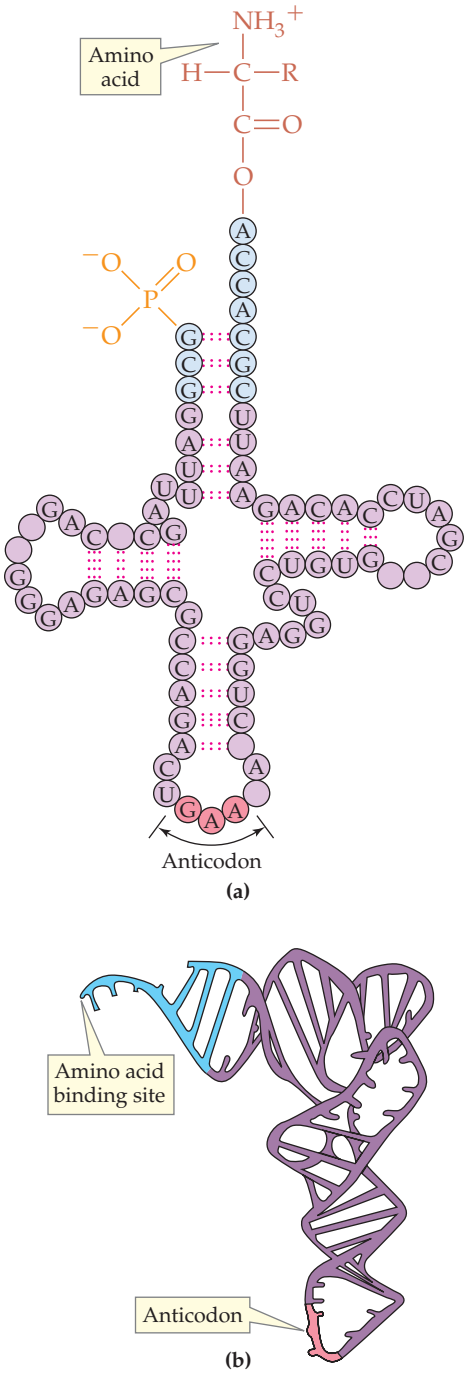
At one end of the L-shaped tRNA molecule, an amino acid is bonded to its specific tRNA by an ester linkage between the —COOH of the amino acid and an —OH group on the last ribose at the 3′ end of the tRNA chain. Individual synthetase enzymes are responsible for connecting each amino acid with its partner tRNA in an energy-requiring reaction. This reaction is referred to as *charging* the tRNA. Once charged, the tRNA is ready to be used in the synthesis of new protein.

At the other end of the tRNA, "L" is a sequence of three nucleotides called an **anticodon** (Figure 26.7). The anticodon of each tRNA is complementary to an mRNA codon—*always the one designating the particular amino acid that the tRNA carries.* For example, the tRNA carrying the amino acid leucine, which is coded for by 5′ CUG 3′ in mRNA, has the complementary sequence 3′ GAC 5′ as its anticodon on the tRNA. This is how the genetic message of nucleotide triplets, the codons, is translated into the sequence of amino acids in a protein. When the tRNA anticodon pairs off with its complementary mRNA codon, leucine is delivered to its proper place in the growing protein chain. The three stages in protein synthesis are *initiation, elongation,* and *termination.* These stages in translation are illustrated in Figure 26.8 and described in detail in the following sections.



▲ Overview of protein synthesis. The codons of mature mRNA are translated in the ribosomes, where tRNAs deliver amino acids to be assembled into proteins (polypeptides).

Anticodon A sequence of three ribonucleotides on tRNA that recognizes the complementary sequence (the codon) on mRNA.



▲ **Figure 26.7**
Structure of tRNA.
(a) Schematic, flattened tRNA molecule. The cloverleaf-shaped tRNA contains an anticodon triplet on one "leaf" and a covalently bonded amino acid at its 3′ end. The example shown is a yeast tRNA that codes for phenylalanine. All tRNAs have similar structures. The nucleotides not identified (blank circles) are slightly altered analogs of the four normal ribonucleotides. (b) The three-dimensional shape (the tertiary structure) of a tRNA molecule. Note how the anticodon is at one end and the amino acid is at the other end.

Ribozyme RNA that acts as an enzyme.

Translation Initiation

Each ribosome in a cell is made up of two subunits of markedly different sizes, called, logically enough, the *small subunit* and the *large subunit*. Each subunit contains protein enzymes and rRNA. Protein synthesis begins with the binding of an mRNA to the small subunit of a ribosome, joined by the first tRNA. The first codon on the 5′ end of mRNA, an AUG, acts as a "start" signal for the translation machinery and codes for a methionine-carrying tRNA. Initiation is completed when the large ribosomal subunit joins the small one and the methionine-bearing tRNA occupies one of the two binding sites on the united ribosome. Not all proteins have methionine at one end. If it is not needed, the methionine from chain initiation is removed by *posttranslational modification* before the new protein goes to work.

Translation Elongation

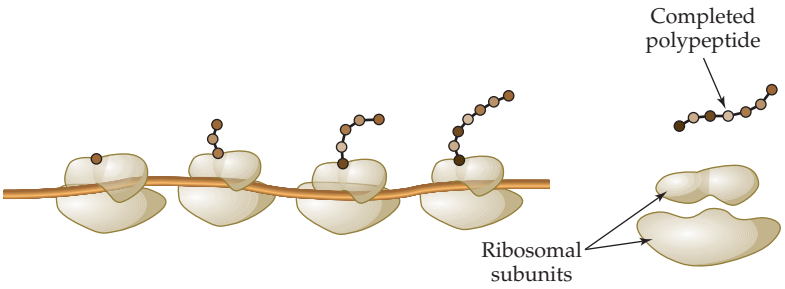
Next to the first binding site on the ribosome is a second binding site where the next codon on mRNA is exposed and the tRNA carrying the next amino acid will be attached. All available tRNA molecules can approach and try to fit, but only one with the appropriate anticodon sequence can bind. Once the tRNA with amino acid 2 arrives, a **ribozyme** in the large subunit catalyzes formation of the new peptide bond and breaks the bond linking amino acid 1 to its tRNA. These energy-requiring steps are fueled by the hydrolysis of guanosine triphosphate (GTP) to guanosine diphosphate (GDP). The first tRNA then leaves the ribosome, and the entire ribosome shifts one codon (three positions) along the mRNA chain. As a result, the second binding site is opened up to accept the tRNA carrying the next amino acid.

The three elongation steps now repeat:

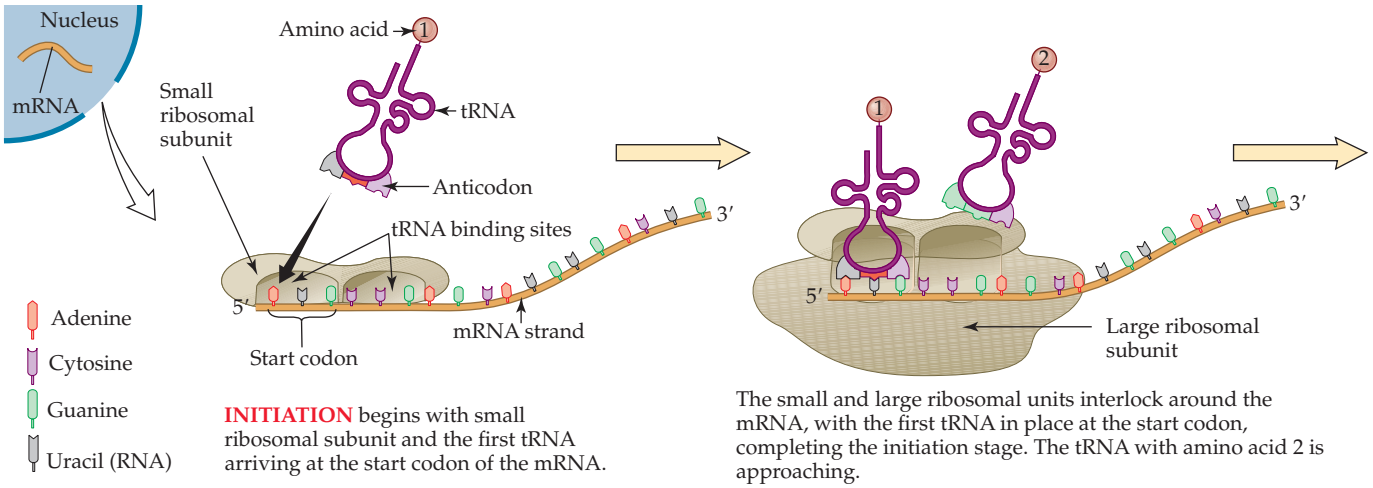
- The next appropriate tRNA binds to the ribosome.
- Peptide bond formation attaches the newly arrived amino acid to the growing chain, and the tRNA carrying it is released.
- Ribosome position shifts to free the second binding site for the next tRNA.

A single mRNA can be "read" simultaneously by many ribosomes. The growing polypeptides increase in length as the ribosomes move down the mRNA strand.

Translation Termination

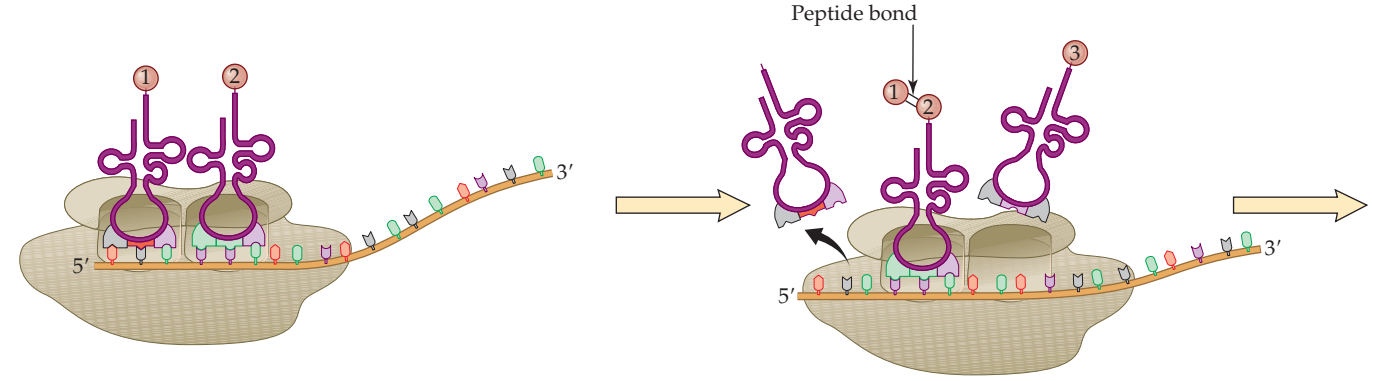


When synthesis of the protein is completed, a "stop" codon signals the end of translation. An enzyme called a *releasing factor* then catalyzes cleavage of the polypeptide chain from the last tRNA; the tRNA and mRNA molecules are released from the ribosome, and the two ribosome subunits separate. This step also requires energy from GTP. Overall, to add one amino acid to the growing polypeptide chain requires four molecules of GTP, excluding the energy needed to charge the tRNA.



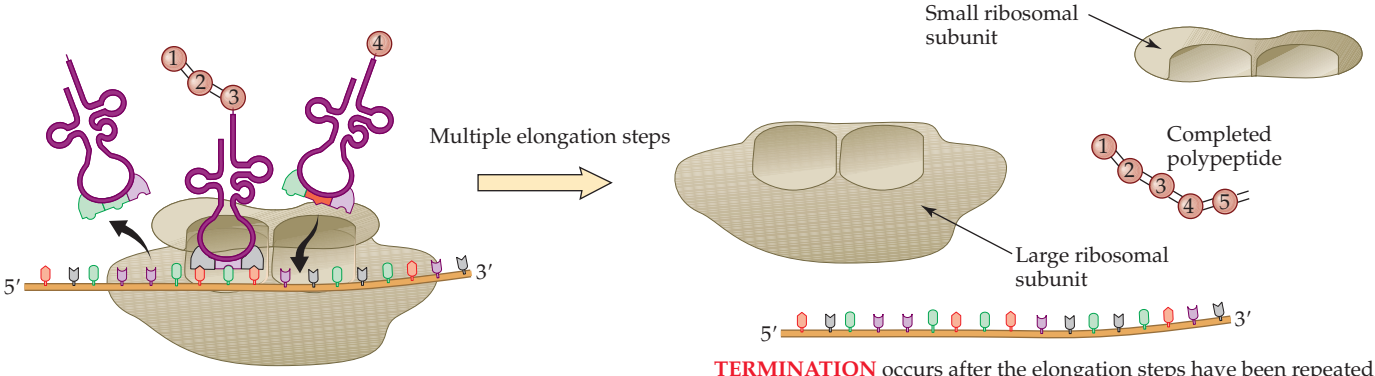
INITIATION begins with small ribosomal subunit and the first tRNA arriving at the start codon of the mRNA.

The small and large ribosomal units interlock around the mRNA, with the first tRNA in place at the start codon, completing the initiation stage. The tRNA with amino acid 2 is approaching.



ELONGATION begins as the tRNA with amino acid 2 binds to its codon at the second site within the ribosome.

A peptide bond forms between amino acid 1 and 2, the first tRNA is released, the ribosome moves one codon to the right, and the tRNA with amino acid 3 is arriving.



Elongation continues with three amino acids in the growing chain and the fourth one arriving with its tRNA.

TERMINATION occurs after the elongation steps have been repeated until the stop codon is reached. The ribosomal units, the mRNA, and the polypeptide separate.

▲ **Figure 26.8**
Translation: The initiation, elongation, and termination stages in protein synthesis.

PROBLEM 26.20

What amino acid sequence is coded for by the mRNA base sequence CUC-AUU-CCA-UGC-GAC-GUA?

PROBLEM 26.21

What anticodon sequences of tRNAs match the mRNA codons in Problem 25.20?

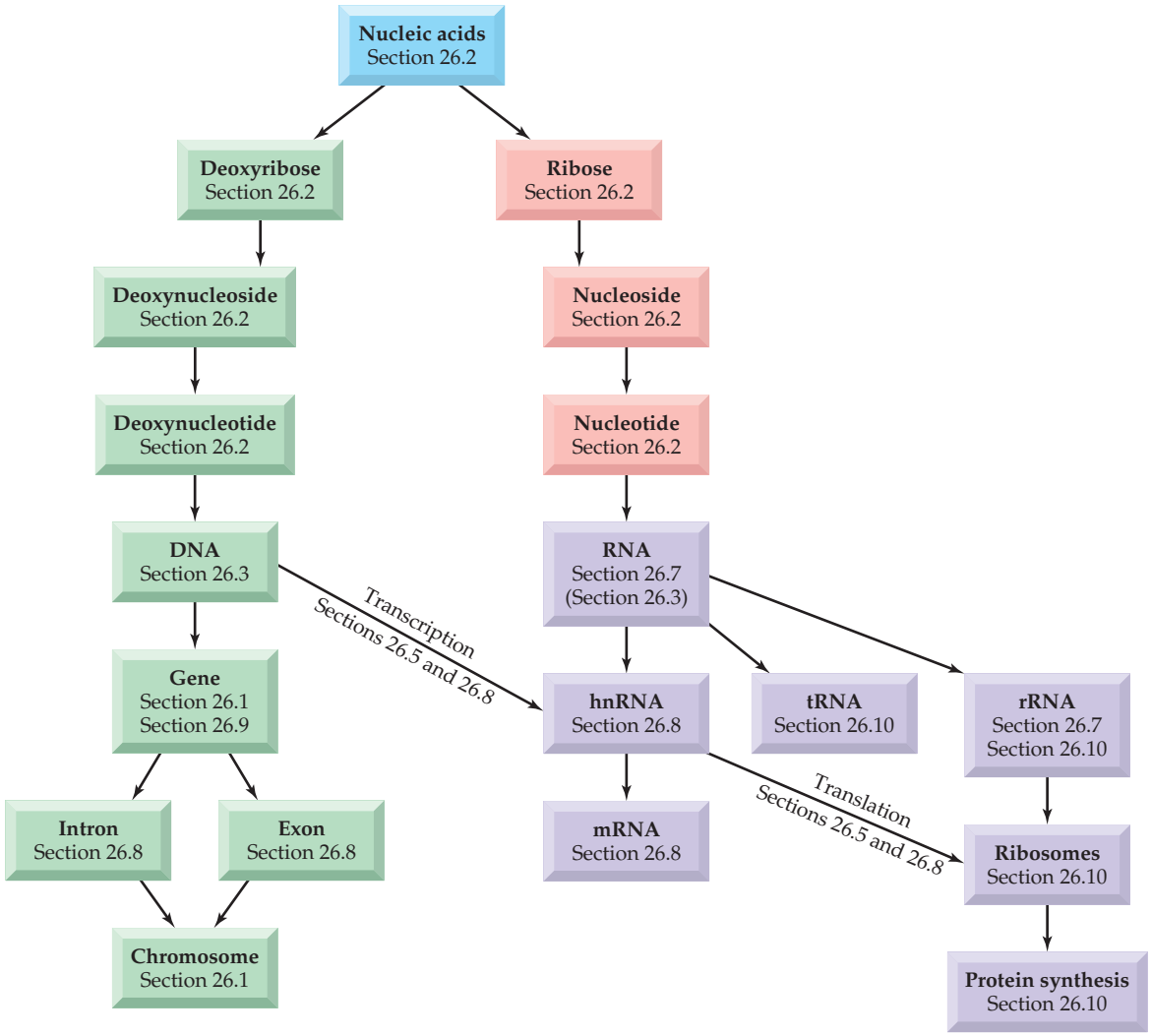
SUMMARY REVISITING THE CHAPTER LEARNING OBJECTIVES

- **Explain the role of chromosomes, genes, and DNA, and describe their basic function in the human body.** Chromosomes are molecular packages that contain all the information necessary for an organism to duplicate. Within chromosomes are genes that encode the synthesis of specific proteins primary structure or other functional molecules. Genes have a molecular makeup of DNA, which are very large molecules that contain genetic information *(see Problems 28–31).*
- **Describe, identify, and draw the components of nucleosides and nucleotides.** *Nucleic acids* are polymers of *nucleotides.* Each nucleotide contains a sugar, a base, and a phosphate group. The sugar is D-ribose in *RNAs* and 2-deoxy-D-ribose in *DNAs.* The C5 — OH of the sugar is bonded to the phosphate group, and the anomeric carbon of the sugar is connected by an *N*-glycosidic bond to one of five heterocyclic nitrogen bases (Table 26.1). A *nucleoside* contains a sugar and a base but not the phosphate group *(see Problems 32–35).*
- **Describe and identify nucleic acid chains in DNA and RNA.** In DNA and RNA, the nucleotides are connected by phosphate diester linkages between the 3′ — OH group of one nucleotide and the 5′ phosphate group of the next nucleotide. DNA and RNA both contain adenine, guanine, and cytosine; thymine occurs in DNA and uracil occurs in RNA *(see Problems 36–41).*
- **Interpret the structure of DNA, and write complementary sequences.** The DNA in each *chromosome* consists of two polynucleotide strands twisted together in a *double helix.* The sugar–phosphate backbones are on the outside, and the bases are in the center of the helix. The bases on the two strands are complementary—opposite every thymine is an adenine, opposite every guanine is a cytosine. The base pairs are connected by hydrogen bonds (two between T and A; three between G and C). Because of the *base pairing,* the DNA strands are *antiparallel:* One DNA strand runs in the 5′ to 3′ direction and its complementary partner runs in the 3′ to 5′ direction *(see Problems 42–46).*
- **Describe how genetic information is duplicated, transferred, and expressed.** Human heredity is the combination of a full complement of chromosomes and genes. These 23 pairs of chromosomes are DNA molecules copied from the fertilized egg. However, in an ongoing process when a cell divides, the genetic information can be passed on to daughter cells. This genetic information not only depends on the number and kinds of bases in the DNA but also on sequences of the bases in the DNA. Through processes called replication, transcription, and translation, gene expression can occur through the encoded DNA *(see Problems 47 and 50).*
- **Explain the process of DNA replication.** *Replication* (Figure 26.5) requires DNA polymerases and deoxyribonucleoside triphosphates. The DNA helix partially unwinds and the enzymes move along the separated DNA strands, synthesizing a new strand with bases complementary to those on the unwound DNA strand being copied. The enzymes move only in the 3′ to 5′ direction along the template strand (and thus new DNA strands only grow in the 5′ to 3′ direction), so that one strand is copied continuously and the other strand is copied in segments as the replication fork moves along. In each resulting double helix, one strand is the original template strand and the other is the new copy *(see Problems 48 and 49).*
- **List the types of RNA, their locations in the cell, and their functions.** *mRNA* carries the genetic information out of the nucleus to the *ribosomes* in the cytosol, where protein synthesis occurs. *tRNAs* circulate in the cytosol, where they bond to amino acids that they then deliver to ribosomes for protein synthesis. *rRNAs* are incorporated into ribosomes *(see Problems 50 and 51).*
- **Explain the process of transcription, and write complementary strands through mRNA.** In *transcription* (Figure 26.6), one DNA strand serves as the template and the other, the informational strand, is not copied. Nucleotides carrying bases complementary to the template bases between a control segment and a termination sequence are connected one by one to form mRNA. The primary transcript mRNA (or hnRNA) is identical to the matching segment of the informational strand but with uracil replacing thymine. *Introns,* which are base sequences that do not code for amino acids in the protein, are cut out before the final transcript mRNA leaves the nucleus *(see Problems 52–55).*
- **Interpret mRNA codons from the genetic code, and write the primary sequence of a protein.** The genetic information is read as a sequence of codons—triplets of bases in DNA that give the sequence of amino acids in a protein. Of the 64 possible codons (Table 26.3), 61 specify amino acids and three are stop codons *(see Problems 56–67).*
- **Identify the initiation, elongation, and termination steps in translation for protein synthesis.** Each tRNA has at one end an *anticodon* consisting of three bases complementary to those of the mRNA codon that specifies the amino acid it carries. Initiation of *translation* (Figure 26.8) is the coming together of the large and small subunits of the ribosome, an mRNA, and the first amino acid–bearing tRNA connected at the first of the two binding sites in the ribosome. *Elongation* proceeds as the next tRNA arrives at the second binding site, its amino acid is bonded to the first one, the first tRNA leaves, and the ribosome moves along so that once again there is a vacant second site. These steps repeat until the stop codon is reached. The termination step consists of separation of the two ribosome subunits, the mRNA, and the protein *(see Problems 68 and 69).*

KEY WORDS

Anticodon, *p. 833*
Base pairing, *p. 823*
Chromosome, *p. 815*
Codon, *p. 830*
Deoxyribonucleotide, *p. 818*
DNA (deoxyribonucleic acid), *p. 815*
Double helix, *p. 822*
Exon, *p. 829*
Gene, *p. 815*
Genetic code, *p. 830*
Genome, *p. 827*
Heterogeneous nuclear RNA (hnRNA), *p. 829*
Intron, *p. 829*
Messenger RNA (mRNA), *p. 827*
Nucleic acid, *p. 815*
Nucleoside, *p. 816*
Nucleotide, *p. 815*
Replication, *p. 824*
Ribonucleotide, *p. 818*
Ribosome, *p. 827*
Ribosomal RNA (rRNA), *p. 827*
Ribozyme, *p. 834*
RNA (ribonucleic acid), *p. 816*
Transcription, *p. 824*
Transfer RNA (tRNA), *p. 827*
Translation, *p. 824*

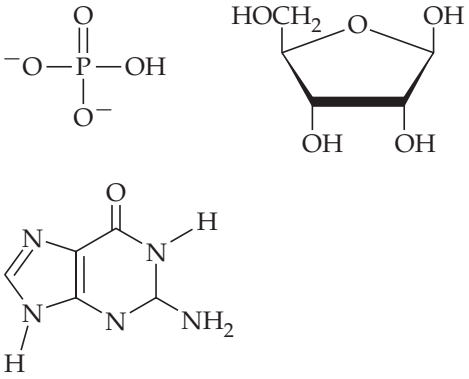
CONCEPT MAP



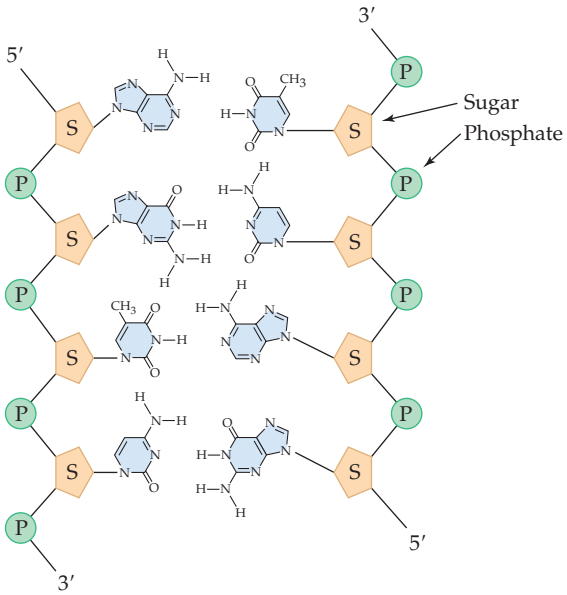
▲ **Figure 26.9 Concept Map.** This concept map shows the molecular structures in DNA and RNA as well as the process for protein synthesis.

UNDERSTANDING KEY CONCEPTS

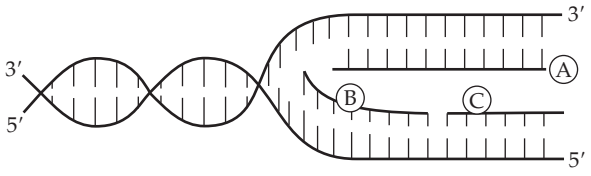
26.22 Combine the following structures to create a ribonucleotide. Show where water is removed to form an *N*-glycosidic linkage and where water is removed to form a phosphate ester. Draw the resulting ribonucleotide structure, and name it.



26.23 Copy the diagram to the right and use dotted lines to indicate where hydrogen bonding occurs between the complementary strands of DNA. What is the sequence of each strand of DNA drawn (remember that the sequence is written from the 5′ to 3′ end)?



26.24 Copy the following simplified drawing of a DNA replication fork:



(a) On the drawing, indicate the direction of synthesis of the new strand labeled A and the location of DNA polymerase on the strand.

(b) On the drawing, indicate the direction of synthesis of the new strand labeled B and the location of DNA polymerase on the strand.

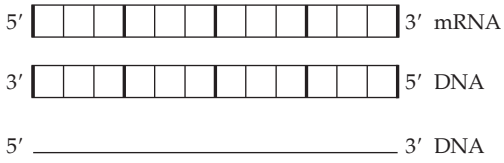
(c) How will strand C and strand B be connected?

26.25 What groups are found on the exterior of the DNA double helix? In the nucleus, DNA strands are wrapped around proteins called histones. Would you expect histones to be neutral, positively charged, or negatively charged? Based on your answer, which amino acids do you expect to be abundant in histones and why?

26.26 In addition to RNA polymerase, transcription of DNA for the synthesis of mRNA requires (a) a control segment of DNA (also called an initiation sequence), (b) an informational strand of DNA, (c) a template strand of DNA, and (d) an end of the sequence (termination sequence). Determine the direction of RNA synthesis on the RNA strand in the following diagram. Draw in the locations of elements (a)–(d).

26.27 Gln-His-Pro-Gly is the sequence of a molecule known as progenitor thyrotropin-releasing hormone (pro-TRH). If we were searching for pro-TRH genes, we would need to know what sequence of bases in DNA we should be looking for. Use the following boxes to indicate answers to parts (a)–(d).

Gln ----- His ----- Pro ----- Gly



(a) What RNA sequence could code for these four amino acids?

(b) What double-stranded DNA sequence (gene) could code for these amino acids?

(c) Which strand of DNA is the template strand, and which is the informational strand?

(d) How many possible DNA sequences are there?

ADDITIONAL PROBLEMS

DNA, CHROMOSOMES, AND GENES (SECTION 26.1)

26.28 What is the difference between a gene and a chromosome?

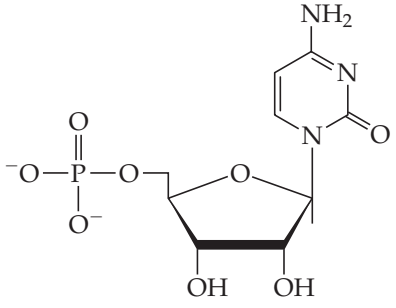
26.29 What are the two major components of chromatin?

26.30 What genetic information does a single gene contain?

26.31 How many chromosomes are present in a human cell?

STRUCTURE AND FUNCTION OF NUCLEIC ACIDS (SECTIONS 26.2 AND 26.3)

26.32 For the following molecule:



(a) Label the three nucleic acid building blocks it contains.

(b) Draw a box around the nucleoside portion of the molecule.

(c) Draw a circle around the nucleotide portion of the molecule.

26.33 What are the sugars in DNA and RNA, and how do they differ?

26.34 **(a)** What are the four major heterocyclic bases in DNA?

(b) What are the four major heterocyclic bases in RNA?

(c) Structurally, how do the heterocyclic bases in RNA differ from those in DNA? (See Table 26.1.)

26.35 What are the two structural types of bases in DNA and RNA? Which bases correspond to each type?

26.36 Draw structures to show how the phosphate and sugar components of a nucleic acid are joined. What kind of linkage forms between the sugar and the phosphate?

26.37 Draw structures to show how the sugar and heterocyclic base components of a nucleic acid are joined. What small molecule is formed?

26.38 What is the difference between the 3′ end and the 5′ end of a polynucleotide?

26.39 Are polynucleotides synthesized 3′ to 5′ or 5′ to 3′?

26.40 Draw the complete structure of uridine 5′-phosphate, one of the four major ribonucleotides.

26.41 Draw the complete structure of the RNA dinucleotide U-C. Identify the 5′ and 3′ ends of the dinucleotide.

BASE PAIRING (SECTION 26.4)

26.42 **(a)** What is meant by the term *base pairing*?

(b) Which bases pair with which other bases?

(c) How many hydrogen bonds does each base pair have?

26.43 What kind of intermolecular attraction holds the DNA double helix together?

26.44 What does it mean to speak of bases as being *complementary*?

26.45 The DNA from sea urchins contains about 32% A and about 18% G. What percentages of T and C would you expect in sea urchin DNA? Explain.

26.46 If a double-stranded DNA molecule is 22% G, what is the percentage of A, T, and C? Explain.

NUCLEIC ACIDS, REPLICATION OF DNA, AND STRUCTURE AND FUNCTION OF RNA (SECTIONS 26.5–26.7)

26.47 How are replication, transcription, and translation similar? How are they different?

26.48 Why is more than one replication fork needed when human DNA is duplicated?

26.49 Why do we say that DNA replication is semiconservative?

26.50 What are the three main kinds of RNA, and what are their functions?

26.51 Rank the following in order of size: tRNA, DNA, mRNA.

TRANSCRIPTION: RNA SYNTHESIS (SECTION 26.8)

26.52 The segment of DNA that encompasses a gene typically contains *introns* and *exons*. Define each of these terms.

26.53 What are some possible roles introns might have? What roles do exons have?

26.54 Transcribed RNA is complementary to which strand of DNA?

26.55 What is a codon and on what kind of nucleic acid is it found?

THE GENETIC CODE AND TRANSLATION (SECTIONS 26.9 AND 26.10)

26.56 What is an anticodon, and on what kind of nucleic acid is it found?

26.57 Which amino acid(s) have the most codons? Which amino acid(s) have the fewest codons? Can you think of a reason why multiple codons code for certain amino acids but other amino acids are coded for by very few codons?

26.58 Look at Table 26.3 and find codons for the following amino acids:

(a) Val **(b)** Arg **(c)** Ser

26.59 What amino acids are specified by the following codons?

(a) C-C-C **(b)** G-C-G **(c)** U-U-A

26.60 What anticodon sequences are complementary to the codons listed in Problem 26.59? (Remember that the anticodons are opposite in direction to the codons, so label the 3′ and 5′ ends!)

26.61 What anticodon sequences are complementary to the codons for the amino acids given in Problem 26.58? (Remember that the anticodons are opposite in direction to the codons, so label the 3′ and 5′ ends!)

26.62 If the sequence T-A-C-C-C-T appears on the informational strand of DNA, what sequence appears opposite it on the template strand? Label your answer with 3′ and 5′ ends.

26.63 Refer to Problem 26.62. What sequence appears on the mRNA molecule transcribed from the DNA sequence T-A-C-C-C-T? Label your answer with 3′ and 5′ ends.

26.64 Refer to Problems 26.62 and 26.63. What dipeptide is synthesized from the informational DNA sequence T-A-C-C-C-T?

26.65 What tetrapeptide is synthesized from the informational DNA sequence G-T-C-A-G-T-A-C-G-T-T-A?

26.66 Metenkephalin is a small peptide found in animal brains that has morphine-like properties. Give an mRNA sequence that could code for the synthesis of metenkephalin: Tyr-Gly-Gly-Phe-Met. Label your answer with 3′ and 5′ ends.

26.67 Refer to Problem 26.66. Give a double-stranded DNA sequence that could code for metenkephalin. Label your answer with 3′ and 5′ ends.

26.68 What is the general shape and structure of a tRNA molecule?

26.69 There are different tRNAs for each amino acid. What is one major way to differentiate among the tRNAs for each amino acid?

CONCEPTUAL PROBLEMS

26.70 A normal hemoglobin protein has a glutamic acid at position 6; in sickle-cell hemoglobin, this glutamic acid has been replaced by a valine. List all the possible mRNA codons that could be present for each type of hemoglobin. Can a single base change result in a change from Glu to Val in hemoglobin?

26.71 Insulin is synthesized as preproinsulin, which has 81 amino acids. How many heterocyclic bases must be present in the informational DNA strand to code for preproinsulin (assuming no introns are present)?

26.72 Human and horse insulin are both composed of two polypeptide chains with one chain containing 21 amino acids and the other containing 30 amino acids. Human and horse insulin differ at two amino acids: position 9 in one chain (human has serine and horse has glycine) and position 30 on the other chain (human has threonine and horse has alanine). How must the DNA differ to account for this? Identify the 5′ and 3′ ends of the four trinucleotide complementary DNA sequences.

26.73 If the initiation codon for proteins is AUG, how do you account for the case of a protein that does not include methionine as its first amino acid?

26.74 Suppose that 22% of the nucleotides of a DNA molecule are deoxyadenosine and during replication the relative amounts of available deoxynucleoside triphosphates are 22% dATP, 22% dCTP, 28% dGTP, and 28% dTTP. What deoxynucleoside triphosphate is limiting to the replication? Explain.

GROUP PROBLEMS

26.75 Imagine that you are part of a research team investigating new cures for HIV/AIDS. Discuss the HIV infection and locate stages in the infection that might be problematic to drug designs and cure.

26.76 Describe how the avian influenza virus is transmitted to humans. (See the Chemistry in Action "Influenza: Variations on a Theme," p. 832.)

26.77 Find 10 subtypes of influenza A, then divide the subtypes up. For each subtype, determine which species would be most infected by the subtype. In addition, find out if the subtype can be transmitted to another species.

26.78 The influenza virus H1N1 can infect both humans and other animals. Use the Internet to collect information that allows you to describe some of the similarities and some of the differences between the H1N1 virus and the virus responsible for avian influenza. (See the Chemistry in Action "Influenza: Variations on a Theme," p. 832.)

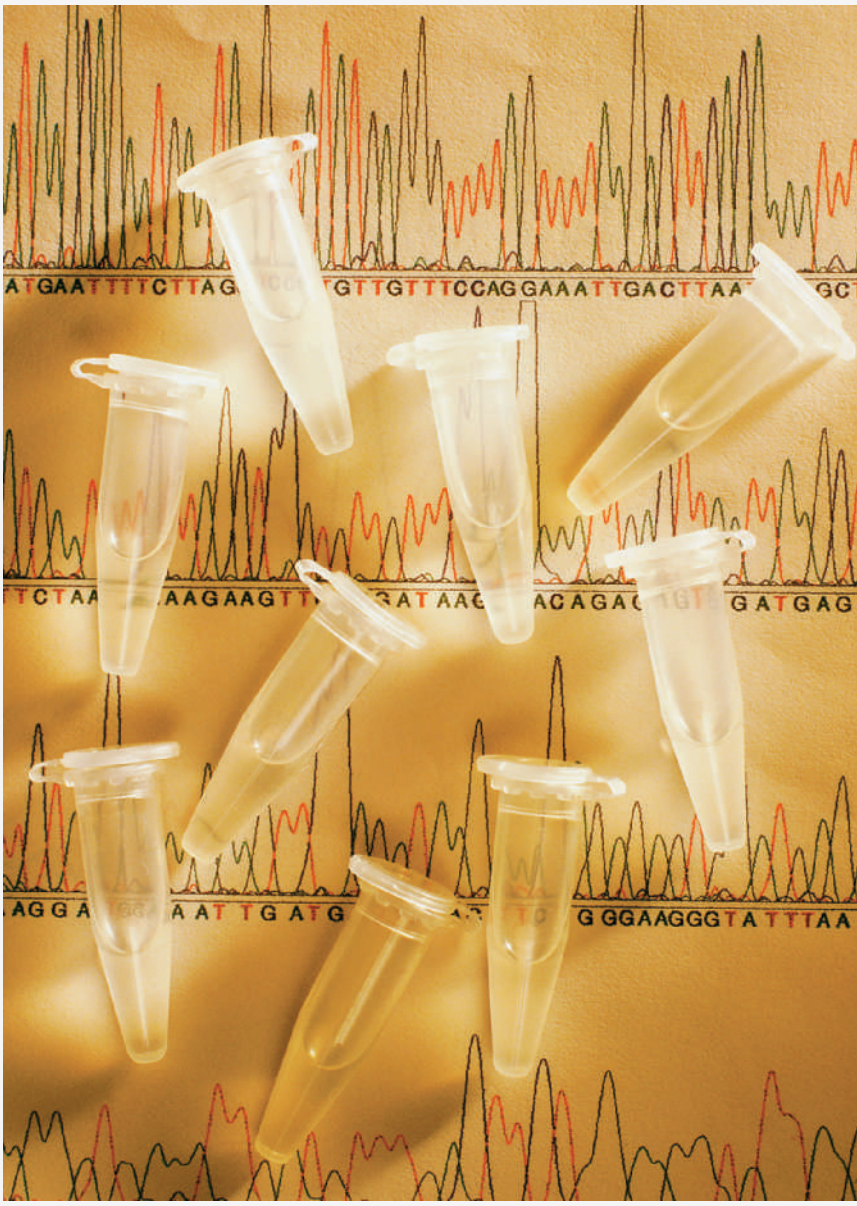
27

Genomics

CONTENTS

CONCEPTS TO REVIEW

A. Structure, Synthesis, and Function of DNA (Sections 26.2 and 26.3)
B. Base Pairing and Heredity (Sections 26.4 and 26.5)
C. Replication of DNA (Section 26.6)
D. Transcription, Translation, and the Genetic Code (Sections 26.8–26.10)



▲ The sequencing of DNA samples has led to advances in everything from medicine to criminal investigation.

Imagine this: A "perfect" crime has been committed and all the investigators can find is a drop of the criminal's blood, or a cigarette butt, or some other trace evidence. Yet from that trace evidence they are able to get a deoxyribonucleic acid (DNA) sample and identify, catch, and convict the criminal. This "DNA fingerprinting" has arisen from the scientific revolution that research on DNA has provided. But how is DNA fingerprinting actually done, and why is it so important in criminal forensics? You will read about this in the Chemistry in Action "DNA Fingerprinting" found at the end of this chapter.

Scientifically, the crowning achievement of DNA research has been the complete and accurate mapping of the human genome. Creation of this map has been compared to such landmark achievements as harnessing nuclear power and flight into outer space. In significance for individual human beings, there has never been anything like it. In this chapter, we will examine how the human genome was mapped, the variations in the content of the DNA in each chromosome, how DNA can be manipulated, and ways in which genomic information can be put to use.

27.1 Mapping the Human Genome

Learning Objective:

- Describe how a genome is mapped.

Genomics has a simple and straightforward definition: It is the study of whole sets of genes and their functions. For example, the study of bacterial genomics not only gives us a better understanding of how bacteria cause disease, but has also led to new treatments. The analysis of plant genomics is allowing the production of agricultural crops with enhanced value and utility, whereas the genomic study of farm animals is leading to improvements in animal health. Humans ultimately benefit from these studies, and applying the techniques learned will eventually lead to improvements in our own health. All work in genomics begins with developing a genetic map for the organism being studied.

Genomics The study of whole sets of genes and their functions.

How to Map a Genome

What exactly is a genetic "map," and how is it established? While it is easy to think of it as a "turn-by-turn" set of directions one might get from a global positioning system (GPS), in reality a genetic map is more like a map you get when you visit a large amusement park. You may see the scary mansion in one corner of the map, the thrill rides in another, the kiddie-ride area in another, and so on, with all the paths that lead to them shown. The typical map of this type is made up of landmarks and their location with respect to each other. A genetic map is no different, with one huge exception: We do not know exactly what many of the landmarks represent. For example, one genetic landmark (or *marker*) might represent a gene for eye color, or it might simply be a specific pattern of repeating nucleotides. So, in effect, a genomic map is a physical representation of all the landmarks in a genome and where they are with respect to one another.

▲ A sample of DNA ready for analysis.

Mapping the genes on a eukaryotic chromosome is no easy feat. When you consider that the nucleotides that code for proteins (the *exons*) are interrupted by noncoding nucleotides (the *introns*) (see Section 26.8), it should be clear what mapping challenges exist for any organism whose genome contains only a few dozen genes. These challenges are greatly magnified for the human genome, which contains between twenty and twenty-five *thousand* genes! Another challenge to consider is that there is neither spacing between "words" in the genetic code nor any "punctuation." Using the English language as an analogy, try to find a meaningful phrase in the following:

sfdggmaddrydkdkdkrrrsjfljhadxccctmctmaqqqoumlittgklejagkjghjoailambrsslj

The phrase is "mary had a little lamb":

sfdgg**ma**dd**ry**dkdkdkrrrsjflj**had**xccctmctm**a**qqqoum**litt**gk**le**jagkjghjoai**lambr**sslj

Now consider how hard finding meaning would be if the phrase you were looking for was in an unfamiliar language! It has been estimated that the string of Cs, Gs, Ts, and As that make up the human genome would fill 75,490 pages of standard-size type in a newspaper like *The New York Times*.

Two organizations led the effort to map the human genome: the Human Genome Project (HGP; a collection of 20 groups at not-for-profit institutes and universities) and Celera Genomics (a commercial biotechnology company). These two groups used different approaches to taking DNA apart, analyzing its base sequences, and reassembling the information. The HGP created a series of maps of finer and finer resolution (think

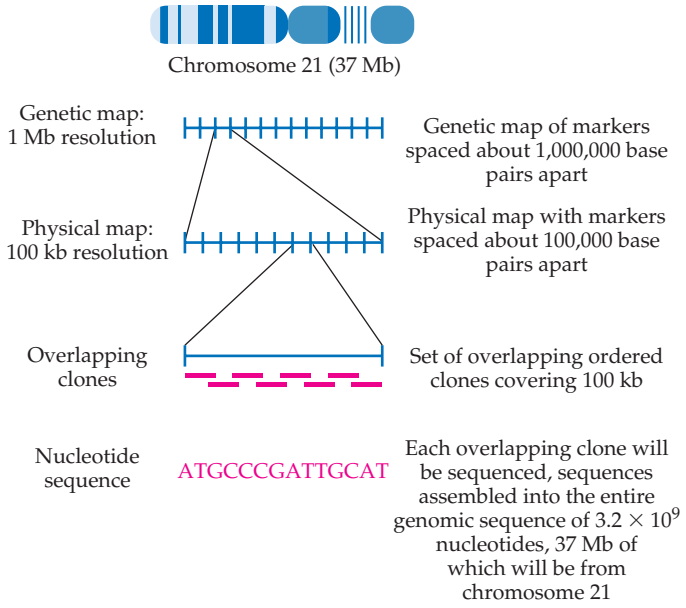
of a satellite map program such as Google Earth, where you can progress from a satellite photo of the United States to a map of your state to a map of the city where you live to the street you live on and, ultimately, to a picture of the house you live in). Celera followed a seemingly random approach in which they fragmented DNA and then relied on instrumental and computer-driven techniques to establish the sequence (think of breaking a piece of glass into thousands of shards and then piecing them back together). It was believed that data obtained via the combination of these two approaches would speed up the enormous task of sequencing the human genome.

In October 2004, the HGP reported that 99% of the gene-containing parts of the genome were sequenced and declared to be 99.999% accurate. Additionally, the mapped sequence reportedly identifies correctly almost all known genes (99.74% of them, to be exact). At a practical level, this "gold-standard" sequence data allows researchers to rely on highly accurate sequence information, priming new biomedical research.

The strategy utilized by the HGP for generating the complete map is shown in Figure 27.1. Pictured at the top is a type of chromosome drawing, known as an ideogram (pronounced *id-ee-uh-gram),* for human chromosome 21. The light- and dark-blue shadings represent the location of banding visible in electron micrographs, first discussed in Section 26.6. Chromosome 21 is the smallest human chromosome, with 37 million base pairs (abbreviated 37 Mb) and was the second chromosome to be mapped (chromosome 22 was the first).

The first step is to generate a *genetic map.* A genetic map shows the physical location of *markers,* identifiable DNA sequences (some within genes, some within noncoding DNA) that are known to be inherited. In the human genome, the markers were an average of 1 million nucleotides apart. This is known as a genetic map because the order and locations of the markers are established by genetic studies of inheritance in related individuals.

The next map, the *physical map,* refines the distance between markers to about 100,000 base pairs. The physical map includes markers identified by a variety of experimental methods, most notably the use of *restriction enzymes* (discussed in Section 27.4).



▸ Figure 27.1
Human Genome Project mapping strategy.

Clones Identical copies of organisms, cells, or DNA segments from a single ancestor.

To proceed to a map of finer resolution, a chromosome was cut into large segments and multiple copies of the segments were produced. The segment copies are called **clones,** a term that refers to identical copies of organisms, cells, or in this case, DNA segments. The overlapping clones, which covered the entire length of the chromosome, were arranged to produce the final level of the map (see Figure 27.1).

Each clone was cut into fragments containing 500 base pairs, and the order of bases in each fragment was determined. In the final step, all the different 500 base-pair sequences are assembled into a completed nucleotide map of the chromosome.

The approach taken by Celera Genomics was much bolder. In what has come to be known as their "shotgun approach," Celera broke the human genome into fragments without identifying the origin of any given fragment. The fragments were copied many times to generate many clones of each area of the genome; ultimately, they were cut into 500-base-long pieces and modified with fluorescently labeled bases that could be sequenced by high-speed machines. The resulting sequences were reassembled by identifying overlapping ends. At Celera, this monumental reassembly task was carried out using the world's largest nongovernmental supercomputing center.

CONCEPTS TO REVIEW In Chapter 18, we saw how electrophoresis is used as a technique to separate proteins by charge or size (Chemistry in Action "Protein Analysis by Electrophoresis"). Gel electrophoresis is also routinely used with DNA to separate DNA molecules by size.

PROBLEM 27.1

Decode the following sequence of letters to find an English phrase made entirely out of three-letter words. (Hint: First look for a word you recognize and then work forward and backward from there.)

uouothedtttrrfatnaedigopredsldjflsjfxxratponxbvateugfaqqthenqeutbadpagfratmeabrrx

27.2 DNA and Chromosomes

Learning Objective:

- Identify the genetic roles of telomeres, centromeres, exons and introns, and noncoding DNA.

Let us now examine the major regions and structural variations in the DNA folded into each chromosome. Understanding how DNA is structured should provide insight into the biotechnology revolution ushered in by the HGP.

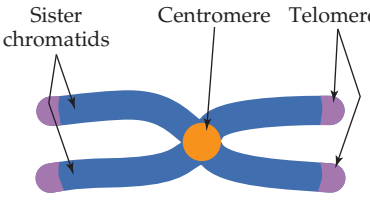
Telomeres and Centromeres

At both ends of every linear chromosome are specialized regions of DNA called **telomeres.** Each telomere in human DNA is a long, noncoding series of a repeating sequence of nucleotides, $(TTAGGG)_n$. Telomeres act as "endcaps," or "covers," protecting the ends of the chromosome from accidental damage. Telomeres also prevent the DNA ends from fusing to the DNA in other chromosomes or to DNA fragments.

Telomeres The ends of chromosomes; in humans, telomeres contain long series of repeating groups of nucleotides.

Another chromosomal region that contains large repetitive base sequences that do not code for proteins is the **centromere.** As the DNA in each chromosome is duplicated in preparation for cell division, the two copies remain joined together at a constricted point in the middle of the chromosome; this is the centromere. The duplicated chromosomes bound together at the centromere are known as *sister chromatids.*

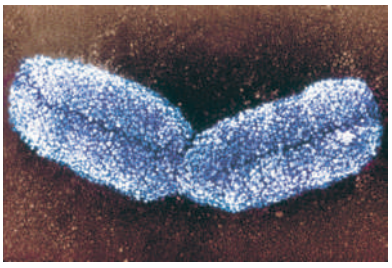
Centromeres The central regions of chromosomes.



Because of the repetitive nature of their sequences, neither telomeres nor centromeres were sequenced in the mapping projects described in Section 27.1.

Each new cell starts life with a long stretch of telomeric DNA on each of its chromosome ends, with over 1000 copies of the repeating group; in humans and other mammals this sequence is usually TTAGGG. Some of this repeating sequence is lost with each cell division, so that as the cell ages, the telomere gets shorter and shorter. A very short telomere is associated with the stage at which a cell stops dividing (known as *senescence).* Continuation of shortening beyond this stage is associated with DNA instability and cell death.

Telomerase is the enzyme responsible for adding telomeres to DNA. It is active during embryonic development. In adults, telomerase is only active in the germ cells destined to become egg and sperm. Under normal, healthy conditions, telomerase is not active in other adult cells (the *somatic* cells). There is widespread speculation that telomere-shortening plays a role in the natural progression of human aging. Some support for this concept comes from experiments with mice whose telomerase activity has been destroyed ("knocked out" in genetic research vernacular). These mice age prematurely, and if they become pregnant, their embryos do not survive.



▲ Top: A duplicated chromosome immediately prior to cell division showing the locations of the telomeres and the centromere. Bottom: Color-enhanced electron microscope image showing the constriction of the centromere during metaphase.

What would happen if telomerase remains active in a cell rather than declining in activity with age? With the length of its telomeres constantly being replenished by telomerase, the cell would not age and instead would continue to divide. Continuing division is one characteristic of cancer cells; in fact, the majority of cancer cells are known to contain active telomerase, which is thought to confer immortality on these

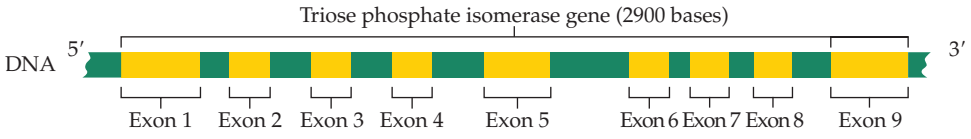
tumor cells. Where this activity stands in relation to the presence of cancer-causing genes and environmental factors is not yet understood because neither amplification nor mutation of the telomerase gene has been identified in tumors; it is simply active when normally it would not be. As a result, a causal role for telomerase in tumor formation has yet to be established. Current research suggests that it is the genes responsible for regulating telomerase expression that are altered in cancer cells. As you might suspect, there are ongoing experiments on the consequences of telomerase inactivation on cancer cells. Additionally, scientists are examining the role that telomerase might play in achieving a sort of human "immortality," at least from a cellular standpoint.

Noncoding DNA

In addition to the noncoding telomeres, centromeres, and introns along a chromosome, there are noncoding promoter sequences, which are regulatory regions of DNA that determine which of its genes are turned on. All of your cells (except red blood cells) contain all of your genes, but only the genes needed by any individual cell will be activated in that cell. As of 2014, researchers have confirmed the existence of approximately 19,000 protein-coding genes in the human genome (versus the 100,000 genes originally estimated to exist); this number keeps shrinking as more research is done. This current data suggests that only about 1.5% of all DNA in the human genome actually codes for protein. It is interesting to note that the human genome has much more noncoding DNA (once referred to as "junk" DNA) than do the genomes known for other organisms. This evidence raises the question of the role played by the vast amount of noncoding DNA present in our genome. The question arises out of the observation that genome size does not correlate with organismal complexity, with one example being that many plants have larger genomes than humans. Some scientists have suggested that the segments of noncoding DNA are needed to accommodate the folding of DNA within the nucleus, others think these segments may have played a role in evolution, while still others argue that the segments are functional but the functions are not yet understood. The function of noncoding DNA remains to be discovered; meanwhile the debate over its role continues to this day.

Genes

In learning about transcription (Section 26.8), you saw that the nucleotides of a single gene are not consecutive along a stretch of DNA but have coding (expressed) segments (the *exons*) that alternate with noncoding (interruption) segments (the *introns).* As an example, consider a "small," 2900-nucleotide sequence found in a much simpler organism (corn) that codes for the enzyme triose phosphate isomerase.



This gene consists of nine exons (in yellow) that account for 759 of the 2900 nucleotides (26%), with the eight introns (in green) accounting for the remaining bases. Now consider a more complex genome such as ours, where only 1–2% of genetic material is coding sequence. Take, for example, chromosome 22. It is one of the smaller human chromosomes and was the first to have all of its nonrepetitive DNA sequenced and mapped. Chromosome 22 is of medical interest because it carries genes known to be associated with the immune system as well as disorders such as congenital heart disease, schizophrenia, leukemia, various cancers, and many other genetically related conditions. The chromosome map identified 49 million bases containing approximately 693 genes, with an average of eight exons and seven introns per gene. The map also revealed several hundred previously unknown genes. With the signal (exon) to noise (intron) ratio being so low (meaning more noise to hide the signal) in the human genome, it will be challenging to completely identify all the coding sequences present.

27.3 Mutations and Polymorphisms

Learning Objectives:

- Describe a mutation and what can result from one.
- Define polymorphisms and SNPs, and explain the significance of the locations of SNPs.

The base-pairing mechanism of DNA replication and ribonucleic acid (RNA) transcription provides an extremely efficient and accurate method for preserving and using genetic information, but it is not perfect. Occasionally, an error occurs, resulting in the incorporation of an incorrect base at some point.

▲ An error in nucleic acid composition that occurs once in 3–4 million lobsters is responsible for the beautiful color of this crustacean.

An occasional error during the transcription of a messenger RNA (mRNA) molecule may not create a serious problem, since large numbers of mRNA molecules are continually being produced. An error that occurs perhaps one out of a million times would hardly be noticed in the presence of many correct mRNAs. If an error occurs during the replication of a DNA molecule, however, the consequences can be far more damaging. Each chromosome in a cell contains only *one* kind of DNA, and if this template is miscopied during replication, then the error is passed on when the cell divides.

An error in base sequence that is carried along during DNA replication is called a **mutation.** Mutation commonly refers to variations in DNA sequence found in a very small number of individuals of a species. Some mutations result from spontaneous and random events. Others are induced by exposure to a **mutagen**—an external agent that can cause a mutation. Viruses, chemicals, and ionizing radiation can all be mutagenic.

Mutation A rare DNA variant; an error in base sequence that is carried along in DNA replication and passed on to the offspring.

Mutagen A substance that causes mutations.

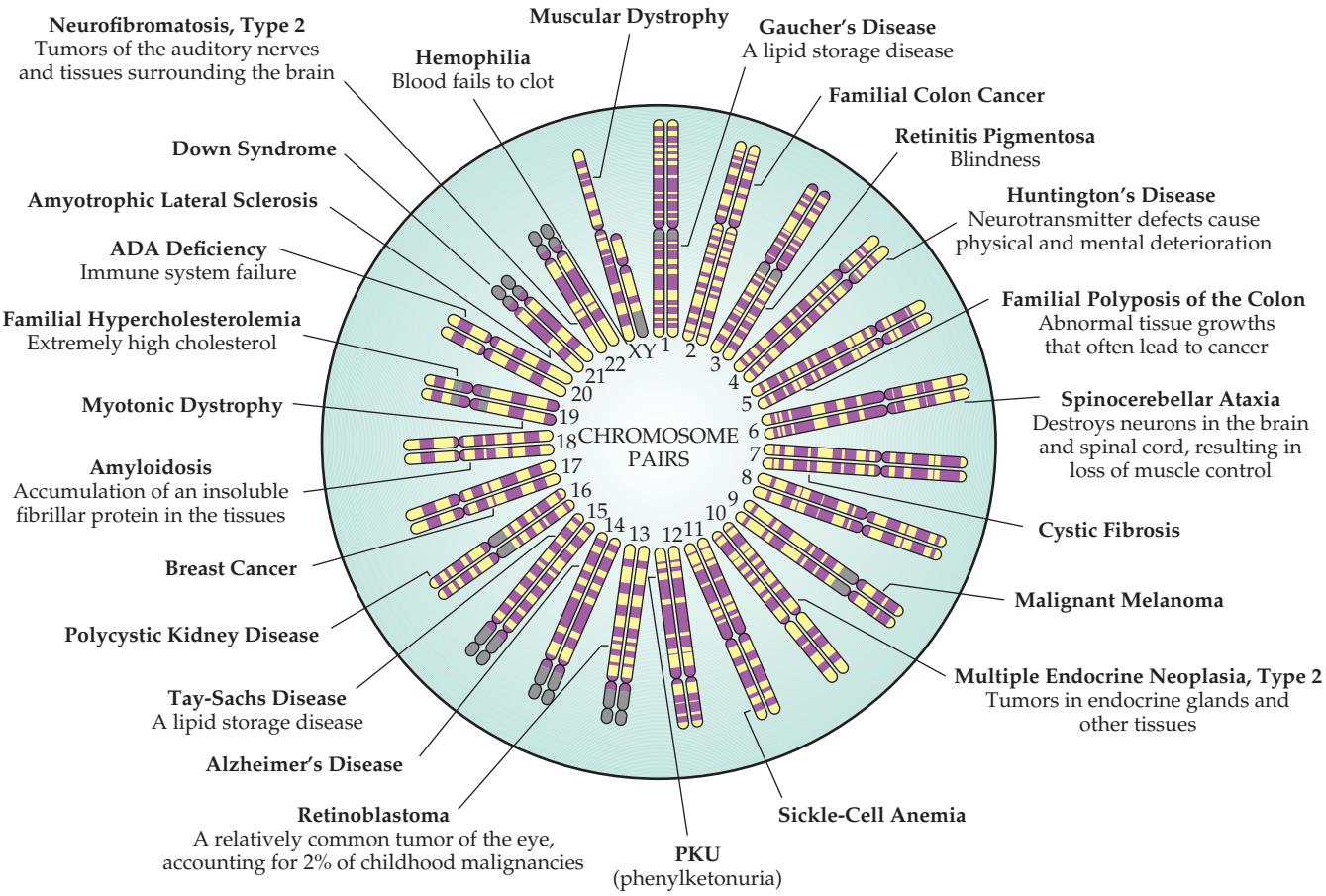
The biological effects of incorporating an incorrect amino acid into a protein range from negligible to catastrophic, depending on both the nature and location of the change. There are thousands of known human hereditary diseases. Some of the more common ones are listed in Table 27.1. Mutations, or sometimes the combination of several mutations, can also produce vulnerability to certain diseases, which may or may not develop in an individual.

Table 27.1 Some Common Hereditary Diseases, Their Causes, and Their Prevalence

Name	Nature and Cause of Defect	Prevalence in Population
Phenylketonuria (PKU)	Brain damage in infants caused by the defective enzyme phenylalanine hydroxylase	1 in 40,000
Albinism	Absence of skin pigment caused by the defective enzyme tyrosinase	1 in 20,000
Tay-Sachs disease	Mental retardation caused by a defect in production of the enzyme hexosaminidase A	1 in 6000 (Ashkenazi Jews); 1 in 100,000 (General population)
Cystic fibrosis	Bronchopulmonary, liver, and pancreatic obstructions by thickened mucus; defective gene and protein identified	1 in 3000
Sickle-cell anemia	Anemia and obstruction of blood flow caused by a defect in hemoglobin	1 in 185 (African Americans)

Polymorphisms are also variations in the nucleotide sequence of DNA within a given population. Most polymorphisms are simply differences in the DNA sequence between individuals due to geographical and ethnic differences and are part of the biodiversity exhibited by life on earth. While the vast majority of polymorphisms recorded have neither advantageous nor deleterious effects, some do and have been shown to give rise to various disease states. The locations of polymorphisms responsible for some inherited human diseases are shown in Figure 27.2.

Polymorphism A variation in DNA sequence within a population.



▲ **Figure 27.2**
A human chromosome map.
Regions on each chromosome that have been identified as responsible for inherited diseases are indicated.

HANDS-ON CHEMISTRY 27.1

Table 27.1 shows five common hereditary diseases, but there are many more. In this exercise you are going to choose one of the diseases listed next and research various aspects of it. This exercise may be assigned as a class project, if your instructor wishes, by assigning a group of students to each disease and having 5–10 minute classroom presentations on their findings. You will need an internet connection to do this activity.

a. Choose one of the following genetic disorders to study:

- Angelman syndrome
- Canavan disease
- Charcot–Marie–Tooth disease
- Cri du chat
- Klinefelter syndrome
- Prader–Willi syndrome
- Becker's muscular dystrophy
- Hemochromatosis

(If done as a class project, your instructor may choose which to assign.)

b. For the disorder you have chosen, determine the following:

1. History (including other names it may be known by)
2. Prevalence in the population of your country and worldwide
3. Genetic mutation and where the mutation is found
4. Symptoms and treatment
5. Prognosis
6. Current research, including gene therapy if applicable.

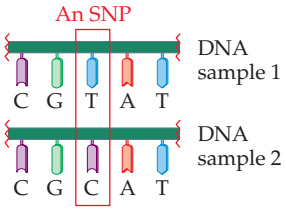
c. Finally, pretend you are a physician, a nurse, or a genetic counselor. Write a short paragraph outlining what and how you would tell the parents of a child who you had diagnosed with the disorder. Remember, the person you are going to talk to may have NEVER taken this class!

Single-Nucleotide Polymorphism and Disease

Single-nucleotide polymorphism (SNP) Common single base-pair variation in DNA.

The replacement of one nucleotide by another in the same location along the DNA sequence is known as a **single-nucleotide polymorphism** (**SNP,** pronounced "snip"). In other words, two different nucleotides at the same position along two defined stretches of DNA are SNPs. An SNP is expected to occur in at least 1% of a specific population and therefore provides a link to a genetic characteristic of that population.

The biological effects of SNPs can be wide ranging, from being negligible to being normal variations such as those in eye or hair color, to being genetic diseases. *SNPs are the most common source of variations between individual human beings.* Most genes carry one or more SNPs, and in different individuals most SNPs occur in the same location.



Imagine that the sequence A-T-G on the informational strand of DNA is replaced with the sequence A-C-G (an SNP); now the mRNA produced will have the codon sequence A-C-G rather than the intended sequence A-U-G. Because A-C-G codes for threonine, whereas A-U-G codes for methionine, threonine will be inserted into the corresponding protein during translation. Furthermore, every copy of the protein will have the same variation. The seriousness of the outcome depends on the function of the protein and the effect of the amino acid change on its structure and activity.

In addition to producing a change in the identity of an amino acid, an SNP might specify the same amino acid (e.g., changing GUU to GUC, both of which code for valine) or it might terminate protein synthesis by introducing a stop codon (like changing CGA to UGA).

Industrial and academic scientists are compiling a catalog of SNPs. Their frequency is roughly one SNP for about every 300 nucleotides, with many of them in coding regions. Knowing their exact locations may one day help doctors to predict an individual's risk of developing a disease.

We have described the single amino acid change that results in sickle-cell anemia. It took years of research to identify the SNP responsible for that disease. Had a computerized catalog of SNPs been available at the time, it might have been found in a few hours. Another known SNP is associated with the risk of developing Alzheimer's disease. Not all SNPs create susceptibility to diseases; for example, there is also one that imparts a resistance to human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS). Most SNPs have neither advantageous nor deleterious effects on the organism.

The mutation leading to sickle-cell anemia is described in the Chemistry in Action "What Is Sickle-Cell Anemia?" found in Chapter 18.

The SNP catalog, although far from complete, has been valuable from the start. It has been used to locate SNPs responsible for 30 abnormal conditions, including total color blindness, one type of epilepsy, and susceptibility to the development of breast cancer. For example, examination of the DNA from prostate cancer patients showed that cataloged SNPs occur in four combinations in these people. The next step is to hunt down the role of each of those four genetic variations in the disease. It is hoped that this information will inspire the development of new treatments for diseases. As of June 2015, the SNP catalog maintained by the National Human Genome Research Institute contains over 147 *million* SNP entries and correlation to diseases is growing at an ever increasing pace (one estimate is over 14,000 diseases have been correlated to SNPs).

The cataloging of SNPs has ushered in the era of genetic medicine. Ultimately, the SNP catalog may allow physicians to predict for an individual the potential age at which inherited diseases will become active, their severity, and their reactions to various types of treatment. The therapeutic course will be designed to meet the distinctive genomic profile of the person.

CHEMISTRY IN ACTION

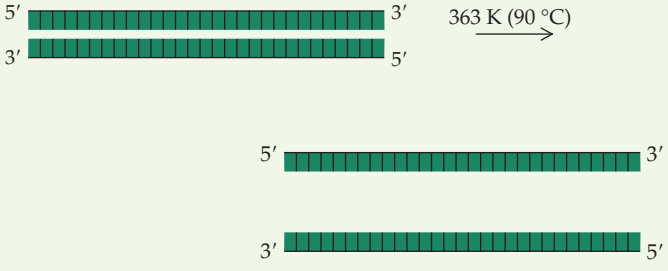
The Polymerase Chain Reaction

Before the 1980s, studying DNA involved the frustration of working with very small, hard-to-obtain samples. Everyone wished there was a way to copy DNA, to make millions of copies of a sample. As a result, scientists focused on making this wish a reality. The outcome was the development and automation of the *polymerase chain reaction (PCR),* which today can be carried out easily in any molecular biology lab. PCR is so common and so simple a technique that it is routinely taught and carried out in undergraduate lab courses.

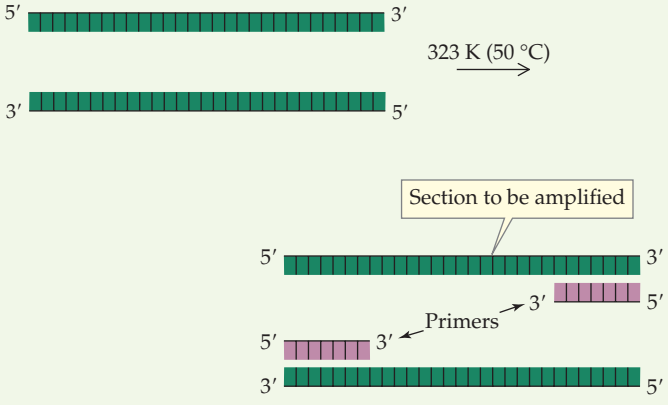
The goal of PCR is to produce many copies of a specific segment of DNA. The DNA might be part of a genome study, it might be from a crime scene or a fossil, or it might be from a specimen preserved as a medical record. The raw materials required for the reaction are a DNA sample that contains the nucleotide sequence to be amplified, *primers* (short synthetic oligonucleotides with bases complementary to the sequences flanking the sequence of interest), the deoxyribonucleoside triphosphates that carry the four DNA bases, and a DNA polymerase enzyme that will create a copy of the DNA between the primers.

The reaction is carried out in three steps:

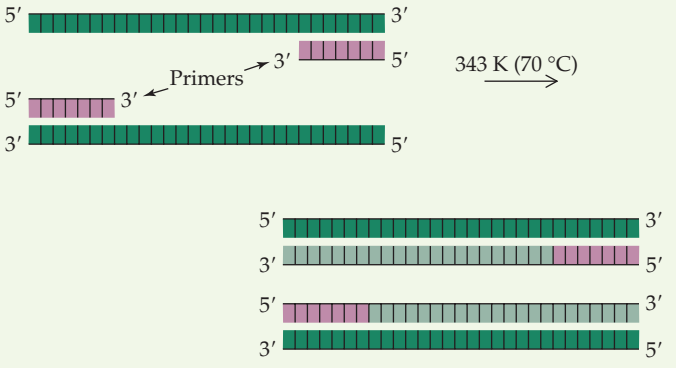
STEP 1: Heating of the DNA sample to cause the helix to unravel into single strands:



STEP 2: Addition of primers complementary to the DNA flanking the single-stranded DNA sequence to be amplified. It is necessary to create double-stranded DNA at the point where copying is to start, because DNA polymerase needs a free existing 3′ end to which it adds nucleotides. The primers indicate this starting point:



STEP 3: Extension of the primers by DNA polymerase to create double-stranded DNA identical to the original. The DNA polymerase adds nucleotides to the ends of the primers so that the new DNA segment includes the primer DNA:



The reactants are combined in a closed container and the temperature cycled from about 363 K (90 °C) for step 1, to about 323 K (50 °C) for step 2, and to about 343 K (70 °C) for step 3. The temperature cycle requires only a few minutes and can be repeated over and over again for the same mixture. The first cycle produces two molecules of DNA; the second produces four molecules; and so on, with doubling at each cycle. Just 25 amplification cycles yield over 30 million copies of the original DNA segment.

Automation of the PCR was made possible by the discovery of a heat-stable polymerase *(Taq polymerase)* isolated from a bacterium that lives in hot springs. Because the enzyme survives the temperature needed for separating the DNA strands, it is not necessary to add fresh enzymes for each three-step cycle.

CIA Problem 27.1 What is the purpose of the PCR?

CIA Problem 27.2 Briefly describe how the PCR works.

CIA Problem 27.3 In automated PCR experiments, why is *Taq* polymerase used instead of the DNA polymerase found in humans?

Worked Example 27.1 Determining the Effect of Changes in DNA on Proteins

The severity of a mutation in a DNA sequence that changes a single amino acid in a protein depends on the type of amino acid replaced and the nature of the new amino acid. (a) What kind of change would have little effect on the protein containing the alternative amino acid? (b) What kind of change could have a major effect on the protein that contains the alternative amino acid? Give an example of each type of mutation.

ANALYSIS The result of exchanging one amino acid for another depends on the change in the nature of the amino acid side chains. To speculate on the result of such a change requires us to think again about the structure of the side chains, which are shown in Table 18.3. The question to consider is whether the mutation introduces an amino acid with such a different side chain character that it is likely to alter the structure and function of the resulting protein.

SOLUTION

(a) Exchange of an amino acid with a small nonpolar side chain for another with the same type of side chain (e.g., glycine for alanine) or exchange of amino acids with very similar side chains (say, serine for threonine) might have little effect.

(b) Conversion of an amino acid with a nonpolar side chain to one with a polar, acidic, or basic side chain could have a major effect because the side-chain interactions that affect protein folding may change (see Figure 18.4). Some examples of this type include exchanging threonine, glutamate, or lysine for isoleucine. In hemoglobin, a single replacement of glutamic acid (a hydrophilic, acidic amino acid) with a valine (a hydrophobic, neutral amino acid) leads to sickle-cell anemia.

KEY CONCEPT PROBLEM 27.2

Consider that an SNP alters the base sequence in an mRNA codon by changing UGU to UGG (see Table 26.3). Speculate on the significance of this change.

27.4 Recombinant DNA

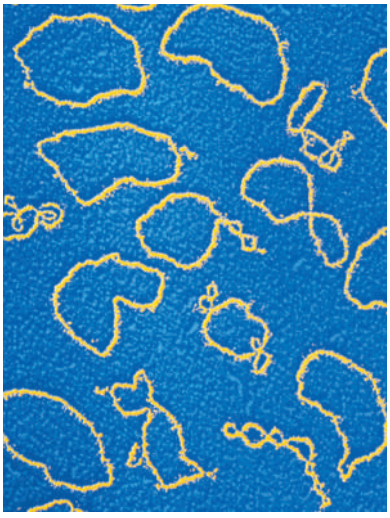
Learning Objective:

- Describe recombinant DNA and its uses.

In this section, we describe a technique for manipulating, altering, and reproducing pieces of DNA. The technique requires the creation of **recombinant DNA**—DNA that joins two or more DNA segments not found together in nature. Progress in all aspects of genomics has built upon information gained in the application of recombinant DNA. The two other techniques that play major roles in DNA studies are the PCR and electrophoresis. PCR is a method by which large quantities of identical pieces of DNA can be synthesized (see the Chemistry in Action "The Polymerase Chain Reaction"). Electrophoresis, which can be carried out simultaneously on large numbers of samples, separates proteins or DNA fragments according to their size (see the Chemistry in Action "Protein Analysis by Electrophoresis" in Chapter 18).

Recombinant DNA DNA that contains two or more DNA segments not found together in nature.

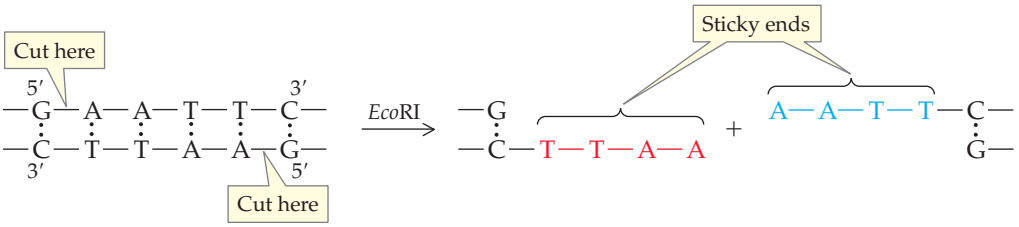
Using recombinant DNA technology, it is possible to cut a gene out of one organism and splice it into (*recombine* it with) the DNA of a second organism. Bacteria provide excellent hosts for recombinant DNA. Bacterial cells, unlike the cells of higher organisms, contain part of their DNA in small circular pieces called *plasmids,* each of which carries just a few genes. Plasmids are extremely easy to isolate, several copies of each plasmid may be present in a cell, and each plasmid replicates through the normal base-pairing pathway. The ease of isolating and manipulating plasmids plus the rapid replication of bacteria create ideal conditions for production of recombinant DNA and the proteins whose synthesis it directs in bacteria.



▲ Plasmids from the bacterium *Escherichia coli,* hosts for recombinant DNA.

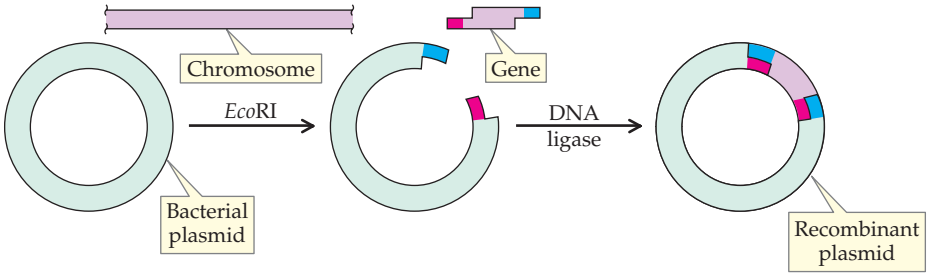
To prepare a plasmid for insertion of a foreign gene, the plasmid is cut open with a bacterial enzyme, known as a *restriction endonuclease* or *restriction enzyme,* that recognizes a specific sequence in a DNA molecule and cleaves between the same two nucleotides in that sequence. For example, the restriction endonuclease *Eco*RI recognizes the sequence G-A-A-T-T-C and cuts between G and A. This restriction enzyme makes its cut at the same spot in the sequence of both strands of the double-stranded DNA when read

in the same 5′ to 3′ direction. As a result, the cut is offset so that both DNA strands are left with a few unpaired bases on each end. These groups of unpaired bases are known as *sticky ends* because they are available to match up with complementary base sequences.



Recombinant DNA is produced by cutting the two DNA segments to be combined with the same restriction endonuclease. The result is DNA fragments with sticky ends that are complementary to each other.

Consider a gene fragment that has been cut from human DNA and is to be inserted into a plasmid. The gene and the plasmid are both cut with the same enzyme, one that produces sticky ends. Thus, the sticky ends on the gene fragment are complementary to the sticky ends on the opened plasmid. The two are mixed in the presence of DNA ligase, an enzyme that joins them together by re-forming their phosphodiester bonds and reconstitutes the now-altered plasmid.



Once the altered plasmid is made, it is inserted back into a bacterial cell, where the normal processes of transcription and translation take place to synthesize the protein encoded by the inserted gene. Since bacteria multiply rapidly, there are soon a large number of them, all containing the recombinant DNA and all manufacturing the protein encoded by the recombinant DNA. Huge numbers of the bacteria can be put to work as a protein factory.

As ideal as this strategy sounds, there are tremendous technical hurdles that have to be overcome before a protein manufactured in this way can be used commercially. One hurdle is getting the recombinant plasmid back into a bacterium. Another is finding a host organism that does posttranslationally modify the protein you are trying to make; for example, yeast cells are known to attach carbohydrates to various amino acids in a protein, rendering the protein inactive. The most serious hurdle of all is isolation of the protein of interest from unwanted endotoxins. *Endotoxins* are potentially toxic natural compounds (usually structural components released when bacteria are lysed) found inside the host organism. Because the presence of even small amounts of endotoxins can lead to serious inflammatory responses, rigorous purification and screening protocols are necessary before the protein can be used in humans.

Despite the aforementioned obstacles, proteins manufactured in this manner have already reached the marketplace, and many more are on the way. Human insulin was the first such protein to become available. Others now include human growth hormone used for children who would otherwise be abnormally small and blood-clotting factors for hemophiliacs. A major advantage of this technology is that large amounts of these proteins can be made, thus allowing their practical therapeutic use.

PROBLEM 27.3

A restriction enzyme known as *Bgl*II cuts DNA in the place marked below.

5′–A–//–G–A–T–C–T–3′

Draw the complementary 3′ to 5′ strand and show where it is cut by the same enzyme.

PROBLEM 27.4

A restriction enzyme known as *EcoR*I cuts DNA in the place marked below.

5′–G–/–A–A–T–T–C–3′

Draw the complementary 3′ to 5′ strand and show where it is cut by the same enzyme.

PROBLEM 27.5

Are the following base sequences "sticky" (complementary) or not? All sequences are written 5′ to 3′.

(a) A-C-G-G-A and T-G-C-C-T **(b)** G-T-G-A-C and C-A-T-G-G

(c) G-T-A-T-A and A-C-G-C-G

27.5 Genomics: Using What We Know

Learning Objective:

- Identify the possible applications of genomic mapping.

To see where genomics may be headed, Table 27.2 provides descriptions of some of its applications. These descriptions are not quite definitions; many of these fields are so new that their scope is viewed differently by different individuals. We stand at the beginning of a revolution. Let us examine in a little more depth three developments that have arisen from this work.

1. Genetically Modified Plants and Animals

The development of new varieties of plants and animals has been proceeding for centuries as the result of natural accidents and occasional success in the hybridization of known varieties. Now, the mapping and study of plant and animal genomes can greatly accelerate our ability to generate crop plants and farm animals with desirable characteristics and lacking undesirable ones.

Some genetically modified crops have already been planted in large quantities in the United States. Each year millions of tons of corn are destroyed by a caterpillar (the European corn borer) that does its damage deep inside the corn stalk and out of reach of pesticides. To solve this problem, a bacterial gene (from *Bacillus thuringiensis,* Bt) has been transplanted into corn. The gene causes the corn to produce a toxin that kills the caterpillars. In 2000, one-quarter of all corn planted in the United States was Bt corn. Tests are under way with genetically modified coffee beans that are caffeine-free, potatoes that absorb less fat when they are fried, and "golden rice," a yellow rice that provides the vitamin A desperately needed in poor populations where insufficient vitamin A causes death and blindness.

▲ "Golden rice" has been genetically modified to provide vitamin A.

Will genetically modified plants and animals intermingle with natural varieties and cause harm to them? Should food labels state whether the food contains genetically modified ingredients? Might unrecognized harmful substances enter the food supply? These are hotly debated questions and have led to the establishment of the Non-GMO Project, where the GMO stands for genetically modified organism. The goal of this project is to offer consumers a non-GMO choice for organic and natural products that are produced without genetic engineering or recombinant DNA technologies. Many foods found in stores are labeled "Non-GMO."

Genetic modifications can also be used to produce previously unseen beauty. Consider the blue rose, a flower that is currently produced by dyeing white roses. Suntory Limited, in a joint venture with Florigene, has recently been able to successfully implant into roses a gene from petunias that leads to the synthesis of blue pigments; these roses are currently being grown in test batches in Japan. Even more exciting is the expectation that the introduction of blue pigments into roses will lead to an explosion in the variety of possible rose colors available to the average consumer.

Table 27.2 Genomics-Related Fields of Study

Biotechnology
A collective term for the application of biological and biochemical research to the development of products that improve the health of humans, other animals, and plants.
Bioinformatics
The use of computers to manage and interpret genomic information and to make predictions about biological systems. Applications of bioinformatics include studies of individual genes and their functions, drug design, and drug development.
Functional genomics
Use of genome sequences to solve biological problems.
Comparative genomics
Comparison of the genome sequences of different organisms to discover regions with similar functions and perhaps similar evolutionary origins.
Proteomics
Study of the complete set of proteins coded for by a genome or synthesized within a given type of cell, including the quest for an understanding of the role of each protein in healthy or diseased conditions. This understanding has potential application in drug design and is being pursued by more than one commercial organization.
Pharmacogenomics
The genetic basis of responses to drug treatment. Goals include the design of more effective drugs and an understanding of why certain drugs work in some patients but not in others.
Pharmacogenetics
The matching of drugs to individuals based on the content of their personal genome in order to avoid administration of drugs that are ineffective or toxic and focus on drugs that are most effective for that individual.
Toxicogenomics
A newly developing application that combines genomics and bioinformatics in studying how toxic agents affect genes and in screening possibly harmful agents.
Genetic engineering
Alteration of the genetic material of a cell or an organism. The goals may be to make the organism produce new substances or perform new functions. Examples are introduction of a gene that causes bacteria to produce a desired protein or allows a crop plant to withstand the effects of a pesticide that repels harmful insects.
Gene therapy
Alteration of an individual's genetic makeup with the goal of curing or preventing a disease.
Bioethics
The ethical implications of how knowledge of the human genome is used.

2. Gene Therapy

Gene therapy, to put it simply, is the use of DNA to treat disease. It is based on the premise that a disease-causing gene within an individual's cells can be corrected or replaced by inserting a functional, healthy gene into the cells. The most clear-cut expectations for gene therapy lie in treating *monogenic* diseases, those that result from defects in a single gene.

The focus has been on using nonpathogenic viruses as *vectors,* the agents that deliver therapeutic quantities of DNA directly into cell nuclei. The expectation was that this method could result in lifelong elimination of an inherited disease, and many studies have been undertaken. Unfortunately, expectations remain greater than achievements thus far. Investigations into the direct injection of "naked DNA" have begun, with one early report of success in encouraging blood vessel growth in patients with inadequate blood supply to their hearts. The Food and Drug Administration (FDA) has, as of 2014, not yet approved any human gene therapy product for sale, although over 2000 clinical trials are currently approved or under way. While currently gene therapy is still experimental, vigorous research into this area continues as new approaches continue to be examined.

3. Personal Genomic Survey

One outcome of the genome mapping project is that the cost of genetic mapping and testing has decreased dramatically, from about $1000 in 2007 to around $100 in 2014, making it available to the average consumer. Suppose that prior to diagnosis and treatment for a health problem that your entire genome could be surveyed. It is possible that the choice of drugs could be directed toward those that would be most effective for you. It is no secret that not everyone reacts in the same manner to a given medication. Perhaps a patient lacks an enzyme needed for a drug's metabolism, or has a monogenic defect, a flaw in a single gene that is the direct cause of the disease. Such a patient might, at some time in the future, be a candidate for gene therapy.

In cancer therapy, there may be advantages in understanding the genetic differences between a patient's normal cells and tumor cells. Such knowledge could assist in chemotherapy, where the goal is the use of an agent that kills the tumor cells but does the least possible amount of harm to noncancerous cells.

Another possible application is the genetic screening of infants. The immediate use of gene therapy might eliminate the threat of a monogenically based disease, or perhaps a lifestyle adjustment would be in order for an individual with one or more SNPs that predict a susceptibility to heart disease, diabetes, or some other disease that results from combinations of genetic and environmental influences. In addition, an individual's genetic map would be available for the rest of his or her life; they may even carry a wallet card encoded with their genetic information. With this knowledge, however, also come ethical dilemmas that have made this use of genomics a hotly debated topic.

Bioethics

Finally, one area of major concern that has arisen from the genomics revolution is that of the ethical and social implications this groundbreaking work has brought to the fore. The ELSI program of the National Human Genome Research Institute was formed to examine and comment on these concerns. ELSI deals with the Ethical, Legal, and Social Implications of human genetic research. The scope of ELSI is broad and thought-provoking. It deals with many questions such as the following:

- Who should have access to personal genetic information and how will it be used?
- Who should own and control genetic information?
- Should genetic testing be performed when no treatment is available?
- Are disabilities diseases? Do they need to be cured or prevented?
- Preliminary attempts at gene therapy are exorbitantly expensive. Who will have access to these therapies? Who will pay for their use?
- Should we re-engineer the genes we pass on to our children?

If you are interested in the ELSI program, their web page is an excellent resource (www.genome.gov/ELSI).

PROBLEM 27.6

Classify the following activities according to the fields of study listed in Table 27.2.

(a) Identification of genes that perform identical functions in mice and humans.

(b) Creation of a variety of wheat that will not be harmed by an herbicide that kills weeds that threaten wheat crops.

(c) Screening of an individual's genome to choose the most appropriate pain-killing medication for that person.

(d) Computer analysis of base-sequence information from groups of people with and without a given disease to discover where the disease-causing polymorphism lies.

CHEMISTRY IN ACTION

DNA Fingerprinting

A crime scene does not always yield fingerprints. It may, instead, yield samples of blood, semen, or bits of hair. As we learned at the beginning of the chapter, DNA analysis of such samples provides a new kind of "fingerprinting" for identifying criminals or proving suspects innocent.

DNA fingerprinting relies on finding variations between two or more DNA samples; for example, DNA isolated from a crime scene can be examined to determine if its variations match those of a suspect or a victim. The naturally occurring variability of the base sequence in DNA is like a fingerprint. It is the same in all cells from a given individual and is sufficiently different from that of other individuals that it can be used for identification.

In the human genome, there are regions of noncoding DNA that contain repeating nucleotide sequences. The repetitive patterns used in DNA fingerprinting are known as *variable number tandem repeats (VNTRs).* As the name suggests, a VNTR is a short DNA sequence that is repeated multiple times in a tandem array (end to end to end). The key feature that makes VNTRs useful in fingerprinting is that *for any given VNTR, the number of copies of the repeated sequence varies between individuals.* One person may have a sequence repeated 15 times, whereas another may have the sequence repeated 40 times. For statistical significance, lab technicians examine several of the known VNTRs across multiple chromosomes to create a DNA fingerprint. The probability of a DNA-fingerprint match with someone other than the correct individual is estimated at 1 in 1.5 billion.

There are two common techniques used for DNA fingerprinting today: the restriction fragment length polymorphism (RFLP) approach and the PCR method.

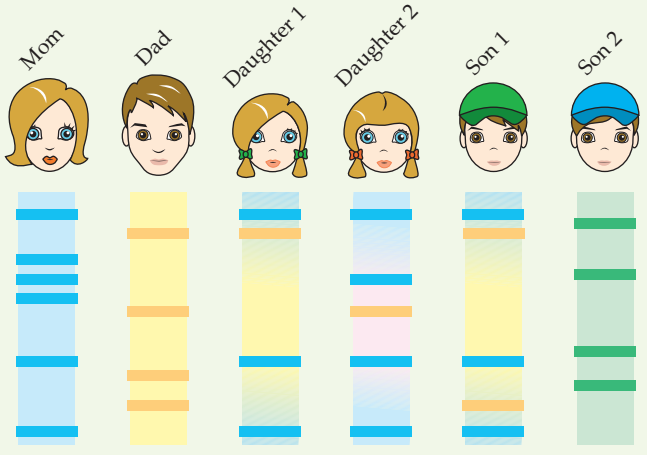
RFLP relies on use of a restriction endonuclease (an enzyme used to cut DNA) that recognizes and cuts sequences on either side of a given VNTR. The general procedure is as follows:

- Digest the DNA sample with the restriction endonuclease.
- Separate the resulting DNA fragments according to their size by gel electrophoresis.
- Transfer the fragments to a nylon membrane (a *blotting* technique).
- Treat the blot with a radioactive DNA probe complementary to the repeating VNTR sequence, so that the probe binds the fragment containing the VNTR sequence.
- Identify the locations of the now-radioactive fragments by exposing an X-ray film to the blot. (The film result of this procedure is known as an *autoradiogram.*)

An autoradiogram resembles a bar code, with dark bands arrayed in order of increasing molecular size of the DNA fragments. To compare the DNA of different individuals, the DNA samples are run in parallel columns on the same electrophoresis gel. In this way, the comparison is validated by having been run under identical conditions. While this method is very accurate, it requires a significant amount of DNA and can take two to four weeks to carry out; it is used primarily for genetic screening.

A more recent method for DNA fingerprinting involves the use of PCR (see the Chemistry in Action "The Polymerase Chain Reaction," p. 848). In this method, one can use primers directed toward regions of the DNA that are known to contain variations; these can then be copied using PCR. This amplification process is repeated about 30 times (about four minutes per cycle) so that in two hours more than 1 billion copies are produced. These fragments can then be separated according to size by gel electrophoresis, stained using a blue dye that binds to DNA, and compared against other samples. Unlike the RFLP method, the PCR system, from amplification to analysis, can be carried out in about 24 hours. It can be performed on small amounts of DNA, and even on DNA that has begun to degrade, and is successful with almost every sample. This method has become the primary technique used in crime scene forensic analysis.

How useful is DNA fingerprinting? The following illustration shows hypothetical DNA-fingerprint patterns of six members of a family, where three of the children share the same mother and father and the fourth has been adopted. As you can see, even individuals in the same family will have distinguishably different DNA fingerprints; only identical twins have identical DNA fingerprints. There are always some similarities in the DNA patterns of offspring and their parents, making such fingerprints valuable in proving or disproving paternity.



CIA Problem 27.4 In 2011, the population of the world was estimated to be about 7 billion. How many people in the world could theoretically have the same DNA fingerprint?

CIA Problem 27.5 State the five basic steps of DNA fingerprinting using the RFLP method. Why do you think the PCR method is of more use in crime scene investigations?

CIA Problem 27.6 What is a VNTR? What is its significance for DNA fingerprinting?

SUMMARY REVISITING THE CHAPTER GOALS

- **Describe how a genome is mapped.** The HGP, an international consortium of not-for-profit institutions, along with Celera Genomics, a for-profit company, have working drafts of the human genome. With the exception of large areas of repetitive DNA, the DNA base sequences of all chromosomes have been examined. The HGP utilized a series of progressively more detailed maps to create a collection of DNA fragments with known location. Celera began by randomly fragmenting all of the DNA without first placing it within the framework of a map. In both groups the fragments were cloned, labeled, ordered, and the individual sequences assembled by computers. The results of the two projects are generally supportive of each other. There are about 3 billion base pairs and about 19,000 genes in the human genome. The bulk of the genome consists of noncoding, repetitive sequences. About 200 of the human genes are identical to those in bacteria *(see Problems 7, 8, and 14–20).*
- **Identify the genetic roles of telomeres, centromeres, exons and introns, and noncoding DNA.** Telomeres, which fall at the ends of chromosomes, are regions of noncoding, repetitive DNA that protect the ends from accidental changes. At each cell division, the telomeres are shortened, with significant shortening associated with senescence and death of the cell. Telomerase, the enzyme that lengthens telomeres, is typically inactivated in adult cells but can become reactivated in cancer cells. Centromeres are the constricted regions of chromosomes that form during cell division and also carry noncoding DNA. Exons are the protein-coding regions of DNA and the noncoding regions separating the exons that make up a gene are the introns. The exons, when strung together, make up the genes that direct protein synthesis. The repetitive, noncoding segments of DNA are of either no function or unknown function *(see Problems 9 and 21–25).*
- **Describe a mutation and what can result from one.** A mutation is an error in the base sequence of DNA that is passed along during replication. Mutations arise by random error during replication but may also be caused by ionizing radiation, viruses, or chemical agents (*mutagens*). Mutations can cause inherited diseases and increase the tendency to acquire others *(see Problems 10, 26, 27, 32–35, and 47–52).*
- **Define polymorphisms and SNPs, and explain the significance of the locations of SNPs.** A polymorphism is a variation in DNA that is found within a population. An SNP is the replacement of one nucleotide by another. The result might be the replacement of one amino acid by another in a protein, no change because the new codon specifies the same amino acid, or the introduction of a "stop codon." Many inherited diseases are known to be caused by SNPs, but they can also be beneficial or neutral. Understanding the location and effect of SNPs is expected to lead to new therapies *(see Problems 28–32, 50, and 52).*
- **Describe recombinant DNA and its uses.** Recombinant DNA is produced by joining DNA segments that do not normally occur together. A gene from one organism is inserted into the DNA of another organism. Recombinant DNA techniques can be used to create large quantities of a particular protein. The gene of interest is inserted into bacterial plasmids (small, extrachromosomal circular DNA). Bacteria carrying these plasmids then serve as factories for the synthesis of large quantities of the encoded protein *(see Problems 11 and 36–41).*
- **Identify the possible applications of genomic mapping.** Mapping the human genome holds major promise for applications in health and medicine. Drugs can be precisely chosen based on a patient's own DNA, thereby avoiding drugs that are ineffective or toxic for that individual. Perhaps one day inherited diseases will be prevented or cured by gene therapy. By genetic modification of crop plants and farm animals, the productivity, marketability, and health benefits of these products can be enhanced. Progress in each of these areas is bound to be accompanied by controversy and ethical dilemmas *(see Problems 12 and 42–46).*

KEY WORDS

Clones, *p. 842*
Centromeres, *p. 843*
Genomics, *p. 841*
Mutagen, *p. 845*
Mutation, *p. 845*
Polymorphism, *p. 845*
Recombinant DNA, *p. 849*
Single-nucleotide polymorphism (SNP), *p. 847*
Telomeres, *p. 843*

UNDERSTANDING KEY CONCEPTS

27.7 What steps are necessary in the mapping of the human genome, as outlined by the Human Genome Project?

27.8 Clearly, all humans have variations in their DNA sequences. How is it possible to sequence the human genome if every individual is unique? How was the diversity of the human genome addressed?

27.9 List the four types of noncoding DNA (see Section 27.2). Give the function of each, if it is known.

27.10 In general, what are the differences between mutations and polymorphisms?

27.11 What is recombinant DNA? How can it be used to produce human proteins in bacteria?

27.12 Identify some major potential benefits of the applications of genomics and some major negative outcomes.

ADDITIONAL PROBLEMS

THE HUMAN GENOME MAP (SECTION 27.1)

27.13 What is genomics?

27.14 How did the private corporation Celera Genomics approach the sequencing of the human genome? What was the advantage of this approach?

27.15 How did the competition that developed between the groups developing the human genome map benefit the HGP?

27.16 Approximately what portion of the human genome is composed of repeat sequences?

27.17 Approximately how many base pairs were identified in the human genome working drafts?

27.18 Among the results of the genome working drafts, (a) were any human genes found to be identical to genes in bacteria and (b) what was learned about the number of proteins produced by a given gene?

27.19 What is the most surprising result found thus far in the human genome studies?

27.20 You may have heard of Dolly, the cloned sheep grown from an embryo created in a laboratory. But in the context of DNA mapping, what are clones and what essential role do they play?

CHROMOSOMES, MUTATIONS, AND POLYMORPHISMS (SECTIONS 27.2 AND 27.3)

27.21 What is thought to be the primary purpose of telomeres?

27.22 How is the age of a cell predicted by its telomeric sequences?

27.23 What is the role of the enzyme telomerase? In what kind of cell is it normally most active and most inactive?

27.24 What is the centromere?

27.25 What is a mutagen?

27.26 Why is a mutation of a base in a DNA sequence much more serious than a mutation in a transcribed mRNA sequence?

27.27 What are the two general and common ways that mutations occur in a DNA sequence?

27.28 What is an SNP?

27.29 How are SNPs linked to traits in individual human beings?

27.30 List some potential biological effects of SNPs.

27.31 What would be a medical advantage of having a catalog of SNPs?

27.32 Does a single base-pair substitution in a strand of DNA always result in a new amino acid in the protein coded for by that gene? Why or why not?

27.33 What determines the significance of a change in the identity of an amino acid in a protein?

27.34 Compare the severity of DNA mutations that produce the following changes in mRNA codons (Consult Table 26.3 for help):

(a) UCA to UCG **(b)** UAA to UAU

27.35 Compare the severity of DNA mutations that produce the following changes in mRNA codons:

(a) GCU to GCC **(b)** ACU to AUU

RECOMBINANT DNA (SECTION 27.4)

27.36 Why are bacteria excellent hosts for recombinant DNA experiments?

27.37 What is an advantage of using recombinant DNA to make proteins such as insulin, human growth hormone, or blood-clotting factors?

27.38 How can DNA fragments be separated by size?

27.39 In the formation of recombinant DNA, a restriction endonuclease cuts a bacterial plasmid to give sticky ends. The DNA segments that are to be added to the plasmid are cleaved with the same restriction endonuclease. What are sticky ends and why is it important that the target DNA and the plasmid it will be incorporated into have complementary sticky ends?

27.40 Give the sequence of unpaired bases that would be sticky with the following sequences:

(a) GGTAC **(b)** ACCCA **(c)** GTGTC

27.41 Are the following base sequences sticky or not sticky? Each piece is written 5′ to 3′.

(a) TTAGC and GCTAA

(b) CGTACG and CCTTCG

USING GENOMICS (SECTION 27.5)

27.42 What is pharmacogenomics and how might it benefit patient care?

27.43 Genetic engineering and gene therapy are similar fields within genomics. What do they have in common and what distinguishes them?

27.44 Provide two examples of genetically engineered crops that are improvements over their predecessors.

27.45 Imagine that you become a parent in an age when a full genetic workup is available for every baby. What advantages and disadvantages might there be to having this information?

27.46 Why is the field of bioethics so important in genomics?

CONCEPTUAL PROBLEMS

27.47 What is a monogenic disease?

27.48 What is the role of a vector in gene therapy?

27.49 Write the base sequence that would be sticky with the sequence T-A-T-G-A-C-T.

27.50 If the DNA sequence A-T-T-G-G-C-C-T-A on an informational strand mutated and became A-C-T-G-G-C-C-T-A, what effect would the mutation have on the sequence of the protein produced?

27.51 What is a restriction endonuclease?

27.52 In the DNA of what kind of cell must a mutation occur for the genetic change to be passed down to future generations?

GROUP PROBLEMS

27.53 Discuss the advantages and drawbacks to having your own personal genomic map. Have half the members of your group take the pro side and the others take the con side of the discussion.

27.54 One of the most actively pursued areas in genomics is that of gene therapy. Have each member of your group research and then discuss the current state of research and development into gene therapy for a disease of their choosing. Some suggestions are Parkinson's disease, Huntington's disease, prostate and pancreatic cancers, and muscular dystrophy.

27.55 Do a keyword search for "unlocking life's code" and see if you can find a timeline for the human genome. Have each member of your group choose a decade and discuss the important strides made during it.

28

Chemical Messengers: Hormones, Neurotransmitters, and Drugs

CONTENTS

CONCEPTS TO REVIEW

A. Amino Acids (Section 18.3)
B. Tertiary and Quaternary Protein Structure (Sections 18.8 and 18.9)
C. How Enzymes Work (Section 19.4)
D. Sterol Structure (Section 23.6)
E. Amines (Chapter 16)

▲ Unwittingly surfing with sharks may result in high anxiety due to the hormone epinephrine.

Imagine you are on a hike, enjoying the scenery when all of the sudden a mother bear appears with her cubs; or, you are paddling out on the ocean to catch a big wave while surfing when a shark approaches your surfboard. Imagine walking casually into class when you abruptly realize there is an important exam that you forgot to study for. In each case, your body initially had a metabolic level where your internal biochemical conditions were in a relaxed state, a condition called homeostasis. However, once fear, stress, or anxiety set in, you are likely to feel shaky, your body's response to an increase in epinephrine.

Epinephrine is one example of a hormone your body produces to signal dangerous or stressful situations. Similar responses occur throughout your body on a daily basis to signal an abundance of situations. How do these rapid, body-wide responses happen? Furthermore, how does the biochemistry in our body maintain a constant internal environment despite these responses?

There are thousands of enzymatic reactions in our bodies that maintain balance for our normal internal biochemistry in response to our external environment. Many metabolic reactions work hard and constantly to maintain body temperature, produce chemicals for energy, eliminate waste products, sustain normal metabolic processes, transport nutrients to various cells, and even stabilize oxygen concentrations.

Two systems share the major responsibility for regulating body chemistry—the *endocrine system* and the *nervous system.* The endocrine system depends on *hormones,* chemical messengers that circulate in the bloodstream. The nervous system relies primarily on a much faster means of communication—electrical impulses in nerve cells, triggered by its own chemical messengers, the *neurotransmitters.* Neurotransmitters carry signals from one nerve cell to another and also from nerve cells to their targets, the ultimate recipients of the messages.

If the normal internal environment is compromised in the situation of fear, or, more complex situations such as severe illness, many drugs act by mimicking, modifying, or opposing the action of chemical messengers. To help maintain our biochemistry when normal processes are disturbed, outside medical intervention might assist in restoring the balance of the many biochemical reactions.

28.1 Messenger Molecules

Learning Objective:

- Describe the origins, pathways, and actions of hormones.

Chemical messengers control and coordinate your body's vital functions. Whether the messengers are hormones that arrive via the bloodstream or neurotransmitters released by nerve cells, such messengers ultimately connect with a *target.* The message is delivered by interaction between the chemical messenger and a **receptor** at the target. The receptor then acts like a light switch, causing some biochemical response to occur—the contraction of a muscle, for example, or the secretion of another biomolecule.

Receptor A molecule or portion of a molecule with which a hormone, neurotransmitter, or other biochemically active molecule interacts to initiate a response in a target cell.

Noncovalent attractions draw messengers and receptors together, much as a substrate is drawn into the active site of an enzyme (Sections 18.8 and 19.4). These attractions hold the messenger and receptor together long enough for the message to be delivered but without any permanent chemical change to the messenger or the receptor. The results of this interaction are chemical changes within the target cell.

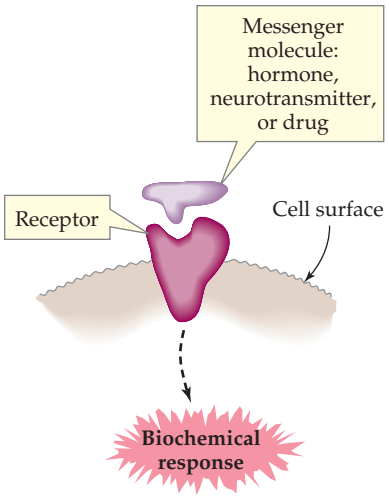
CONCEPTS TO REVIEW Figure 18.3 shows the various types of noncovalent forces that govern the shape of protein molecules. These same types of interactions mediate substrate–enzyme binding, as described in Section 19.4.

Hormones are the chemical messengers of the endocrine system. Endocrine glands and tissues in various parts of the body produce these molecules, often at distances far from their ultimate site of action. Because of this, hormones must travel through the bloodstream to their targets, and the responses they produce can require anywhere from seconds to hours to begin. The action or actions they elicit, however, may last a long time and can be wide-ranging. A single hormone will often affect many different tissues and organs—any cell with the appropriate receptors is a target. Insulin, for example, is a hormone secreted by the pancreas in response to elevated blood glucose levels. At target cells throughout the body, insulin accelerates uptake and utilization of glucose; in muscles it accelerates formation of glycogen, a glucose polymer that is metabolized when muscles need quick energy; and in fatty tissue it stimulates storage of triacylglycerols.

Hormone A chemical messenger secreted by cells of the endocrine system and transported through the bloodstream to target cells with appropriate receptors, where it elicits a response.

The chemical messengers of the nervous system are a set of molecules referred to as **neurotransmitters.** The electrical signals of the nervous system travel along nerve fibers, taking only a fraction of a second to reach their highly specific destinations. Most nerve cells, however, do not make direct contact with the cells they stimulate. A neurotransmitter must carry the message across the tiny gap separating the nerve

Neurotransmitter A chemical messenger that travels between a neuron and a neighboring neuron or other target cell to transmit a nerve impulse.



▲ A general representation of the interaction between a messenger molecule and a cellular receptor.

Endocrine system A system of specialized cells, tissues, and ductless glands that secretes hormones and shares with the nervous system the responsibility for maintaining constant internal body conditions and responding to changes in the environment.

cell from its target. Because neurotransmitters are released in very short bursts and are quickly broken down or reabsorbed by the nerve cell, their effects are short-lived. The nervous system is organized so that nearly all of its vital switching, integrative, and information-processing functions depend on neurotransmitters. Neurotransmitters are typically synthesized and released very close to their site of action.

PROBLEM 28.1

While thinking about how a messenger molecule and receptor molecule interact, list three possible intermolecular forces that involve noncovalent interations.

28.2 Hormones and the Endocrine System

Learning Objectives:

- Distinguish between the different types of hormonal control.
- List the different chemical types of hormones and give examples of each.

The **endocrine system** includes all cells that secrete hormones into the bloodstream. Some of these cells are found in organs that also have non-endocrine functions (e.g., the pancreas, which also produces digestive enzymes); others occur in glands devoted solely to hormonal control (e.g., the thyroid gland). It is important to note, however, that hormones do not carry out chemical reactions. Hormones are simply messengers that alter the biochemistry of a cell by signaling the inhibition or activation of an existing enzyme, by initiating or altering the rate of synthesis of a specific protein, or in other ways.

The major endocrine glands are the thyroid gland, the adrenal glands, the ovaries and testes, and the pituitary gland (found in the brain). The hypothalamus, a section of the brain just above the pituitary gland, controls the endocrine system. It communicates with other tissues in the following three ways:

- *Direct neural control* A nervous system message from the hypothalamus initiates release of hormones by the adrenal gland. For example,

$$\text{Hypothalamus} \xrightarrow{\text{Nerve message}} \text{Adrenal gland} \longrightarrow \text{Epinephrine}$$

  Epinephrine is targeted to many cells; it increases heart rate, blood pressure, and glucose availability.
- *Direct release of hormones* Hormones move from the hypothalamus to the posterior pituitary gland, where they are stored until needed. For example,

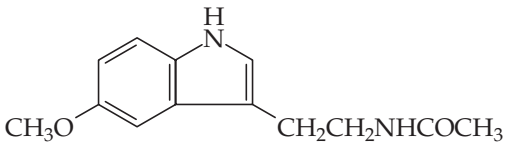
$$\text{Hypothalamus} \longrightarrow \text{Antidiuretic hormone}$$

  Antidiuretic hormone, which is stored in the posterior pituitary gland, targets the kidneys and causes retention of water and elevation of blood pressure.
- *Indirect control through release of regulatory hormones* In the most common control mechanism, *regulatory hormones* from the hypothalamus stimulate or inhibit the release of hormones by the anterior pituitary gland. Many of these pituitary hormones in turn stimulate release of still other hormones by their own target tissues. For example,

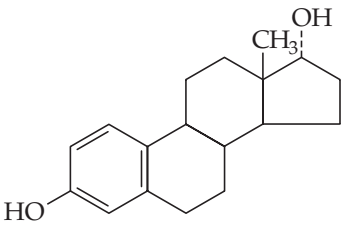
$$\text{Hypothalamus} \xrightarrow{\text{Releasing factor}} \text{Pituitary gland} \longrightarrow$$
$$\text{Thyrotropin (a regulatory hormone)} \longrightarrow$$
$$\text{Thyroid gland} \longrightarrow \text{Thyroid hormones}$$

  Thyroid hormones are targeted to cells throughout the body; they affect oxygen availability, blood pressure, and other endocrine tissues.

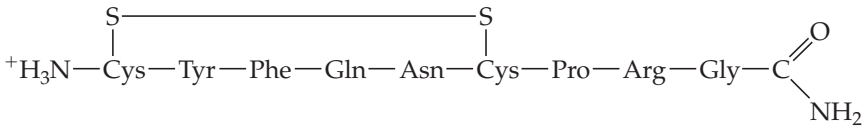
Chemically, hormones are of three major types: (1) amino acid derivatives, such as epinephrine; (2) polypeptides, which range from just a few amino acids to several hundred amino acids; and (3) steroids, which are lipids with the distinctive molecular structure based on four connected rings common to all sterols (see Section 23.6).



Melatonin, an amino acid derivative
(regulates day–night cycle)



Estradiol, a steroid
(an estrogen that acts in ovulation)



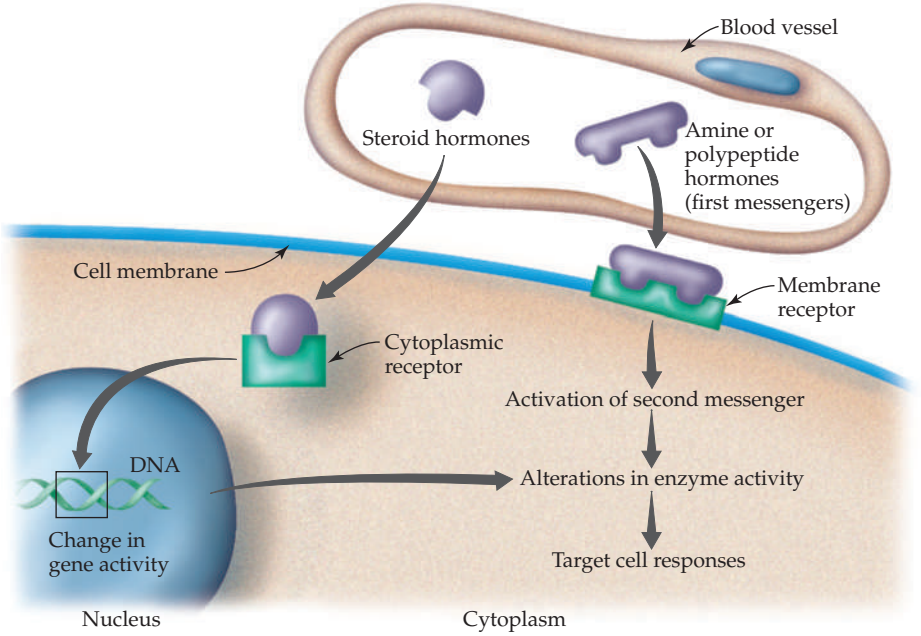
Vasopressin, a polypeptide
(controls urine volume)

Table 28.1 gives examples of the targets and actions of each type of hormone.

Table 28.1 Examples of Each Chemical Class of Hormones

Chemical Class	Hormone Examples	Source	Target	Major Action
Amino acid derivatives	Epinephrine and norepinephrine	Adrenal medulla	Most cells	Release glucose from storage; increase heart rate and blood pressure
	Thyroxine	Thyroid gland	Most cells	Influence energy use, oxygen consumption, growth, and development
Polypeptides (regulatory hormones)	Adrenocorticotropic hormone	Anterior pituitary	Adrenal cortex	Stimulate release of glucocorticoids (steroids), which control glucose metabolism
	Growth hormone	Anterior pituitary	Peripheral tissues	Stimulate growth of muscle and skeleton
	Follicle-stimulating hormone, luteinizing hormone (LH)	Anterior pituitary	Ovaries and testes	Stimulate release of steroid hormones
	Vasopressin	Posterior pituitary	Kidneys	Cause retention of water, elevation of blood volume and blood pressure
	Thyrotropin	Anterior pituitary	Thyroid gland	Stimulates release of thyroid hormones
Steroids	Cortisone and cortisol (glucocorticoids)	Adrenal cortex	Most cells	Counteract inflammation; control metabolism when glucose must be conserved
	Testosterone; estrogen, progesterone	Testes; ovaries	Most cells	Control development of secondary sexual characteristics, maturation of sperm and eggs

Upon arrival at its target cell, a hormone must deliver its signal to create a chemical response inside the cell. The signal enters the cell in ways determined by the chemical nature of the hormone (Figure 28.1). Because the cell is surrounded by a membrane composed of hydrophobic molecules, only nonpolar, hydrophobic molecules can move across it on their own. The steroid hormones are nonpolar, so they can enter the cell directly by diffusion; this is one of the ways a hormone delivers its message. Once within the cell's cytoplasm, a steroid hormone encounters a receptor molecule that carries it to its target, DNA in the nucleus of the cell. The result is some change in production of a protein governed by a particular gene.



▶ **Figure 28.1**
Interaction of hormones and receptors at the cellular level. Steroid hormones are hydrophobic and can cross the cell membrane to find receptors inside the cell. Amine and polypeptide hormones are hydrophilic and, because they cannot cross the cell membrane, act via second messengers.

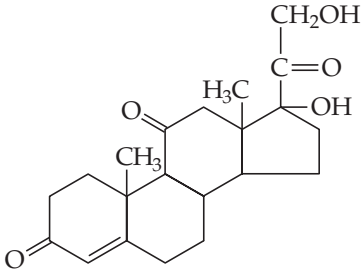
In contrast, the polypeptide and amine hormones are water-soluble molecules and cannot cross the hydrophobic cell membranes. Rather than entering cells, they deliver their messages by bonding noncovalently with receptors on cell surfaces. The result is release of a **second messenger** within the cell. There are several different second messengers, and the specific sequence of events varies. In general, three membrane-bound proteins participate in release of the second messenger: (1) the receptor and (2) a *G protein* (a member of the guanine nucleotide-binding protein family) that transfer the message to (3) an enzyme. First, interaction of the hormone with its receptor causes a change in the receptor (much like the effect of an allosteric regulator on an enzyme; Section 19.7). This stimulates the G protein to activate an enzyme that participates in release of the second messenger.

Second messenger Chemical messenger released inside a cell when a hydrophilic hormone or neurotransmitter interacts with a receptor on the cell surface.

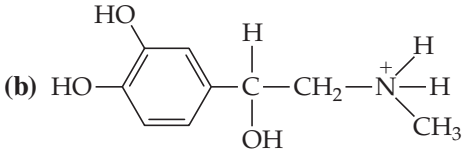
Worked Example 28.1 Classifying Hormones Based on Structure

Classify the following hormones as an amino acid derivative, a polypeptide, or a steroid.

(a)



(b)



(c) $^{+}H_3N$—His—Ser—Glu— ••• Thr—COO^{-}

ANALYSIS Hormones that are amino acid derivatives are recognized by the presence of amino groups. Those that are polypeptides are composed of amino acids. Steroids are recognizable by their distinctive four-ring structures.

SOLUTION
Compound (a) is a steroid, (b) is an amino acid derivative, and (c) is a polypeptide.

PROBLEM 28.2

Look at the structure of epinephrine in Section 28.3. Is it a steroid, an amino acid derivative, or a polypeptide?

PROBLEM 28.3

Review the structure of thyroxine in Section 28.4. Which amino acid could be biochemically altered to synthesize thyroxine? Review the amino acid structures in Chapter 18 for assistance.

PROBLEM 28.4

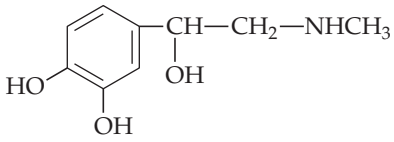
Review the structure of thyrotropin-releasing hormone (TRH) in Section 28.4. This chemical messenger has one chiral carbon, which happens to be an alpha carbon of an amino acid. Which amino acid is part of TRH?

28.3 How Hormones Work: Epinephrine and Fight-or-Flight

Learning Objective:

- Explain the sequence of events in epinephrine's action as a hormone.

Epinephrine (pronounced ep-pin-*eff*-rin), also known as *adrenaline,* is often called the *fight-or-flight hormone* because it is released from the adrenal glands when we need an instant response to danger.

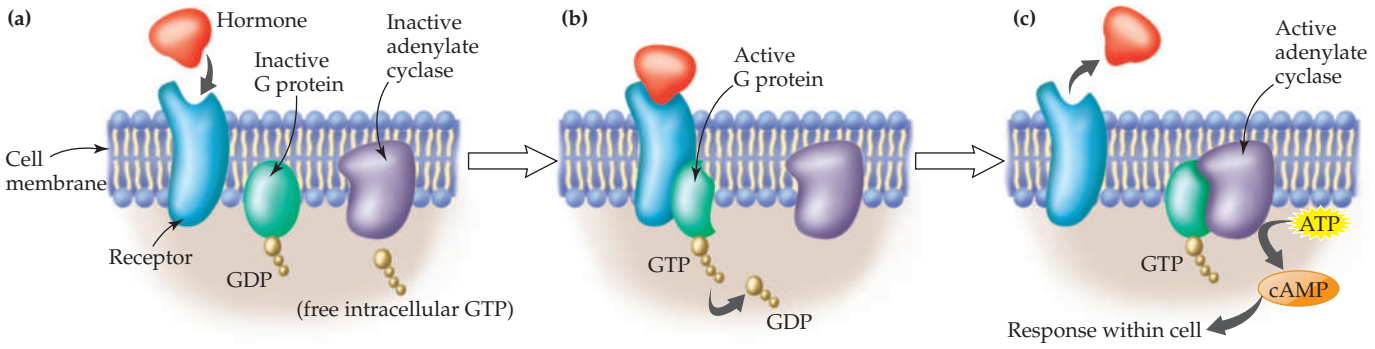


Epinephrine
(adrenaline)

We have all felt the rush of epinephrine that accompanies a near-miss accident or a sudden loud noise. The main function of epinephrine in a "startle" reaction is a dramatic increase in the availability of glucose as a source of energy to deal with whatever stress is immediate. The time elapsed from initial stimulus to glucose release into the bloodstream is only a few seconds.

Epinephrine acts via *cyclic adenosine monophosphate (cyclic AMP,* or *cAMP),* an important second messenger. The sequence of events in this action, shown in Figure 28.2 and described next, illustrates one type of biochemical response to a change in an individual's external or internal environment.

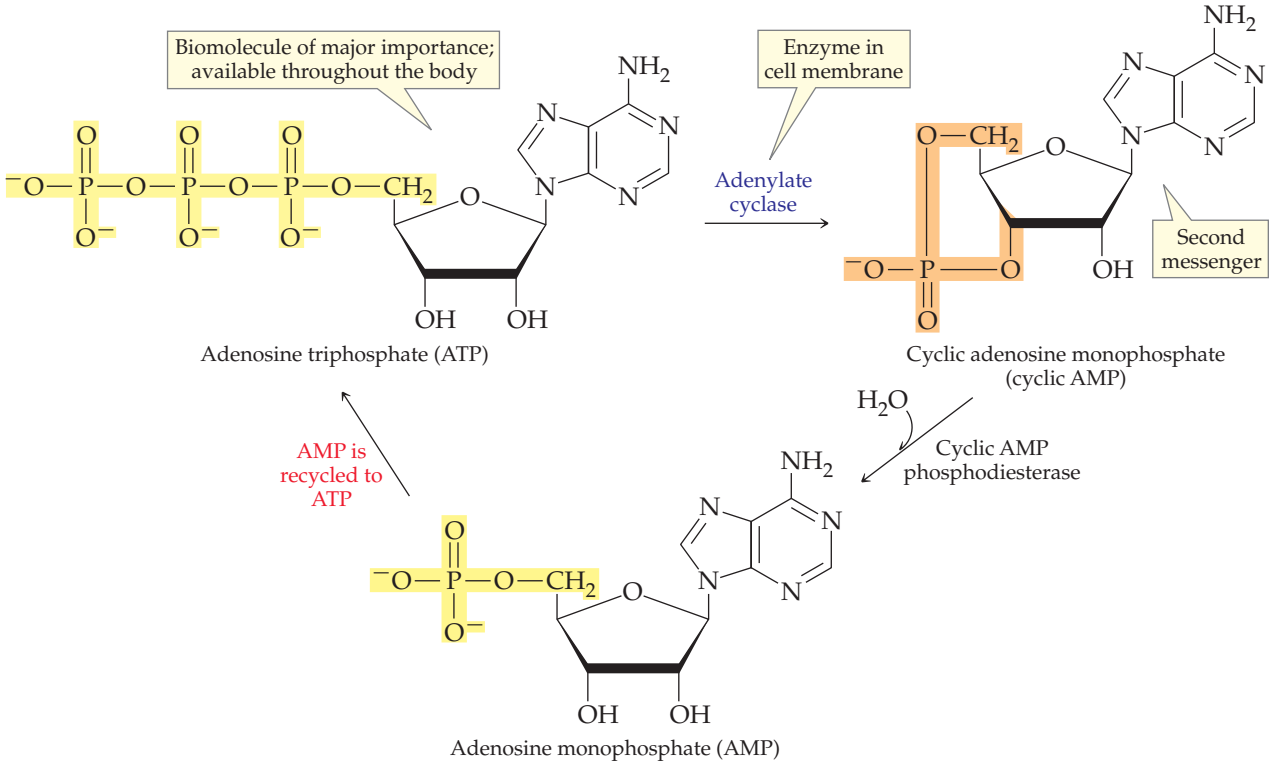
- Epinephrine, a hormone carried in the bloodstream, binds to a receptor on the surface of a cell.
- The hormone–receptor complex activates a nearby G protein embedded in the interior surface of the cell membrane.
- GDP (guanosine diphosphate) associated with the G protein is exchanged for GTP (guanosine triphosphate) from the cytosol.
- The G protein–GTP complex activates *adenylate cyclase,* an enzyme that also is embedded in the interior surface of the cell membrane.
- Adenylate cyclase catalyzes production within the cell of the second messenger—*cyclic AMP*—from adenosine triphosphate (ATP), as shown in Figure 28.3.
- Cyclic AMP initiates reactions that activate glycogen phosphorylase, the enzyme responsible for release of glucose from storage. (Interaction of other hormones with their specific receptors results in initiation by cyclic AMP of other reactions.)
- When the emergency has passed, cyclic AMP is converted back to ATP.



▲ **Figure 28.2**

Activation of cyclic AMP as a second messenger.

(a) The hormone receptor, inactive G protein, and inactive adenylate cyclase enzyme reside in the cell membrane. (b) On formation of the hormone–receptor complex, an allosteric change occurs in the G protein, resulting in the GDP of the G protein being replaced by a free intracellular GTP. (c) The active G protein–GTP complex activates adenylate cyclase, causing production of cyclic AMP inside the cell, where it initiates the action called for by the hormone.



▲ **Figure 28.3**

Production of cyclic AMP as a second messenger.

The reactions shown take place within the target cell after epinephrine or some other chemical messenger interacts with a receptor on the cell surface. (The major role of ATP in providing energy for biochemical reactions was discussed in Section 21.4.)

In addition to making glucose available, epinephrine reacts with other receptors to increase blood pressure, heart rate, and respiratory rate; decrease blood flow to the digestive system (digestion is not important during an emergency); and counteract spasms in the respiratory system. The resulting combined and rapid effects make epinephrine the most crucial drug for treatment of *anaphylactic shock*. Anaphylactic shock is the result of a severe allergic reaction, perhaps to a bee sting, a drug, or even to something seemingly as benign as peanuts; it is an extremely serious medical emergency. The major symptoms include a severe drop in blood pressure due to blood vessel dilation and difficulty breathing due to bronchial constriction. Epinephrine directly counters these symptoms. Individuals who know they are susceptible to these life-threatening allergic responses carry epinephrine with them at all times (typically in the form of an autoinjector known as an "EpiPen").

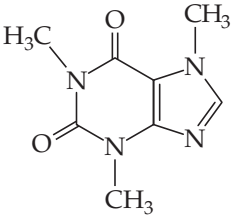
PROBLEM 28.5

A phosphorus-containing anion is removed from ATP in its conversion to cyclic AMP, as shown in Figure 28.3. The anion is often abbreviated as PP_i. Which of the following anions is represented by PP_i?

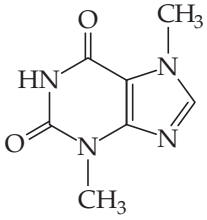
(a) $P_3O_{10}^{5-}$ **(b)** $P_2O_7^{4-}$ **(c)** PO_4^{3-} **(d)** $H_2PO_4^-$

KEY CONCEPT PROBLEM 28.6

Caffeine and theobromine (from chocolate) act as stimulants. They work by altering the cAMP signal. Refer to Figure 28.3 and decide how these molecules might interact with an enzyme in the cAMP pathway to enhance the effect of cAMP.



Caffeine



Theobromine

▲ An epinephrine autoinjection pen. Such devices are carried by individuals at risk of an anaphylactic reaction to an allergen.

28.4 Amino Acid Derivatives, Polypeptides, and Steroid Hormones

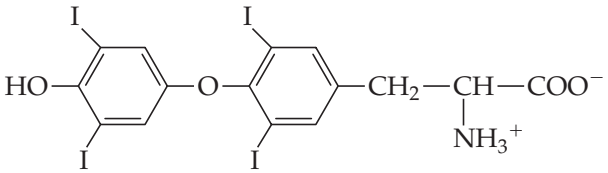
Learning Objective:

- Explain the functions of the three major types of hormones: amino acid derivatives, polypeptides, and steroids.

Amino Acid Derivatives

The biochemistry of the brain is an active area of research. As our understanding of chemical messages in the brain grows, the traditional distinctions between hormones and neurotransmitters are vanishing. Several amino acid derivatives classified as hormones because of their roles in the endocrine system are also synthesized in neurons and function as neurotransmitters in the brain. (Because a barrier—the *blood–brain barrier*—limits entry into the brain of chemicals traveling in the bloodstream, the brain cannot rely on a supply of chemical messengers synthesized elsewhere; see the Chemistry in Action "The Blood–Brain Barrier," Chapter 29.) Epinephrine, the fight-or-flight hormone, is one of the amino acid derivatives that is both a hormone and a neurotransmitter. The pathway for the synthesis of epinephrine is shown in Figure 28.4; several other chemical messengers are also formed in this pathway.

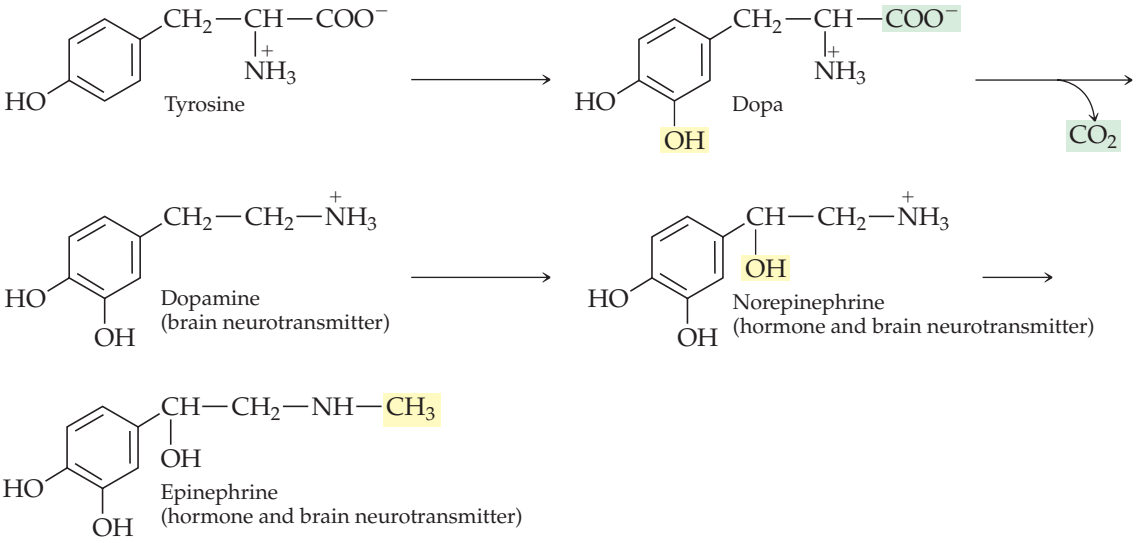
Thyroxine, another amino acid derivative, is also a hormone. It is one of two iodine-containing hormones produced by the thyroid gland, and our need for dietary iodine is due to these hormones. Unlike other hormones derived from amino acids, thyroxine is a nonpolar compound that can cross cell membranes and enter cells, where it activates the synthesis of various enzymes. When dietary iodine is insufficient, the thyroid gland compensates by enlarging in order to produce more thyroxine. Thus, a greatly enlarged thyroid gland (a goiter) is a symptom of iodine deficiency. In developed countries, where iodine is added to table salt, goiter is uncommon. In some regions of the world, however, iodine deficiency is a common and serious problem that results not only in goiter but also in severe mental retardation in infants *(cretinism)*.



Thyroxine

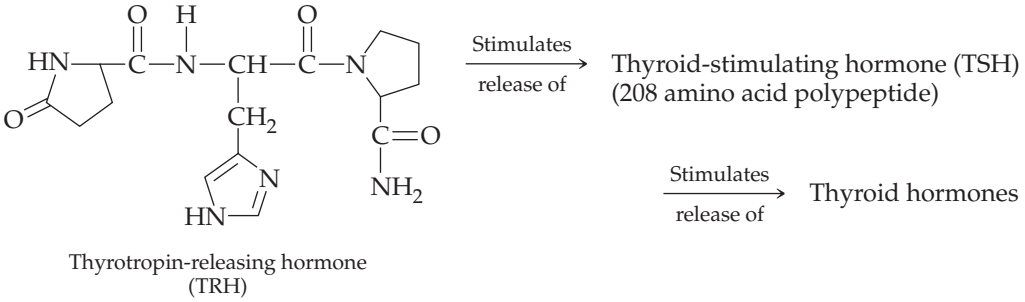
Polypeptides

Polypeptides are the largest class of hormones. They range widely in molecular size and complexity, as illustrated by two hormones that control the thyroid gland, *TRH* and *thyroid-stimulating hormone (TSH)*. TRH, a modified tripeptide, is a regulatory



▲ **Figure 28.4**
Synthesis of chemical messengers from tyrosine.
The changes in each step are highlighted in gold (yellow) for substitution reactions and green for respiratory (elimination) reactions.

hormone released by the hypothalamus. At the pituitary gland, TRH activates release of TSH, a protein that has 208 amino acid residues in two chains. TSH in turn triggers release of amino acid derivative hormones from the thyroid gland.



Because of its importance in glucose metabolism and diabetes mellitus, the function of insulin as a hormone is described in Chapter 22 as part of the discussion of glucose metabolism.

Insulin, a protein containing 51 amino acids, is released by the pancreas in response to high concentrations of glucose in the blood. It stimulates cells to take up glucose to either generate or store energy.

PROBLEM 28.7

Examine the TRH structure and identify the three amino acids from which it is derived. The *N*-terminal amino acid has undergone ring formation, and the carboxyl group at the *C*-terminal end has been converted to an amide.

KEY CONCEPT PROBLEM 28.8

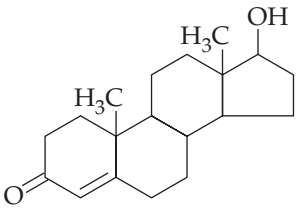
Look at the structure of thyroxine shown earlier in this section. Is thyroxine, an amino acid derivative, hydrophobic or hydrophilic? Explain.

Steroid Hormones

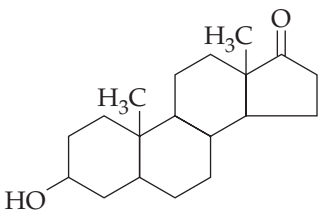
Sterols have a central structure composed of the four connected rings as you saw in Chapter 23. Because sterols are soluble in hydrophobic solvents, they are classified as lipids. Sterol hormones, referred to as steroids, are divided into three types according to function: mineralcorticoids, glucocorticoids (Section 23.6), and the sex hormones that are responsible for male and female hormonal and physical characteristics.

The two most important male sex hormones, or androgens, are testosterone and androsterone. These steroids are responsible for the development of male secondary sex characteristics during puberty and for promoting tissue and muscle growth.

Male sex hormones (androgens)



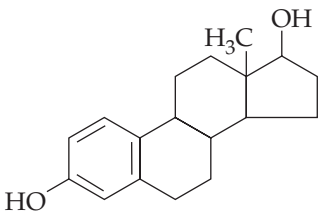
Testosterone



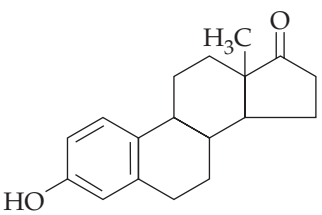
Androsterone

Estrone and *estradiol,* the female steroid hormones known as *estrogens,* are synthesized from testosterone, primarily in the ovaries but also to a small extent in the adrenal cortex. Estrogens govern development of female secondary sex characteristics and participate in regulation of the menstrual cycle. The ovaries release *progestins,* principally *progesterone,* during the second half of the menstrual cycle and prepare the uterus for implantation of a fertilized ovum should conception occur.

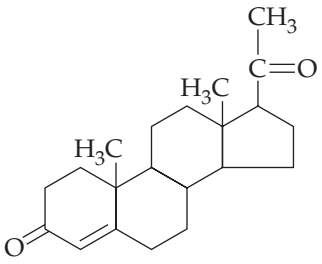
Female sex hormones



Estradiol
(an estrogen)

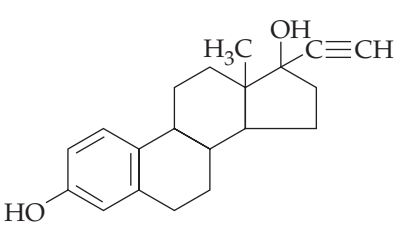


Estrone
(an estrogen)

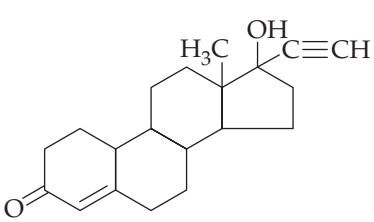


Progesterone
(a progestin)

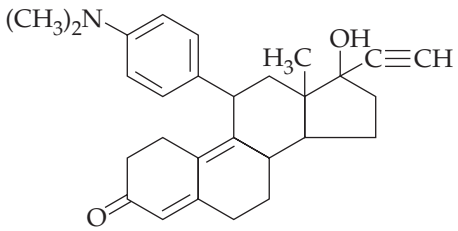
In addition to the several hundred known steroids isolated from plants and animals, others have been synthesized in the laboratory in the search for new drugs. Most birth control pills are a mixture of the synthetic estrogen *ethynyl estradiol* and the synthetic progestin *norethindrone.* These steroids function by tricking the body into a false pregnant state, making it temporarily infertile. The compound known as *RU-486,* or *mifepristone,* is effective as a "morning after" pill. It prevents pregnancy by binding strongly to the progesterone receptor, thereby blocking implantation in the uterus of a fertilized egg cell.



Ethynyl estradiol
(a synthetic estrogen)



Norethindrone
(a synthetic progestin)



RU-486
(Mifepristone)

Anabolic steroids, which have the ability to increase muscle mass and consequently strength, are drugs that resemble androgenic (male) hormones, such as testosterone. These steroids have been used by bodybuilders for decades to change their body shape to a more muscular, bulky form; some professional and semiprofessional athletes (both men and women) have used them in the hope of gaining body mass, strength, power, speed, endurance, and aggressiveness. Unfortunately, many serious side effects can arise from this abuse of anabolic steroids. Stunted bone growth in adolescents, liver, prostate, and kidney

CHEMISTRY IN ACTION

Homeostasis

Homeostasis—the maintenance of a constant internal environment in the body—is as important to the study of living things as atomic structure is to the study of chemistry. The phrase "internal environment" is a general way to describe all the conditions within cells, organs, and body systems. Conditions such as body temperature, the availability of chemical compounds that supply energy, and the disposal of waste products must remain within specific limits for an organism to function properly. Throughout our bodies, sensors track the internal environment and send signals to restore proper balance if the environment changes. If oxygen is in short supply, for example, a signal is sent that makes us breathe harder. When we are cold, a signal is sent to constrict surface blood vessels and prevent further loss of heat.

At the chemical level, homeostasis regulates the concentrations of ions and many different organic compounds so that they stay near normal levels. The predictability of the concentrations of such substances is the basis for *clinical chemistry*—the chemical analysis of body tissues and fluids. In the clinical lab, various tests measure concentrations of significant ions and compounds in blood, urine, feces, spinal fluid, or other samples from a patient's body. Comparing the lab results with "norms" (average concentration ranges in a population of healthy individuals) shows which body systems are struggling, or possibly failing, to maintain homeostasis. To give just one example, urate (commonly known as uric acid) is an anion that helps to carry waste nitrogen from the body. A uric acid concentration higher than the normal range of about 2.5–7.7 mg/dL in blood can indicate the onset of gout or signal possible kidney malfunction.

A copy of a clinical lab report for a routine blood analysis is shown in the following figure. (Fortunately, this individual has no significant variations from normal.) The metal names in the report refer to the various cations, and the heading "Phosphorus" refers to the phosphate anion.

Test	Result	Normal Range
Albumin	4.3 g/dL	3.5–5.3 g/dL
Alk. Phos.*	33 U/L	25–90 U/L
BUN*	8 mg/dL	8–23 mg/dL
Bilirubin T.*	0.1 mg/dL	0.2–1.6 mg/dL
Calcium	8.6 mg/dL	8.5–10.5 mg/dL
Cholesterol	227 mg/dL	120–250 mg/dL
Chol., HDL*	75 mg/dL	30–75 mg/dL
Creatinine	0.6 mg/dL	0.7–1.5 mg/dL
Glucose	86 mg/dL	65–110 mg/dL
Iron	101 mg/dL	35–140 mg/dL
LDH*	48 U/L	50–166 U/L
SGOT*	23 U/L	0–28 U/L
Total protein	5.9 g/dL	6.2–8.5 g/dL
Triglycerides	75 mg/dL	36–165 mg/dL
Uric Acid	4.1 mg/dL	2.5–7.7 mg/dL
GGT*	23 U/L	0–45 U/L
Magnesium	1.7 mEq/L	1.3–2.5 mEq/L
Phosphorus	2.6 mg/dL	2.5–4.8 mg/dL
SGPT*	13 U/L	0–26 U/L
Sodium	137.7 mEq/L	135–155 mEq/L
Potassium	3.8 mEq/L	3.5–5.5 mEq/L

▲ **A clinical lab report for routine blood analysis.** The abbreviations marked with asterisks are for the following tests (alternative standard abbreviations are in parentheses): Alk. Phos., alkaline phosphatase (ALP); BUN, blood urea nitrogen; Bilirubin T., total bilirubin; Chol., HDL, cholesterol, high-density lipoproteins; LDH, lactate dehydrogenase; SGOT, serum glutamic oxaloacetic transaminase (AST); GGT, γ-glutamyl transferase; SGPT, serum glutamic pyruvic transaminase (ALT).

CIA Problem 28.1 One of the responsibilities of the endocrine system is maintenance of homeostasis in the body. Briefly explain what is meant by the term *homeostasis.*

CIA Problem 28.2 What is the goal of the measurements of clinical chemistry?

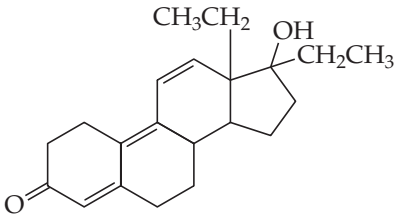
CIA Problem 28.3 In humans, approximately 12% of all genes are regulatory genes necessary to maintain homeostasis within cells. Health checkups often include a blood panel; common compounds measured include blood glucose and triacylglycerols. Based on your knowledge of metabolism, why would these compounds be included in the blood test? What might that have to do with regulatory genes?

cancer, high blood pressure, aggressive behavior, liver damage, irregular heartbeat, and nosebleeds (arising out of blood coagulation disorders) are but a few of the short and long-term side effects of these agents. Today, most organized amateur and professional sports have banned the use of these and other "performance-enhancing" drugs.

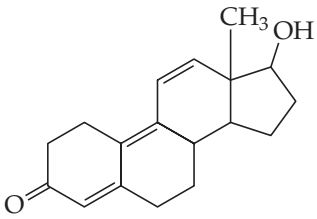
Despite bans, "roids" are still used by some athletes. Baseball, track, wrestling, and cycling have all investigated the use of anabolic steroids, with prominent athletes stripped of their honors. It is legal to use steroids to treat injuries in racehorses, but treatment must stop a month prior to a race. Trainers still abuse this rule. To enforce the ban on anabolic steroids, athletes (human and animal) are subjected to random drug

screening, but some athletes attempt to get around the screenings by using *designer steroids*—steroids that cannot be detected with current screening methods, such as tetrahydrogestrinone (THG), trenbolone (used by cattle ranchers to increase the size of cattle), and gestrinone (used to treat endometriosis in women), because identification depends on knowing the compound's structure. However, analysis of a synthetic steroid to determine its structure is easily done, thwarting athletes' plans.

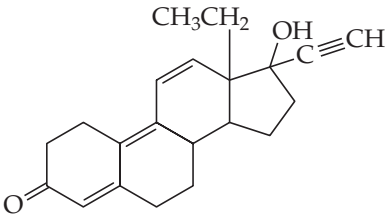
Designer Anabolic Steroids



Tetrahydrogestrinone (THG)



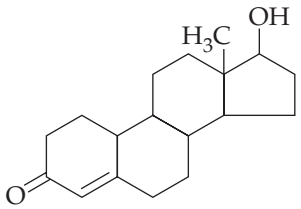
Trenbolone



Gestrinone

PROBLEM 28.9

Nandrolone is an anabolic, or tissue-building, steroid sometimes taken by athletes seeking to build muscle mass (it is banned by the International Olympic Committee as well as other athletic organizations). Among its effects is a high level of androgenic activity. Which of the androgens shown on page 867 does it most closely resemble? How does it differ from that androgen?



Nandrolone (an anabolic steroid)

28.5 Neurotransmitters

Learning Objective:

- Describe the origins, pathways, and actions of neurotransmitters.

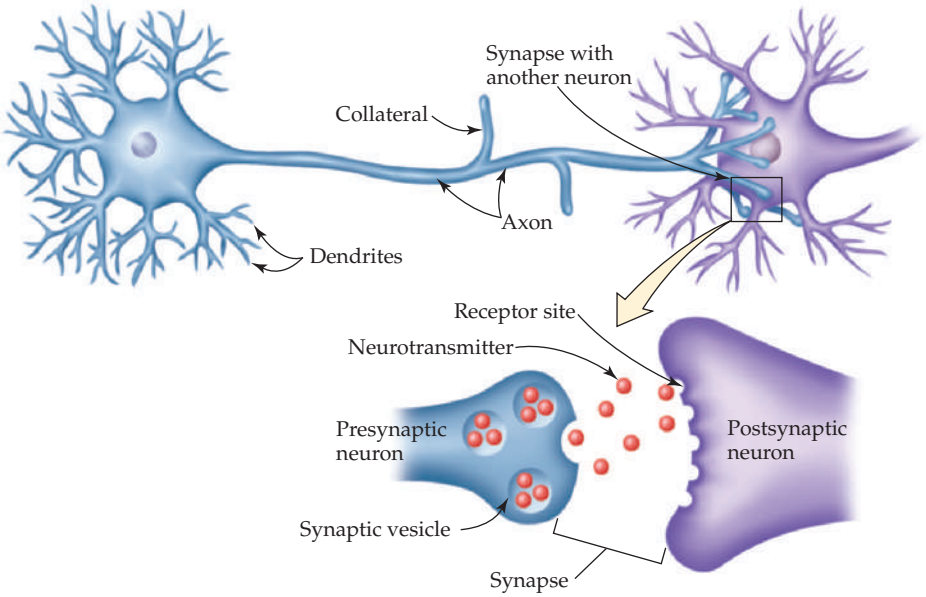
Neurotransmitters are the chemical messengers of the nervous system. Released by nerve cells *(neurons),* they transmit signals to neighboring target cells, such as other nerve cells, muscle cells, or endocrine cells. Structurally, nerve cells that rely on neurotransmitters typically have a bulb-like body connected to a long, thin stem called an *axon* (Figure 28.5). Short, tentacle-like appendages, the *dendrites,* protrude from the bulbous end of the neuron, and numerous filaments protrude from the axon at the opposite end. The filaments lie close to the target cell, separated only by a narrow gap—the **synapse.**

Synapse The place where the tip of a neuron and its target cell lie adjacent to each other.

A nerve impulse is transmitted along a nerve cell by variations in electrical potential caused by the exchange of positive ions across the cell membrane. Chemical transmission of the impulse between a nerve cell and its target occurs when neurotransmitter molecules are released from a *presynaptic neuron,* cross the synapse, and bind to receptors on the target cell. When the target is another nerve cell, it is called a *postsynaptic neuron,* where receptors on the postsynaptic neuron's dendrites receive the neurotransmitter, as shown in Figure 28.5. Once neurotransmitter–receptor binding has occurred, the message has been delivered. The postsynaptic neuron then transmits the nerve impulse down its own axon until a neurotransmitter delivers the message to the next neuron or other target cell.

Neurotransmitter molecules are synthesized in the presynaptic neurons and stored there in small pockets, known as *vesicles,* from which they are released as needed. After a neurotransmitter has done its job, it must be *rapidly* removed from the synaptic cleft so that the postsynaptic neuron is ready to receive another impulse. Removal occurs in one of two ways. Either a chemical change catalyzed by an enzyme available in the synaptic cleft inactivates the neurotransmitter or, alternatively, the neurotransmitter is returned to the presynaptic neuron and placed in storage until it is needed again.

Most neurotransmitters are amines synthesized from amino acids. Figure 28.4 shows the synthesis of dopamine, norepinephrine, and epinephrine from tyrosine. Figure 28.6 shows the synthesis of serotonin and melatonin from tryptophan. Some neurotransmitters act directly by causing changes in adjacent cells as soon as they



▶ **Figure 28.5**
A nerve cell and transmission of a nerve signal by neurotransmitters. Transmission occurs between neurons when a neurotransmitter is released by the presynaptic neuron, crosses the synapse, and fits into a receptor on the postsynaptic neuron or other target cell.

connect with their receptors. Others rely on second messengers, often cyclic AMP, the same second messenger utilized by hormones. Individual neurotransmitters are associated with emotions, drug addiction, pain relief, and other brain functions, as we shall see in the following sections.

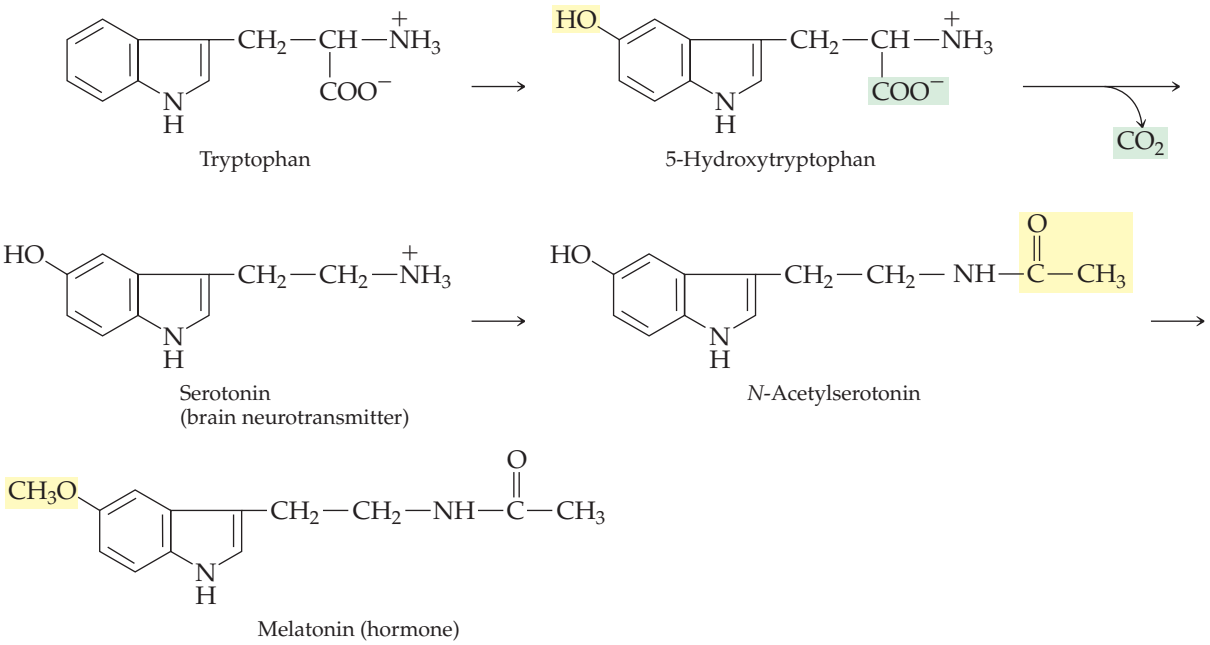
PROBLEM 28.10

Which of the following transformations of amines in Figure 28.6 is (1) an acetylation, (2) a methylation, and (3) a decarboxylation?

(a) 5-Hydroxytryptophan to serotonin

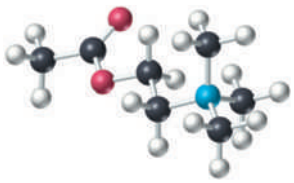
(b) Serotonin to *N*-acetylserotonin

(c) *N*-Acetylserotonin to melatonin



▲ **Figure 28.6**
Synthesis of chemical messengers from tryptophan.
The changes in each step are highlighted in yellow for substitution reactions and in green for elimination reactions.

28.6 How Neurotransmitters Work: Acetylcholine, Its Agonists and Antagonists



Acetylcholine

Learning Objective:

- Outline the sequence of events in acetylcholine's action as a neurotransmitter and give examples of its agonists and antagonists.

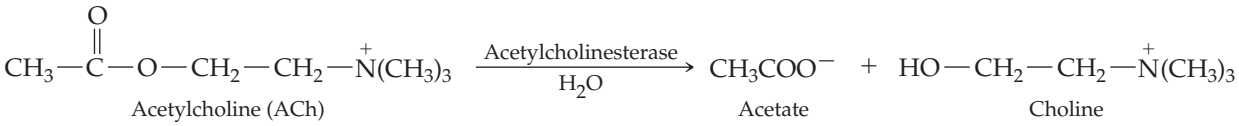
Acetylcholine in Action

Acetylcholine is a neurotransmitter responsible for the control of skeletal muscles. It is also widely distributed in the brain, where it plays a role in the sleep–wake cycle, learning, memory, and mood. *Cholinergic nerves* rely on acetylcholine as their neurotransmitter.

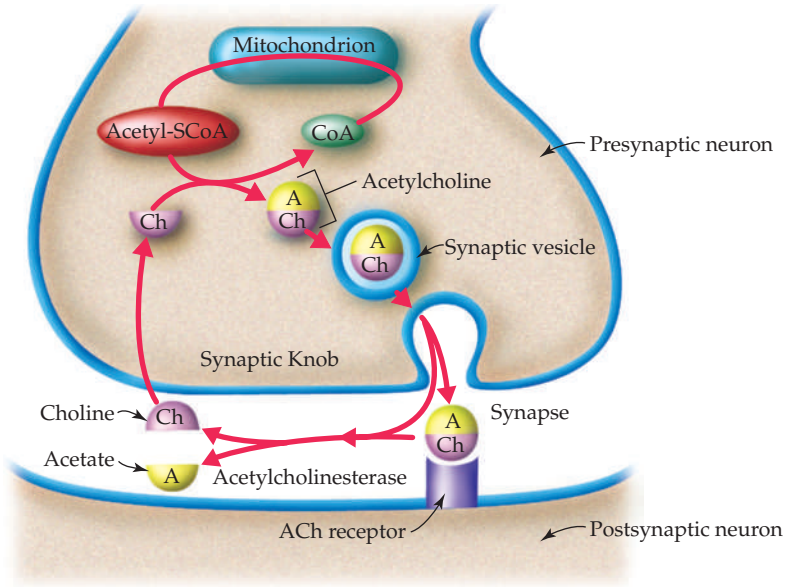
Acetylcholine A vertebrate neurotransmitter that is most commonly found in muscle neurons.

Acetylcholine is synthesized in presynaptic neurons and stored in their vesicles. The rapid sequence of events in Figure 28.7 shows the action of acetylcholine communicating between nerve cells, and the sequence is as follows:

- A nerve impulse arrives at the presynaptic neuron.
- Vesicles move to the cell membrane, fuse with it, and release their acetylcholine molecules (several thousand molecules from each vesicle).
- Acetylcholine crosses the synapse and binds to receptors on the postsynaptic neuron, causing a change in membrane permeability to ions.
- This change in the permeability to ions of the postsynaptic neuron initiates the nerve impulse in that neuron.
- After the message is delivered, acetylcholinesterase present in the synaptic cleft catalyzes the decomposition of acetylcholine.



- Choline is absorbed back into the presynaptic neuron, where new acetylcholine is synthesized.



◂ **Figure 28.7**
Acetylcholine release and re-uptake. Acetylcholine is stored in vesicles in the presynaptic neuron. After it is released into the synapse and connects with its receptor, it is broken down by hydrolysis into acetate and choline in a reaction catalyzed by acetylcholinesterase. The choline is taken back into the synaptic knob and reused to synthesize acetylcholine, which is then stored in the vesicles until needed.

Drugs and Acetylcholine

Drug Any substance that alters body function when it is introduced from an external source.

Many drugs act at acetylcholine synapses, where the tip of a neuron that releases acetylcholine and its target cell lie adjacent to each other. A **drug** is any molecule that alters normal functions when it enters the body from an external source. The action is at the molecular level, and it can be either therapeutic or poisonous. To have an effect, many drugs must connect with a receptor just as a substrate must bind to an enzyme or as a hormone or neurotransmitter must bind to a receptor. In fact, many drugs are designed to mimic a given hormone or neurotransmitter and in so doing elicit either an enhanced or attenuated effect.

Agonist A substance that interacts with a receptor to cause or prolong the receptor's normal biochemical response.

Antagonist A substance that blocks or inhibits the normal biochemical response of a receptor.

Pharmacologists classify some drugs as **agonists**—substances that act to produce or prolong the normal biochemical response of a receptor. Other drugs are classified as **antagonists**—substances that block or inhibit the normal response of a receptor. Many agonists and antagonists compete with normal signaling molecules for interaction with the receptor, just as inhibitor molecules compete with substrate for the active site in an enzyme. To illustrate the ways in which drugs can affect our biochemical activity, we next describe the action of a group of drugs. These drugs are all members of the same family in the sense that their biochemical activity occurs at acetylcholine synapses in the central nervous system. Figure 28.7 shows the locations of their actions and Table 28.2 describes examples of the acetylcholine drug family.

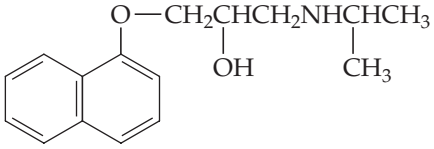
◀◀ Alkaloids are naturally occurring, nitrogen-containing compounds isolated from plants; usually basic, bitter, and poisonous (see Section 16.7).

Table 28.2 Acetylcholine Drug Family (therapeutic or poisonous)

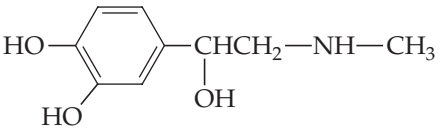
Name *(drug mechanism)*	Origin	Drug Action
Botulinum toxin *(antagonist)*	The botulinum toxin is found in *Clostridium botulinum* that are located in soil. One type of exposure to the toxin is through improperly canned food.	The toxin binds irreversibly to the presynaptic neuron, where acetylcholine would be released. It prevents this release, frequently causing death due to muscle paralysis.
Black widow spider *(agonist)*	Venom from bite	The synapse is flooded with acetylcholine, resulting in muscle cramps and spasms.
Organophosphorus insecticides *(antagonists)*	These are synthesized in the laboratory. Some examples include parathion, diazinon, and malathion.	All of the organophosphorus insecticides prevent acetylcholinesterase from breaking down acetylcholine within the synapse. As a result, the nerves are overstimulated, causing a variety of symptoms including muscle contraction and weakness, lack of coordination, and at high doses, convulsions.
Nicotine *(agonist)* (Chapter 16)	A general nicotine alkaloid source is found in the leaves of nicotiana nightshade plants, which are used for manufacturing tobacco.	Nicotine at low doses is a stimulant because it activates acetylcholine receptors. The sense of alertness and well-being produced by inhaling tobacco smoke is a result of this effect. At high doses, nicotine is an antagonist. It irreversibly blocks the acetylcholine receptors and can cause their degeneration.
Atropine *(antagonist)*	Atropine, found naturally in a variety of nightshade plants, is an alkaloid that is poisonous at high doses.	At controlled doses, its therapeutic uses include acceleration of abnormally slow heart rate, paralysis of eye muscles during surgery, and relaxation of intestinal muscles in gastrointestinal disorders. Most importantly, it is a specific antidote for acetylcholinesterase poisons such as organophosphorus insecticides. By blocking activation of the receptors, it counteracts the excess acetylcholine created by acetylcholinesterase inhibitors.
Tubocurarine *(antagonist)*	Tubocurarine is a purified alkaloid from curare, a mixture of chemicals extracted from a plant found in South America.	Tubocurarine competes with acetylcholine at receptors. It is used to paralyze patients in conjunction with anesthesia drugs prior to surgery.

PROBLEM 28.11

Propranolol (trade name Inderal) is an antagonist for certain epinephrine receptors and is a member of the class of drugs known as beta blockers (because they block what are known as beta receptors). Circle the functional groups in propranolol and name them. Compare the structure of propranolol with the structure of epinephrine and describe the differences.



Propranolol
(Inderal)



Epinephrine
(adrenaline)

PROBLEM 28.12

The LD_{50} values (lethal dose in mg/kg, for rats) for the three organophosphorus insecticides listed in this section are parathion, 3–13 mg/kg; diazinon, 250–285 mg/kg; and malathion, 1000–1375 mg/kg. (a) Find the molecular structures using the Internet. (b) Which would you choose for use in your garden and why? (c) Thinking about hydrophobic and hydrophilic, which is most dangerous for mammals to ingest? Why?

KEY CONCEPT PROBLEM 28.13

Some drugs are classified as agonists, whereas others are classified as antagonists.

(a) Sumatripan, sold as Imitrex, is effective in treating migraine headaches. It acts as an agonist at the serotonin receptor. Explain the effect Imitrex has on the serotonin receptor.

(b) Ondansetron, sold as Zofran, acts on a subclass of serotonin receptors to inhibit nausea and vomiting; it is frequently prescribed to patients in chemotherapy. It acts as an antagonist at these receptors. Explain the effect Zofran has on these receptors.

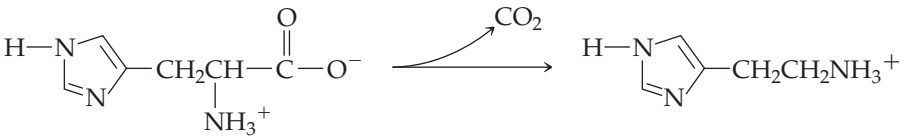
28.7 Histamines, Antihistamines, and Important Neurotransmitters

Learning Objective:

- Describe the neurotransmitters and types of drugs that play roles in allergies, mental depression, and drug addiction.

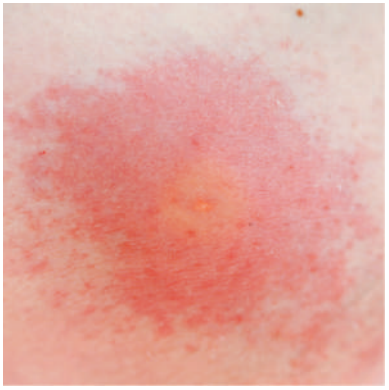
Histamine and Antihistamines

Histamine is the neurotransmitter responsible for the symptoms of the allergic reaction familiar to hay fever sufferers or those who are allergic to animals. It is also the chemical that causes an itchy bump when an insect bites you. In the body, histamine is produced by decarboxylation of the amino acid histidine.



Histidine

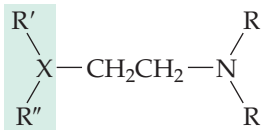
Histamine



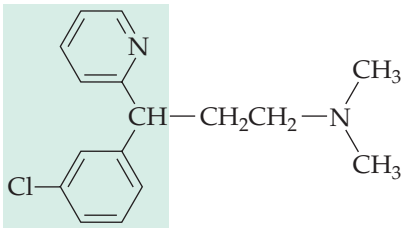
▲ The swelling and inflammation surrounding this insect bite are due to a histamine response.

The *antihistamines* are a family of drugs that counteract the effect of histamine because they are histamine-receptor antagonists. They competitively block the attachment of histamine to its receptors. Members of this family all have in common a

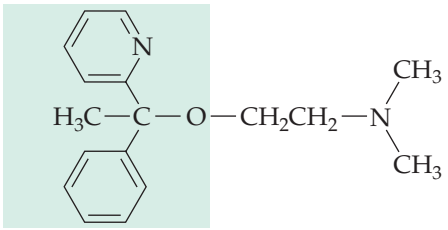
disubstituted ethanamine side chain, usually with two *N*-methyl groups. As illustrated by the following examples, the R′ and R″ groups at the other end of the molecule tend to be bulky and aromatic.



General antihistamine structure

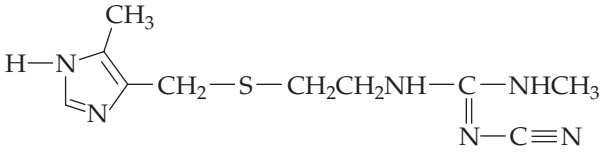


Chlorpheniramine
(an antihistamine)

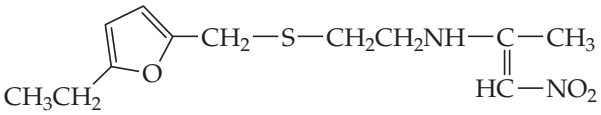


Doxylamine
(an antihistamine)

Histamine also activates secretion of acid in the stomach. After synthesis of about 200 different compounds with systematic variations on the histamine structure, a histamine antagonist was developed. The result was *cimetidine,* widely publicized as a treatment for heartburn under its trade name Tagamet. Today, many other histamine antagonists exist, including ranitidine, sold under its trade name Zantac.



Cimetidine
(Tagamet)

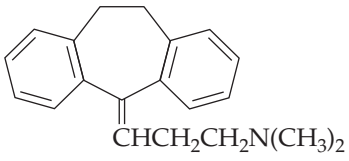


Ranitidine
(Zantac)

Serotonin, Norepinephrine, and Dopamine

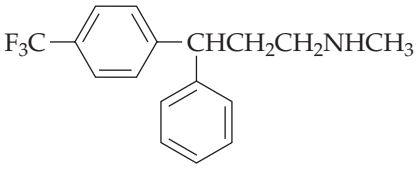
Serotonin, norepinephrine, and dopamine could be called the "big three" of neurotransmitters. Regular news reports appear as discoveries about them accumulate. Collectively, serotonin, norepinephrine, and dopamine are known as *monoamines*. Figures 28.4 and 28.6 show their biochemical syntheses. All are active in the brain and all are associated with mood, fear and pleasure, mental illness, and drug addiction.

The connection between major depression and a deficiency of serotonin, norepinephrine, and dopamine is well-established. The evidence comes from the different modes of action of three families of drugs used to treat depression: amitriptyline, phenelzine, and fluoxetine. Each in its own way increases the concentration of the neurotransmitters at synapses.



Amitriptyline, a tricyclic antidepressant
(Elavil)

Phenelzine, an MAO inhibitor
(Nardil)



Fluoxetine, an SSRI
(Prozac)

- Amitriptyline is representative of the *tricyclic antidepressants,* which were the first generation of these drugs. The tricyclics prevent the re-uptake of serotonin and norepinephrine from within the synapse. Serotonin is important in mood-control pathways and functions more slowly than other neurotransmitters; slowing its re-uptake often improves mood in depressed patients.
- Phenelzine is a *monoamine oxidase (MAO) inhibitor,* one of a group of medications that inhibit the enzyme that breaks down monoamine neurotransmitters. This inhibition of *MAO* allows the concentrations of monoamines at synapses to increase.

- Fluoxetine represents the newest class of antidepressants, the *selective serotonin re-uptake inhibitors (SSRI).* They are more selective than the tricyclics because they inhibit only the re-uptake of serotonin. Fluoxetine (Prozac) has rapidly become the most widely prescribed drug for all but the most severe forms of depression. Most antidepressants cause unpleasant side effects; fluoxetine does not, a major benefit.

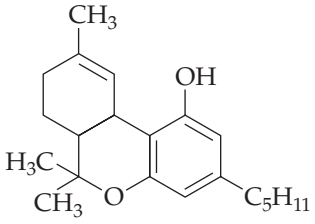
It is important to note that the relief of depression symptoms by these drugs is not evidence that the chemical basis of depression is fully understood nor that increasing neurotransmitter concentration is the only action of these drugs. The brain still holds many secrets. The use of fluoxetine for conditions other than depression illustrates the complex and not yet fully understood relationships between neurotransmitter activity and behavior. It is used to treat obsessive compulsive disorder, bulimia, obesity, panic disorder, body dysmorphic disorder, teen depression, and premenstrual dysphoric disorder (formerly known as PMS). New uses for this class of drugs are constantly being explored.

Dopamine and Drug Addiction

Dopamine plays a role in the brain in processes that control movement, emotional responses, and the experiences of pleasure and pain. It interacts with five different kinds of receptors in different parts of the brain. An oversupply of dopamine is associated with schizophrenia, and an undersupply results in the loss of fine motor control in Parkinson's disease (see the Chemistry in Action "The Blood–Brain Barrier," Chapter 29). Dopamine also plays an important role in the brain's reward system. An ample supply of brain dopamine produces the pleasantly satisfied feeling that results from a rewarding experience—a "natural high." Herein lies the role of dopamine in drug addiction: the more the dopamine receptors are stimulated, the greater the high.

Experiments show that cocaine blocks re-uptake of dopamine from the synapse, and amphetamines accelerate release of dopamine. Studies have linked increased brain levels of dopamine to alcohol and nicotine addiction as well. The higher-than-normal stimulation of dopamine receptors by drugs results in tolerance. In the drive to maintain constant conditions (see the Chemistry in Action "Homeostasis," p. 868), the number of dopamine receptors decreases and the sensitivity of those that remain decreases. Consequently, brain cells require more and more of a drug for the same result, a condition that contributes to addiction.

Marijuana also creates an increase in dopamine levels in the same brain areas where dopamine levels increase after administration of heroin or cocaine. The most-active ingredient in marijuana is tetrahydrocannabinol (THC). The use of marijuana medically for chronic pain relief has become a controversial topic in recent years, as questions about its benefits and drawbacks are debated.



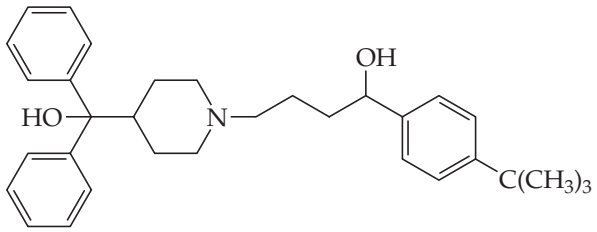
Tetrahydrocannabinol (THC)

KEY CONCEPT PROBLEM 28.14

Identify the functional groups present in THC. Is the molecule likely to be hydrophilic or hydrophobic? Would you expect THC to build up in fatty tissues in the body, or would it be readily eliminated in the urine?

Worked Example 28.2 Predicting Biological Activity Based on Structure

The relationship between the structure of a molecule and its biochemical function is an essential area of study in biochemistry and the design of drugs. Terfenadine (Seldane) was one of the first of the new generation of "nondrowsy" antihistamines (it was removed from the market due to potential heart toxicity). Based solely on what you have learned so far, suggest which of its structural features make it an antihistamine.



Terfenadine

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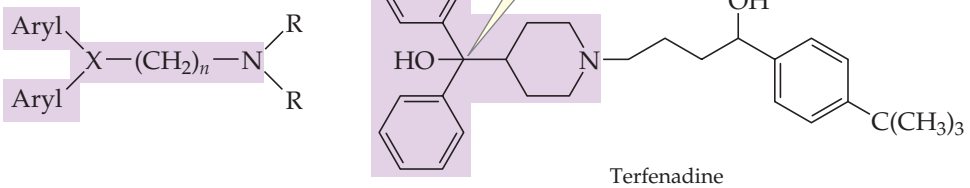
ANALYSIS Members of the antihistamine family have in common the general structure shown here: an X group (usually a CH) to which two aromatic groups (noted as *aryl* in the drawing) are attached. The X is also attached to a disubstituted nitrogen by a carbon chain.

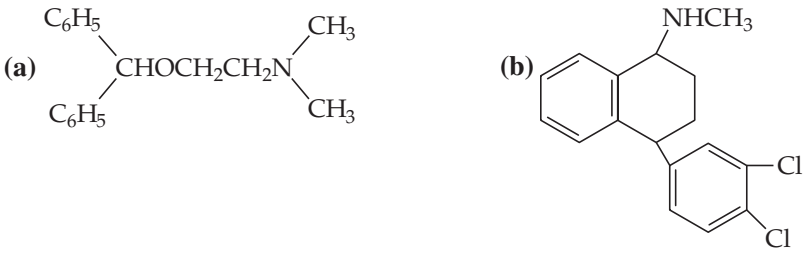


Terfenadine

SOLUTION
Since terfenadine contains the same basic structure as a general antihistamine, its biological function should be similar.

KEY CONCEPT PROBLEM 28.15

Predict which of the following compounds is an antihistamine and which is an antidepressant.



Neuropeptides and Pain Relief

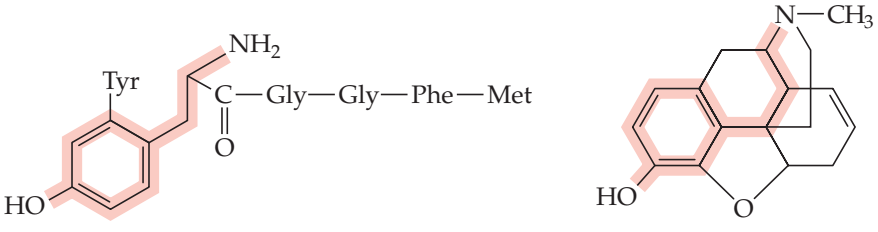
Studies of morphine and other opium derivatives in the 1970s revealed that these addictive but effective pain-killing substances act via their own specific brain receptors, raising some interesting questions: Why are there brain receptors for chemicals from a plant? Could it be that there are animal neurotransmitters that act at the same receptors?

The two pentapeptides, *Met-enkephalin* and *Leu-enkephalin* (Met and Leu stand for the carboxy terminal amino acids, Section 18.3), were discovered to exert morphine-like suppression of pain when injected into the brains of experimental animals.

Met-enkephalin: Tyr-Gly-Gly-Phe-**Met**

Leu-enkephalin: Tyr-Gly-Gly-Phe-**Leu**

The structural similarity between Met-enkephalin and morphine, highlighted in the following figure, supports the concept that both interact with the same receptors, which are located in regions of the brain and spinal cord that act in the perception of pain.



Met-enkephalin Morphine

Subsequently, about a dozen natural pain-killing polypeptides that act via the opiate receptors, classified as *endorphins,* have also been found. A 31-amino acid polypeptide that ends with the same 5-amino acid sequence as Met-enkephalin is one such endorphin and is a more potent pain suppressor than morphine.

HANDS-ON CHEMISTRY 28.1

In this exercise, you will track various biochemical responses during simple activities and may be able to identify some hormones and neurotransmitters discussed in this chapter like serotonin (a neurotransmitter molecule involved in mood or the sleep–wake cycle) or epinephrine (the flight-or-fight molecule that activates the secondary messenger cAMP).

For a few days, you will keep a log that correlates activity or inactivity to alertness.

1. On day one, right before class, record your alertness, mood, and how long it lasts. Also, rank your bodily functions using the following defined scale. Then, if you get a break during class, record your alertness, mood, and bodily functions again using the same scale.
2. Before class on day two, take a five minute walk and record your mood, alertness, and bodily functions. If the class takes a break, repeat the bodily function recording.
3. On day three, repeat day two but walk a little longer and record your alertness, mood, and bodily functions.
4. On day four, repeat day three but walk even longer, and record your alertness, mood, and bodily functions.

Use the following scale to record your bodily functions each day, where 1 = excellent, 2 = above average, 3 = average, 4 = below average, 5 = terrible, and 6 = no change.

Concentration	1	2	3	4	5	6
Heart rate	1	2	3	4	5	6
Cold hands	1	2	3	4	5	6
Quality of sleep	1	2	3	4	5	6
Frustration	1	2	3	4	5	6
Nausea	1	2	3	4	5	6
Headache	1	2	3	4	5	6
Change of appetite	1	2	3	4	5	6
Breathing	1	2	3	4	5	6

Now that you have collected some data; reflect on which hormones might be elevated or lowered and why. Some generalizations might be that if you have a headache or if your heart rate, breathing, and concentration levels are not normal, there could be increased levels of epinephrine or norepinephrine in your body. If your quality of sleep or appetite is affected, serotonin might be involved. In addition, cortisol has been known to give a feeling of nausea or cold hands.

If you are comfortable, discuss your findings with a classmate. Some points of discussion might be: Did your concentration levels change at all on a day you didn't get good sleep, or, did your mood improve at all after taking a walk? Did you notice your heart rate spike when you were frustrated? Can you conclude any patterns or connections that you observed?

SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Describe the origins, pathways, and actions of hormones.** *Hormones* are the chemical messengers of the *endocrine system.* Under control of the hypothalamus, they are released from various locations, many in response to intermediate, regulatory hormones. Hormones travel in the bloodstream to target cells, where they connect with receptors that initiate chemical changes within cells *(see Problems 22–27).*

- **Distinguish between the different types of hormonal control.** There are three basic types of hormonal control that allow communication between the endocrine system and other tissues: direct neural control, direct release of the hormone, and indirect control through the release of regulatory hormones. In direct neural control, a nervous system message from the hypothalamus initiates release of hormones by the adrenal gland. Direct release of the hormones involves their movement from the hypothalamus to the posterior pituitary gland, where they are stored until needed. Lastly, regulatory hormones from the hypothalamus stimulate or inhibit the release of hormones by the anterior pituitary gland. Many of these pituitary hormones in turn stimulate release of still other hormones by their own target tissues *(see Problems 28–31).*

- **List the different chemical types of hormones and give examples of each.** Hormones are *polypeptides, steroids,* or *amino acid derivatives* (Table 28.2). Many are polypeptides, which range widely in size and include small molecules such as vasopressin and oxytocin, larger ones like insulin, and all of the regulatory hormones. Steroids have a distinctive four-ring structure and are classified as lipids because they are hydrophobic. All of the sex hormones are steroids *(see Problems 32–35).*

- **Explain the sequence of events in epinephrine's action as a hormone.** Epinephrine, the fight-or-flight hormone, acts via a cell-surface receptor and a G protein that connects with an enzyme, both of which are embedded in the cell membrane. The enzyme adenylate cyclase transfers the message to a *second messenger,* a cyclic AMP, which acts within the target cell *(see Problems 36–45).*

- **Explain the functions of the three major types of hormones: amino acid derivatives, polypeptides, and steroids.** Hormones that are amino acid derivatives are *synthesized* from amino acids (Figures 28.4 and 28.6). Epinephrine and norepinephrine act as hormones throughout the body and also act as neurotransmitters in the brain. Polypeptide hormones are the largest class of hormones. Steroid hormones are classified as mineralcorticoids, glucocorticoids, or sex hormones. All three types are synthesized from the endocrine system *(see Problems 46–57).*

- **Describe the origins, pathways, and actions of neurotransmitters.** *Neurotransmitters* are synthesized in presynaptic neurons and stored there in vesicles for release when needed. They travel across a *synaptic cleft* to *receptors* on adjacent target cells. Some act directly via their receptors; others utilize cyclic AMP or other second messengers. After their message is delivered, neurotransmitters are either broken down rapidly or taken back into the presynaptic

neuron so that the receptor is free to receive further messages *(see Problems 58–67).*

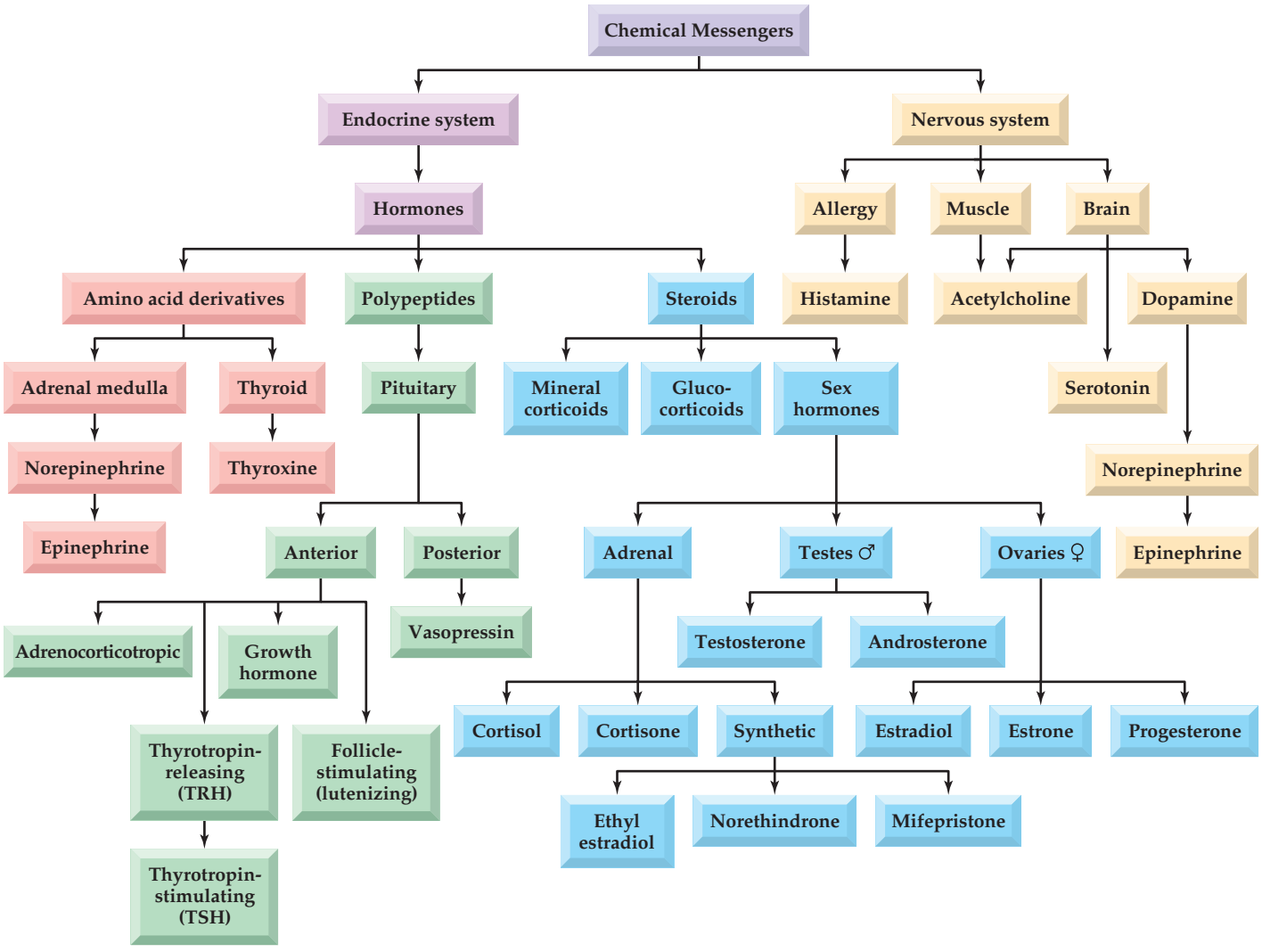
- **Outline the sequence of events in acetylcholine's action as a neurotransmitter and give examples of its agonists and antagonists.** Acetylcholine is released from the vesicles of a presynaptic neuron and connects with receptors that initiate continuation of a nerve impulse in the postsynaptic neuron. It is broken down in the synaptic cleft by acetylcholinesterase to form choline, which is returned to the presynaptic neuron and converted back to acetylcholine. *Agonists*, such as nicotine at low doses, activate acetylcholine receptors and are stimulants. *Antagonists,* such as tubocurarine or atropine, which block activation of the receptors, are toxic in high doses, but at low doses are useful as muscle relaxants *(see Problems 68–70).*

- **Describe the neurotransmitters and types of drugs that play roles in allergies, mental depression, drug addiction, and pain relief.** *Histamine,* an amino acid derivative, causes allergic symptoms. *Antihistamines* are antagonists with a general structure that resembles histamines but with bulky groups at one end. Monoamines (serotonin, norepinephrine, and dopamine) are brain neurotransmitters; a deficiency of any of these molecules is associated with mental depression. *Drugs* that increase their activity include *tricyclic antidepressants* (e.g., amitriptyline), *MAO inhibitors* (e.g., phenelzine), and *SSRI* (e.g., fluoxetine). An increase of dopamine activity in the brain is associated with the effects of most addictive substances. A group of neuropeptides acts as opiate receptors to counteract pain; all may be addictive *(see Problems 71–82).*

KEY WORDS

Acetylcholine, *p. 871*
Agonist, *p. 872*
Antagonist, *p. 872*
Drug, *p. 872*
Endocrine system, *p. 860*
Hormone, *p. 859*
Neurotransmitter, *p. 859*
Receptor, *p. 859*
Second messenger, *p. 862*
Synapse, *p. 869*

CONCEPT MAP



▲ **Figure 28.8 Concept Map.** This concept map shows the categorization of different types of hormones and neurotransmitters.

UNDERSTANDING KEY CONCEPTS

28.16 In many species of animals, at the onset of pregnancy, LH is released; it promotes the synthesis of progesterone—a major hormone in maintaining the pregnancy.

(a) Where is LH produced, and to what class of hormones does it belong?

(b) Where is progesterone produced, and to what class of hormones does it belong?

(c) Do progesterone-producing cells have LH receptors on their surface, or does LH enter the cell to carry out its function?

(d) Does progesterone bind to a cell-surface receptor, or does it enter the cell to carry out its function? Explain.

28.17 The "rush" of epinephrine in response to danger causes the release of glucose in muscle cells so that those muscles can carry out either "fight-or-flight." Very small amounts of the hormone produced in the adrenal gland cause a powerful response. To get such a response, the original signal (epinephrine) must be amplified many times. At what step in the sequence of events (Section 28.3) would you predict that the signal is amplified? Explain. How might that amplification take place?

28.18 Diabetes occurs when there is a malfunction in the uptake of glucose from the bloodstream into the cells. Your friend's youngest brother was just diagnosed with type I diabetes, and she has asked you the following questions. How would you answer them?

(a) What hormone is involved, and what class is it?

(b) Where is the hormone released?

(c) How is this hormone transported to the cells that need it to allow glucose to enter?

(d) Would you expect the hormone to enter the cell to carry out its function? Explain.

28.19 Give two mechanisms by which neurotransmitters exert their effects.

28.20 When an impulse arrives at the synapse, the synaptic vesicles open and release neurotransmitters into the cleft within a thousandth of a second. Within another ten thousandth of a second, these molecules have diffused across the cleft and bound to receptor sites in the effector cell. In what two ways is transmission across a synapse terminated so that the neuron's signal is concluded?

28.21 What is the significance of dopamine in the addictive effects of cocaine, amphetamines, and alcohol?

ADDITIONAL PROBLEMS

CHEMICAL MESSENGERS (SECTION 28.1)

28.22 What do the terms *chemical messenger, target tissue,* and *hormone receptor* mean?

28.23 What is a hormone? What is the function of a hormone? How is the presence of a hormone detected by its target?

28.24 What is the main difference between a hormone and a vitamin?

28.25 What is the main difference between a hormone and a neurotransmitter?

28.26 Is a hormone changed as a result of binding to a receptor? Is the receptor changed as a result of binding the hormone? What are the binding forces between hormone and receptor?

28.27 How is hormone binding to its receptor more like an allosteric regulator binding to an enzyme than a substrate binding to an enzyme?

HORMONES AND THE ENDOCRINE SYSTEM (SECTION 28.2)

28.28 What is the purpose of the body's endocrine system?

28.29 Name as many endocrine glands as you can.

28.30 List the three major classes of hormones.

28.31 Give two examples of each of the three major classes of hormones.

28.32 What is the structural difference between an enzyme and a hormone?

28.33 What is the relationship between enzyme specificity and tissue specificity for a hormone?

28.34 Describe in general terms how a peptide hormone works.

28.35 Describe in general terms how a steroid hormone works.

HOW HORMONES WORK: EPINEPHRINE (SECTION 28.3)

28.36 In what gland is epinephrine produced and released?

28.37 Under what circumstances is epinephrine released?

28.38 How does epinephrine reach its target tissues?

28.39 What is the main function of epinephrine at its target tissues?

28.40 In order of their involvement, name the three membrane-bound proteins involved in transmitting the epinephrine message across the cell membrane.

28.41 What is the "second messenger" inside the cell that results from the epinephrine message? Is the ratio of epinephrine molecules to second messenger less than 1:1, 1:1, or greater than 1:1? Explain.

28.42 What role does the second messenger play in a cell stimulated by epinephrine?

28.43 What enzyme catalyzes hydrolysis of the second messenger to terminate the message? What is the product called? (Hint: Consult Figure 28.2.)

28.44 Epinephrine is used clinically in the treatment of what life-threatening allergic response? (Hint: Think about the use of the EpiPen.)

28.45 People susceptible to anaphylactic shock due to insect stings or certain food allergies must be prepared to treat themselves in case of exposure. How are they prepared and what must they do?

HORMONES (SECTION 28.4)

28.46 Give an example of a polypeptide hormone. How many amino acids are in the hormone? Where is the hormone released? Where does the hormone function? What is the result of the hormone message?

28.47 Give an example of a steroid hormone. What is the structure of the hormone? Where is the hormone released? Where does the hormone function? What is the result of the hormone message?

28.48 What do the three major classes of steroid hormones have in common?

28.49 What molecules are the steroid hormones derived from? How does that make the physical properties of steroid hormones different from the other hormones?

28.50 Name the two primary male sex hormones.

28.51 Name the three principal female sex hormones.

28.52 Until relatively recently, the use of androgens by athletes was a common, legal practice. What are the advantages of using androgens during athletic training and competition?

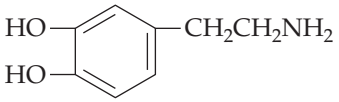
28.53 The use of androgens during athletic training and competition has been banned in national and international sports. What are the disadvantages of using androgens during athletic training and competition?

28.54 List two hormones that also function as neurotransmitters.

28.55 Explain why epinephrine can act as both a neurotransmitter and a hormone without "crossover" between the two functions.

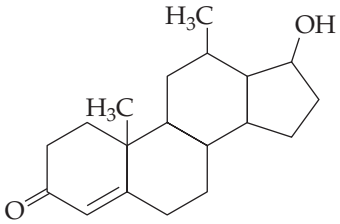
28.56 Identify the class to which each of these following hormones belongs:

(a)



(b) Insulin

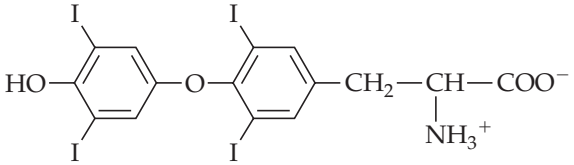
(c)



28.57 Identify the class to which each of these following hormones belongs:

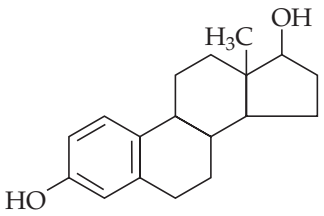
(a) Glucagon

(b)



Thyroxine

(c)



Estradiol

NEUROTRANSMITTERS (SECTION 28.5)

28.58 What is a synapse, and what role does it play in nerve transmission?

28.59 What is an axon, and what role does it play in nerve transmission?

28.60 List three cell types that might receive a message transmitted by a neurotransmitter.

28.61 What kinds of cellular or organ actions would you expect to be influenced by neurotransmitters?

28.62 Describe in general terms how a nerve impulse is passed from one neuron to another.

28.63 What are the two methods for removing the neurotransmitter once its job is done?

28.64 List the three steps in chemical transmission of the impulse between a nerve cell and its target.

28.65 Write an equation for the reaction that is catalyzed by acetylcholinesterase.

28.66 Why are enkephalins sometimes called *neurohormones*?

28.67 Outline the six steps in cholinergic nerve transmission.

CHEMICAL MESSENGERS AND DRUGS (SECTION 28.6)

28.68 Describe the difference between drugs that are agonists and those that are antagonists.

28.69 Give an example of a drug that acts as an agonist for acetylcholine receptors and one that acts as an antagonist for these receptors.

28.70 Give an example of a drug from each family in Problem 28.69.

HISTAMINES, ANTIHISTAMINES, AND IMPORTANT NEUROTRANSMITTERS, NEUROPEPTIDES, AND PAIN RELIEF (SECTION 28.7)

28.71 Give examples of two histamine antagonists that have very different tissue specificities and functions.

28.72 Name three families of drugs used to treat depression.

28.73 Name the "big three" monoamine neurotransmitters.

28.74 What is the impact and mode of action of cocaine on dopamine levels in the brain?

28.75 What is the impact and mode of action of amphetamines on dopamine levels in the brain?

28.76 How is the THC of marijuana similar in action to heroin and cocaine?

28.77 Why do we have brain receptors that respond to morphine and other opium derivatives from plants?

28.78 In schizophrenia, the neurons affected by dopamine are overstimulated. This condition is treated with drugs like chlorpromazine (Thorazine), which bind to the affected receptors and inhibit the dopamine signal. Does chlorpromazine act as an agonist or antagonist?

28.79 Methamphetamine "highs" often are accompanied by behavioral changes that resemble schizophrenia. Does methamphetamine act as an agonist or antagonist?

28.80 What are endorphins? Where in the body are they found?

28.81 Enkephalins and endorphins are referred to as "nature's opiates." Explain this saying.

28.82 Why might it be an advantage for an animal to produce its own pain-suppressing molecules?

CONCEPTUAL PROBLEMS

28.83 Suppose you are hiking in the Alaskan wilderness when your path crosses that of a bear. What hormone is responsible for your immediate response?

28.84 How do curare-treated arrows work?

28.85 What characteristics in their mechanism of action does thyroxine share with the steroid hormones?

28.86 List and describe the functions of the three types of proteins involved in transmission of a hormone signal.

28.87 The cyclic AMP (second messenger) of signal transmission is very reactive and breaks down rapidly after synthesis. Why is this important to the signal-transmission process?

28.88 We say that there is signal amplification in the transmission process. Explain how signal amplification occurs and what it means for transmission of the signal to the sites of cellular activity.

28.89 Compare the structures of the sex hormones testosterone and progesterone. What portions of the structures are the same? Where do they differ?

28.90 When you compare the structures of ethynyl estradiol to norethindrone, where do they differ? Where is ethynyl estradiol similar to estradiol? Where is norethindrone similar to progesterone?

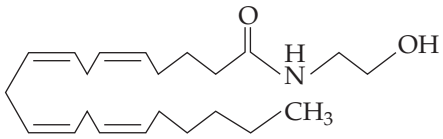
28.91 Identify the structural changes that occur in the first two steps in the conversion of tyrosine to epinephrine (Figure 28.4). To what main classes and subclasses of enzymes do the enzymes that catalyze these reactions belong?

28.92 Look at the structures of the two male sex hormones shown on page 867. Identify the type of functional group change that interconverts testosterone and androsterone. To which class of chemical reactions does this change belong?

28.93 Look at the structures of the three female sex hormones shown on page 867. Identify the type of functional group change that interconverts estradiol and estrone. To which class of chemical reactions does this change belong?

GROUP PROBLEMS

28.94 Anandamides have been isolated from brain tissues and appear to be the natural ligand for the receptor that also binds THC. Anandamides have also been discovered in chocolate and cocoa powder. How might the craving for chocolate be explained?



An anandamide structure

28.95 The phosphodiesterase that catalyzes hydrolysis of cyclic AMP is inhibited by caffeine. What overall effect would caffeine have on a signal that is mediated by cAMP?

29

Body Fluids

CONTENTS

CONCEPTS TO REVIEW

A. Solutions (Sections 9.1, 9.2, and 9.9)
B. Osmosis and Osmotic Pressure (Section 9.10)
C. Dialysis (Section 9.11)
D. pH (Sections 10.5 and 10.6)

▲ An annual blood test can alert your doctor to medical problems before they become life-threatening.

When you were young, going to the doctor's office was something you did when you were sick, and if you had blood drawn it was because your physician was looking for the cause of your illness. As we get older, the need to see a doctor once a year for an annual checkup becomes more important as a preventative measure, and with that comes blood work. But what exactly is your doctor screening for, and why? Blood is the one fluid that touches every part of your body, and in it are clues to the health of your heart, kidneys, liver, and other

organs. In the Chemistry in Action "What's in a Blood Test?," we will examine what is being looked at in a typical blood panel and what variations from normal can mean. For example, why are calcium levels being measured in a comprehensive metabolic panel (CMP)? Or what is a lipid panel screening looking for? Or what is the purpose of a fasting blood glucose analysis?

We have chosen to discuss body fluids last in your text because just about every aspect of chemistry you have studied so far applies to them. Electrolytes, nutrients and waste products, metabolic intermediates, and chemical messengers flow through your body in blood and in lymph fluid and exit as waste in the urine and feces. The chemical compositions of blood and urine mirror chemical reactions throughout the body. Fortunately, samples of these fluids are easily collected and studied. Many advances in understanding biological chemistry have been based on information obtained from analysis of blood and urine. As a result, studies of blood and urine chemistry provide information essential for the diagnosis and treatment of disease.

29.1 Body Water and Its Solutes

Learning Objective:

- Describe the major categories of body fluids, their composition, and the exchange of solutes between them.

The water content of the human body averages about 60% (by mass). Physiologists describe body water as occupying two different "compartments"—the *intracellular* and the *extracellular* compartments. We have looked primarily at the chemical reactions occurring in the **intracellular fluid** (the fluid inside cells), which includes about two-thirds of all body water (Figure 29.1). We now turn our attention to the remaining one-third of body water, the **extracellular fluid,** which includes mainly **blood plasma** (the fluid portion of blood) and **interstitial fluid** (the fluid that fills the spaces between cells).

To be soluble in water, a substance must be an ion, a gas, a small polar molecule, or a large molecule having many polar, hydrophilic or ionic groups on its surface. All four types of solutes are present in body fluids. The majority are inorganic ions and ionized biomolecules (mainly proteins); this is depicted in Figure 29.2. Although these fluids have different compositions, their **osmolarities** are the same; that is, they have the same number of moles of dissolved solute particles (ions or molecules) per liter. The osmolarity is kept in balance by the passage of water across cell membranes by osmosis, which occurs in response to osmolarity differences.

Inorganic ions, known collectively as *electrolytes* (Section 9.8), are major contributors to the osmolarity of body fluids and they move about as necessary to maintain charge balance. Water-soluble proteins make up a large proportion of the solutes in blood plasma and intracellular fluid; 100 mL of blood contains about 7 g of protein. Blood proteins are used to transport lipids and other molecules, and they play essential roles in blood clotting (Section 29.5) and the immune response (Section 29.4). The blood gases (oxygen and carbon dioxide), along with glucose, amino acids, and the nitrogen-containing by-products of protein catabolism, are the major small molecules in body fluids.

Blood travels through peripheral tissue in a network of tiny, hair-like capillaries that connect the arterial and venous parts of the circulatory system (Figure 29.3). This is where nutrients and end products of metabolism are exchanged between blood and interstitial fluid. Water and many small solutes move freely across the capillary walls in response to differences in fluid pressure and concentration (see Figure 29.3).

Solutes that can cross membranes freely (passive diffusion) move from regions of high solute concentration to regions of low solute concentration. On the arterial ends of capillaries, blood pressure is higher than interstitial fluid pressure and solutes and water are pushed into interstitial fluid. On the venous ends of the capillaries, blood pressure is lower, and water and solutes from the surrounding tissues are able to reenter the blood plasma. Except for protein content, blood plasma and interstitial fluid are similar in composition (Figure 29.2).

Intracellular fluid Fluid inside cells.

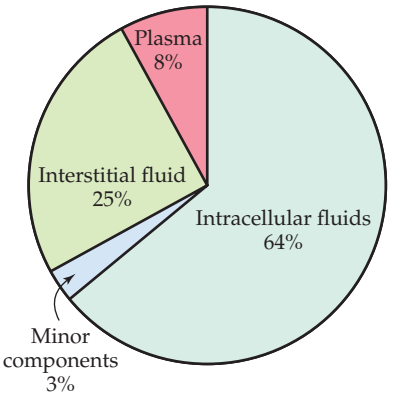
Extracellular fluid Fluid outside cells.

Blood plasma Liquid portion of the blood: An extracellular fluid.

Interstitial fluid Fluid surrounding cells: An extracellular fluid.

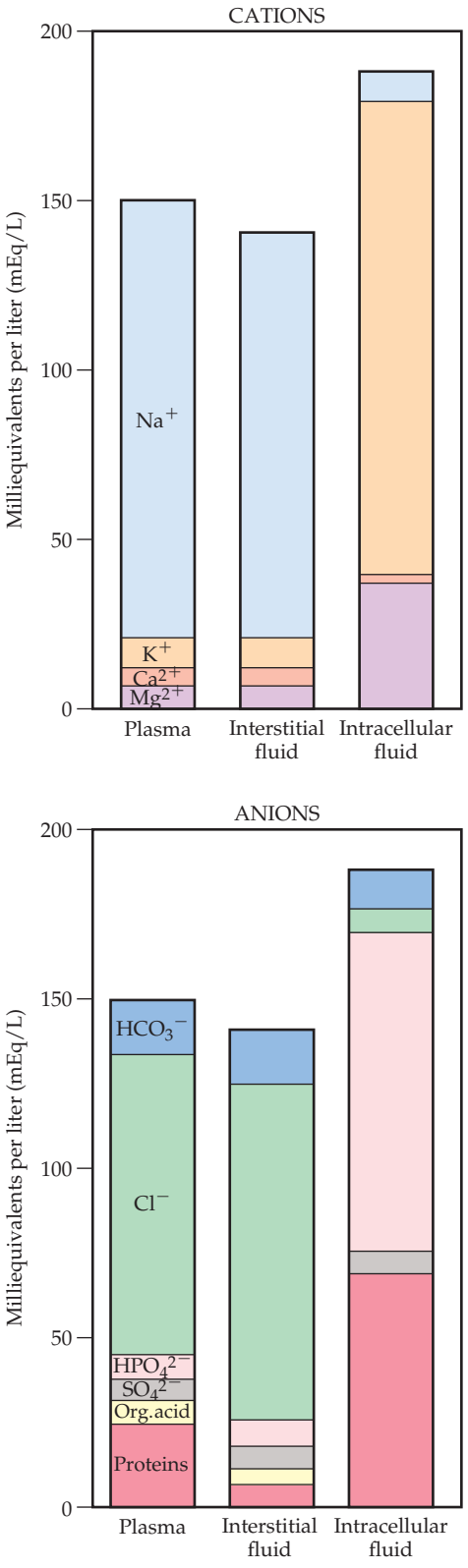
Osmolarity Amount of dissolved solute per volume of solution.

CONCEPTS TO REVIEW The concept of hydrophilic and hydrophobic groups was discussed in Section 14.3, and the idea of ionized biomolecules was discussed in the Chemistry in Action "Medications, Body Fluids, and the 'Solubility Switch,'" found in Chapter 17.

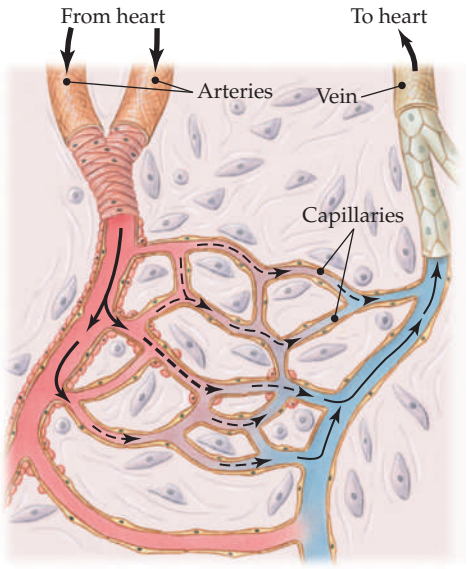


▲ **Figure 29.1**
Distribution of body water. About two-thirds of body water is intracellular—within cells. The extracellular fluids include blood plasma, fluids surrounding cells (interstitial), and such minor components as lymph, cerebrospinal fluid, and the fluid that lubricates joints (synovial fluid).

In osmosis, water moves across a semipermeable membrane from the more dilute solution to the more concentrated solution (see Section 9.10).



▲ **Figure 29.2**
The distribution of cations and anions in body fluids.
Outside cells, Na^+ is the major cation and Cl^- is the major anion. Inside cells, K^+ is the major cation and HPO_4^{2-} is the major anion. Note that at physiological pH, proteins are negatively charged.



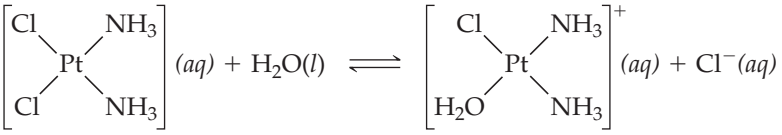
▲ **Figure 29.3**
The capillary network.
Solute exchange between blood and interstitial fluid occurs across capillary walls.

Additionally, peripheral tissue is networked with lymph capillaries (Figure 29.4). The lymphatic system collects excess interstitial fluid, debris from cellular breakdown, and proteins and lipid droplets too large to pass through capillary walls. Interstitial fluid and the substances that accompany it into the lymphatic system are referred to as *lymph,* and the walls of lymph capillaries are constructed so that lymph cannot return to the surrounding tissue. Ultimately, lymph enters the bloodstream at the thoracic duct.

Exchange of solutes between the interstitial fluid and the intracellular fluid occurs by crossing cell membranes. Here, major differences in concentration are maintained by active transport (transport requiring energy) *against* concentration gradients (from regions of *low* concentration to regions of *high* concentration) and by the impermeability of cell membranes to certain solutes, notably the sodium ion (Figure 29.5). Sodium ion concentration is high in extracellular fluids and low in intracellular fluids, whereas potassium ion concentrations are just the reverse: high inside cells and low outside cells (see Figure 29.2).

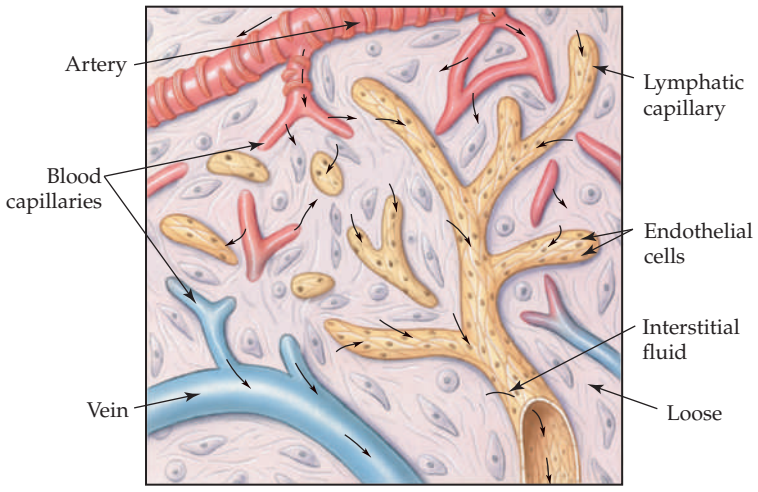
KEY CONCEPT PROBLEM 29.1

The drug cisplatin is used to treat various forms of cancer in humans. As with many other drugs, the difficult part in designing the cisplatin molecule was to have a structure that ensures transport into the cell. The equilibrium reaction that takes place in the body when cisplatin is administered is

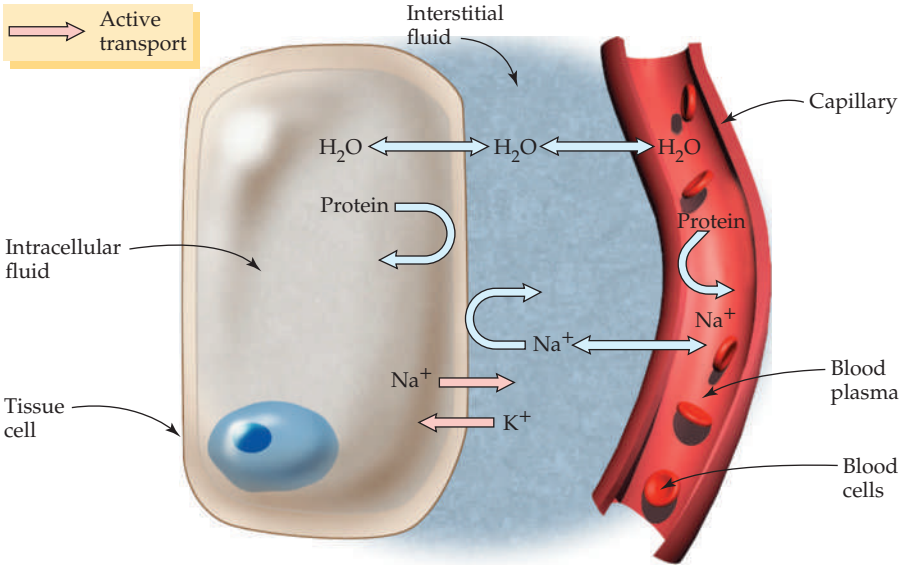


Cisplatin Monoaquacisplatin

Which form of cisplatin would you expect to exist inside the cell (where chloride concentrations are small)? Which form of cisplatin would you expect to exist outside the cell (where chloride concentrations are high)? Which form—cisplatin or monoaquacisplatin—enters the cell most readily? Why?



◂ **Figure 29.4**
Blood and lymph capillaries.
The arrows show the flow of fluids in and out of the various components of peripheral tissue.



◂ **Figure 29.5**
Exchange among body fluids.
Water exchanges freely in most tissues, with the result that the osmolarities of blood plasma, interstitial fluid, and intracellular fluid are the same. Large proteins cross neither capillary walls nor cell membranes, leaving the interstitial fluid protein concentration low. Concentration differences between interstitial fluid and intracellular fluid are maintained by active transport of Na^+ and K^+.

29.2 Fluid Balance

Learning Objective:

- Discuss how fluid balance is maintained.

Preserving fluid balance—a constant amount of fluid in the body—is crucial in maintaining physiological homeostasis. One way to accomplish this is by ensuring that daily intake and output of water are roughly equal as shown in Table 29.1.

What are the physiological effects if this delicate balance is not maintained—a question especially important to endurance athletes. During the course of a typical event, especially when performed in the heat, much fluid loss occurs with minimal fluid intake to counter it. Shown in Table 29.2, this typically results in a loss of body mass during the event and makes it easy to monitor performance versus fluid loss.

Exercise physiologists consider 4% body mass loss and above to be the "danger zone." In fact, the sports drink Gatorade was developed in 1965 for just this reason. Doctors at the University of Florida developed the original formula to solve a serious problem for

Table 29.1 Adult Human Daily Average Water Intake/Output

Water Intake (mL/day)		Water Output (mL/day)	
Drinking water	1200	Urine	1400
Water from food	1000	Skin	400
Water from metabolic oxidation of food	300	Lungs	400
		Sweat	100
		Feces	200
Total	2500		2500

Table 29.2 Effects of Body Mass Loss during Athletic Endurance Events

Body Mass Loss (%)	Symptoms and Performance
0	Normal heat regulation and performance
1	Thirst is stimulated, heat regulation during exercise is altered, performance begins to decline
2–3	Further decrease in heat regulation, increased thirst, worsening performance
4	Exercise performance cut by 20–30%
5	Headache, irritability, "spaced-out" feeling, fatigue
6	Weakness, severe loss of thermoregulation
7	Collapse is likely unless exercise is stopped

the school's football team—dehydration. This formula was so successful that by 1968, Gatorade had become the official sports drink of the National Football League and today commands a major share of the sports-drink market, with gross sales of over $800 million per year. One can see why research into hydration strategies has led to the plethora of "sports drinks" that are now available in your local supermarket. See the Chemistry in Action "Electrolytes, Fluid Replacement, and Sports Drinks" on p. 308.

Physiologically, the intake of water and electrolytes is regulated, but not closely. However, the output of these substances *is very* closely controlled. Both the intake and output of water are controlled by hormones. Receptors in the hypothalamus monitor the concentration of solutes in blood plasma, and as little as a 2% change in osmolarity can cause an adjustment in hormone secretion. For example, when a rise in blood osmolarity indicates an increased concentration of solutes and therefore a shortage of water, secretion of *antidiuretic hormone* (ADH; also known as *vasopressin*) increases. One key role of the kidneys is to keep water and electrolytes in balance by increasing or decreasing the amounts eliminated. In the kidneys, ADH causes a decrease in the water content of the urine. At the same time, osmoreceptors in the hypothalamus and baroreceptors in the heart and blood vessels activate the thirst mechanism, triggering increased water intake.

ADH is so tightly regulated that both oversecretion and undersecretion of this hormone can lead to serious disease states. Excess secretion can lead to what physicians refer to as the *syndrome of inappropriate ADH secretion (SIADH)*. Two of the many causes of SIADH are regional low blood volume arising from decreased blood return to the heart (caused by, for example, asthma, pneumonia, pulmonary obstruction, or heart failure) and misinterpretation by the hypothalamus of osmolarity (due, for example, to central nervous system disorders, barbiturates, or morphine). When ADH secretion is too high, the kidney excretes too little water, the water content of body compartments increases, and serum concentrations of electrolytes drop to dangerously low levels.

The reverse problem, inadequate secretion of ADH, is often a result of injury to the hypothalamus and causes *diabetes insipidus*. In this condition (unrelated to diabetes mellitus), up to 15 L of dilute urine is excreted each day. Administration of synthetic hormone can control the problem.

HANDS-ON CHEMISTRY 29.1

Sports drinks and sports energy bars have become an important part of the athletics scene. With claims of better energy, better performance, and faster recovery, these hydrating sports drinks and snack bars have moved from athletic field into the consumer marketplace. But are the claims that these companies make warranted? In this exercise, you will examine what is in these products and what the science behind them is. You will need to have an internet connection to fully carry out this activity. For this exercise, disregard the so-called energy shots or energy drinks so popular on college campuses today.

a. The American College of Sports Medicine (ACSM) (www.acsm.org) has done extensive studies on selecting and effectively using sports drinks and energy bars; use the ACSM as your primary source of information. First off, begin by looking at exactly what a sports drink is. What is typically found in one? What are the ingredients purported to do? What considerations should be made in selecting one? Would simply drinking water be just as good?

b. Now, consider sports energy bars. What is found in a typical energy bar? What considerations should be made in selecting one? Most energy bars have a high glycemic index. What does this mean and why is it so attractive for an energy bar to have a high index?

c. Finally, based on what you discovered in parts a and b, do you think it is wise for an average person to consume sports drinks and energy bars on a regular basis? Why or why not? By average we mean someone who is not a runner or an endurance athlete; someone who is moderately active, perhaps like yourself.

29.3 Blood

Learning Objective:

- Describe the composition and functions of blood.

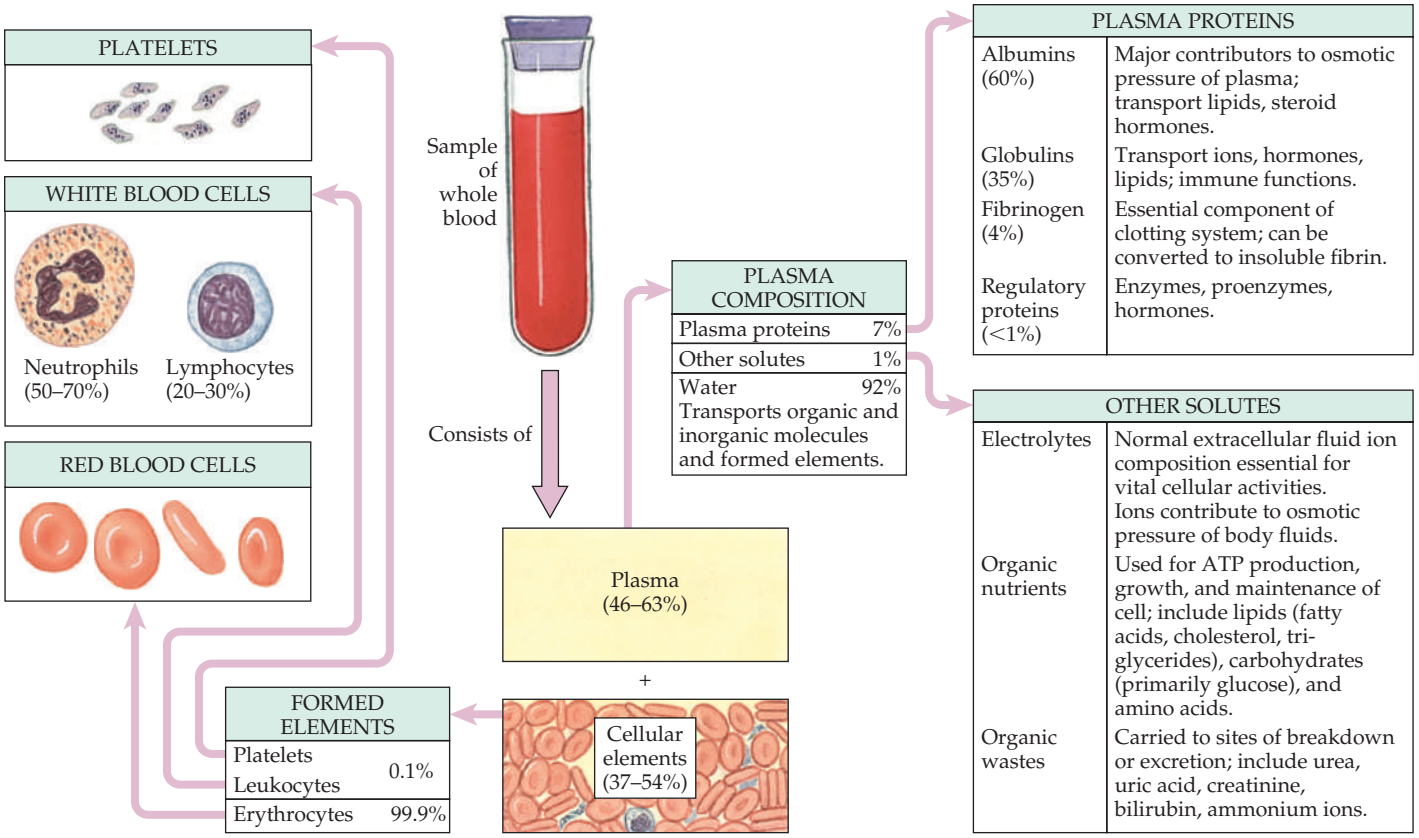
Blood flows through the body in the circulatory system, which in the absence of trauma or disease, is essentially a closed system. About 55% of blood is plasma, which contains the proteins and other solutes shown in Figure 29.6; the remaining 45% is a mixture of red blood cells (**erythrocytes;** RBCs), platelets, and white blood cells (**leukocytes;** WBCs).

Erythrocytes Red blood cells (RBCs); transporters of blood gases.

Leukocytes White blood cells (WBCs).

Whole blood Blood plasma plus blood cells.

The plasma and cells together make up **whole blood,** which is what is usually collected for clinical laboratory analysis. The whole blood sample is collected directly into evacuated tubes that contain an anticoagulant to prevent clotting (which would normally occur within 20–26 minutes at room temperature). Typical anticoagulants include heparin (which interferes with the action of enzymes needed for clotting) and citrate or oxalate ion (either of which form precipitates with calcium ion, which is also needed for blood clotting, thereby removing it from solution). Plasma is separated from blood cells by spinning the sample in a centrifuge, which causes the blood cells to clump together at the bottom of the tube, leaving the plasma at the top.



▲ **Figure 29.6**
The composition of whole blood.

Many laboratory analyses are performed on **blood serum,** the fluid remaining after blood has completely clotted. Blood serum composition is not the same as that of blood plasma—as we'll see in Section 29.5, blood clots are not simply clumps of cells, but also include networks of protein that originated from the plasma. When a serum sample is desired, whole blood is collected in the presence of an agent that hastens clotting. Thrombin, a natural component of the clotting system, is often used for this purpose. Centrifugation separates the clot and cells to leave behind the serum.

Blood serum Fluid portion of blood remaining after clotting has occurred.

Major Components of Blood

- **Whole blood**
  - **Blood plasma**—fluid part of blood containing water-soluble solutes
  - **Blood cells** —RBCs (carry gases)
    —WBCs (part of immune system)
    —platelets (help to initiate blood clotting)
- **Blood serum**—fluid portion of plasma left after blood has clotted

Table 29.3 summarizes the functions of the major protein and cellular components of blood. These functions fall into three categories.

Table 29.3 Protein and Cellular Components of Blood

Blood Component	Function
Proteins	
Albumins	Transport lipids, hormones, drugs; major contributor to plasma osmolarity
Globulins	
Immunoglobulins (γ-globulins, antibodies)	Identify antigens (microorganisms and other foreign invaders) and initiate their destruction
Transport globulins	Transport lipids and metal ions
Fibrinogen	Forms fibrin, the basis of blood clots
Blood cells	
RBCs (erythrocytes)	Transport O_2, CO_2, and H^+
WBCs (leukocytes)	
Lymphocytes	Defend against specific pathogens and foreign substances (T cells and B cells)
Phagocytes	Carry out phagocytosis—engulf foreign invaders (neutrophils, eosinophils, and monocytes)
Basophils	Release histamine during inflammatory response of injured tissue
Platelets	Help to initiate blood clotting

Major Functions of Blood

- **Transport** The circulatory system is the body's equivalent of an interstate highway network, transporting materials from where they enter the system to where they are used or disposed of. Oxygen and carbon dioxide are carried to and from different body parts by RBCs. Nutrients are carried from the intestine to the sites of their catabolism. Waste products of metabolism are carried to the kidneys. Hormones from endocrine glands are delivered to their target tissues.
- **Regulation** Blood redistributes body heat as it flows along, thereby participating in the regulation of body temperature. It also picks up or delivers water and electrolytes as they are needed. In addition, blood buffers are essential to the maintenance of acid-base balance.
- **Defense** Blood carries the molecules and cells needed for two major defense mechanisms: (1) the immune response, which destroys foreign invaders, and (2) blood clotting, which prevents loss of blood and begins the healing of wounds.

CHEMISTRY IN ACTION

The Blood–Brain Barrier

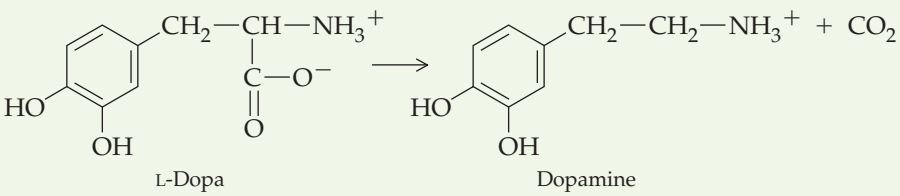
Nowhere in human beings is the maintenance of a constant internal environment more important than in the brain. Because of the fluctuations in blood concentrations of hormones, amino acids, neurotransmitters, and potassium that occur elsewhere in the body, the brain must be rigorously isolated from variations in blood composition.

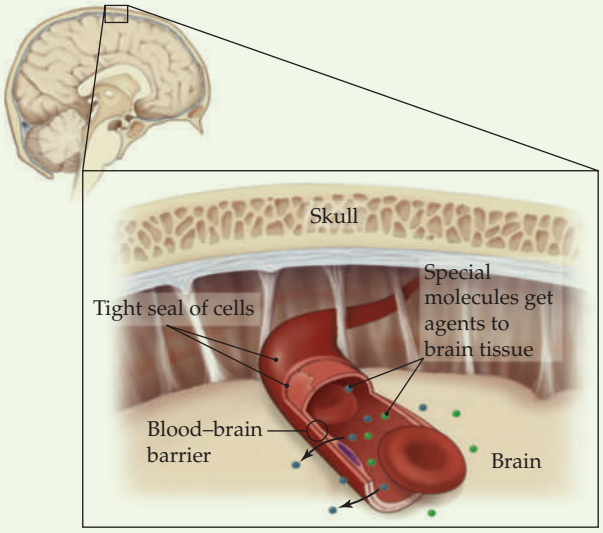
How can the brain receive nutrients from the blood in capillaries and yet be protected? The answer lies in the unique structure of the *endothelial cells* that form the walls of brain capillaries. Unlike the cells in most other capillaries, those in brain capillaries form a series of continuous tight junctions so that nothing can pass between them. To reach the brain, therefore, a substance must cross this blood–brain barrier (BBB) by crossing the endothelial cell membranes. The BBB serves as internal protection for the brain just as the skull serves as the brain's external protection. Scientists have come to the realization that the BBB is itself a vital organ and have begun calling it the neurovascular unit. Finding ways to breach this barrier will undoubtedly lead to new cures for many diseases, from brain cancers to Alzheimer's disease.

Consider glucose, the main source of energy for brain cells. It must have a way to cross the barrier. Also, certain amino acids the brain cannot manufacture must be recognized and brought across the cell membranes; all of this indicates that specific transporters must exist to move substances in and out of the brain. Glycine is another example of a substance that must cross the barrier. As a small amino acid that is a potent neurotransmitter, an asymmetric (one-way) transport system exists for it. Glycine inhibits rather than activates transmission of nerve signals, and its concentration must be held at a lower level in the brain than in the blood. To accomplish this, there is a glycine transport system in the cell membrane closest to the brain, but no matching transport system on the other side. Thus, glycine can be transported out of the brain but not into it.

The brain is also protected by a "metabolic" BBB. In this case, a compound that gets into an endothelial cell is converted within the cell to a metabolite that is unable to enter the brain. A striking demonstration of the metabolic brain barrier is provided by *dopamine,* a neurotransmitter, and L-*dopa,* a metabolic precursor of dopamine.

L-Dopa can both enter and leave the brain because it is recognized by one of these transport systems. However, the brain is protected from an excess of L-dopa entering by its conversion to dopamine within the endothelial cells of the BBB. Like glycine, dopamine, which is also produced from L-dopa within the brain, can leave the brain but cannot enter it. The dopamine deficiency that occurs in Parkinson's disease is therefore treated by administration of L-dopa.





▲ The blood–brain barrier.

Since crossing the endothelial cell membrane is the route into the brain, substances soluble in the membrane lipids readily breach the BBB. Think about heroin, which differs from morphine in having two nonpolar acetyl groups where the morphine has polar hydroxyl groups (Table 16.2). The resulting difference in lipid solubility allows heroin to enter the brain much more efficiently than morphine. Once inside the brain, enzymes remove the acetyl groups to produce morphine, and in doing so, trap it in the brain. For a long time, scientists believed that the BBB was an inviolable wall that should not be meddled with; now finding ways to breach the BBB is of major concern to medicinal chemists. For example, brain tumors are currently treated with either radiation or surgery, as the chemical agents used to typically treat cancer cannot cross the BBB. Researchers have begun to examine *chimeric therapeutics,* materials that are half drug (which do not cross the BBB) and half "molecular Trojan horse" (genetically engineered proteins that do cross the BBB). This strategy has been shown to work in mice, but human trials are still off in the future. As our understanding of this crucial barrier unfolds, we can expect many advances in the treatment of diseases of the brain that thus far have been treatable by only the most invasive of techniques.

CIA Problem 29.1 What is meant by an asymmetric transport system? Give one specific example of such a system.

CIA Problem 29.2 What type of substance is likely to breach the BBB? Would ethanol be likely to cross this barrier? Why or why not?

CIA Problem 29.3 What is the metabolic BBB?

CIA Problem 29.4 Heroin is better able to cross the BBB than morphine. Looking at the structures of these two molecules (refer to Table 16.2), circle the areas where they differ and why this explains the difference between the potencies of heroin and morphine as analgesics.

PROBLEM 29.2

Match each term in the (a)–(e) group with its definition from the (i)–(v) group.

(a) Interstitial fluid	**(i)** Fluid that remains when blood cells are removed
(b) Whole blood	**(ii)** Fluid, solutes, and cells that together flow through veins and arteries
(c) Blood serum	**(iii)** Fluid that fills spaces between cells
(d) Intracellular fluid	**(iv)** Fluid that remains when blood clotting agents are removed from plasma
(e) Blood plasma	**(v)** Fluid within cells

29.4 Plasma Proteins, White Blood Cells, and Immunity

Learning Objective:

- Explain the roles of the blood components that participate in inflammation and the immune response.

Antigen A substance foreign to the body that triggers the immune response.

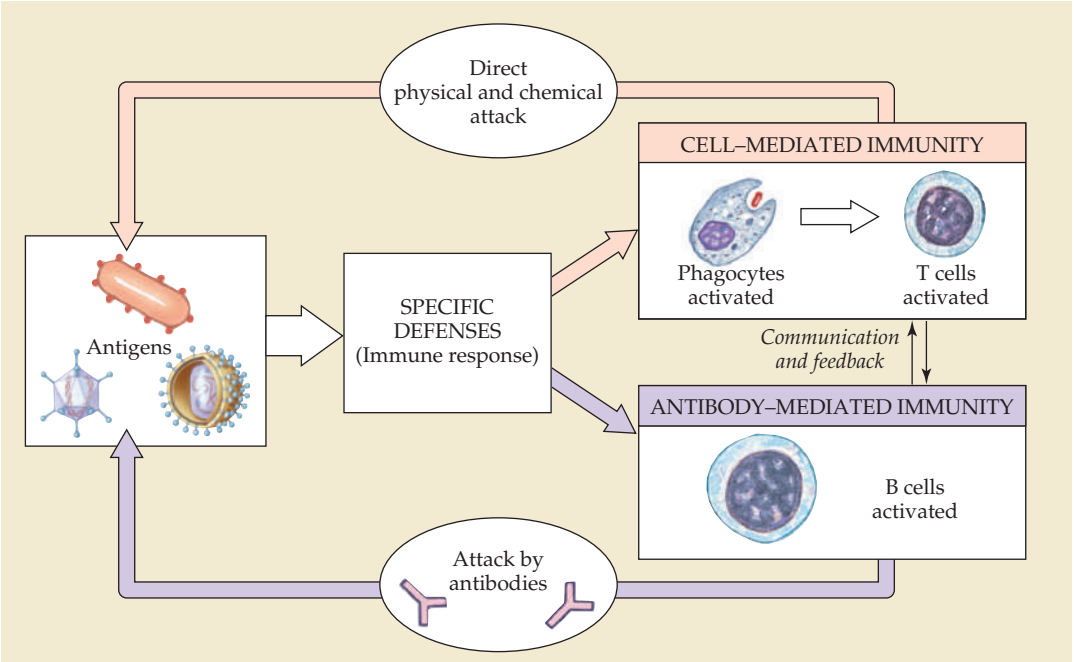
Inflammatory response A nonspecific defense mechanism triggered by antigens or tissue damage.

Immune response Defense mechanism of the immune system dependent on the recognition of specific antigens, including viruses, bacteria, toxic substances, and infected cells; either cell-mediated or antibody-mediated.

Antibody (immunoglobulin) Glycoprotein molecule that identifies antigens.

An **antigen** is any molecule or portion of a molecule recognized by the body as a foreign invader. An antigen might be a molecule never seen before by the body or a molecular segment recognized as an invader (for example, a protein on the surface of a bacterium or virus). Antigens can also be small molecules, known as *haptens*, that are only recognized as antigens after they have bonded to carrier proteins. Haptens include some antibiotics, environmental pollutants, and allergens from plants and animals.

The recognition of an antigen can initiate three different responses. The first, the **inflammatory response,** is a nonspecific, localized response to an antigen. The two remaining types of **immune response** (cell-mediated response and antibody-mediated response) do depend on recognition of *specific* invaders (such as viruses, bacteria, toxic substances, or infected cells; Figure 29.7). At the molecular level, the invading antigen is detected by an interaction very much like that between an enzyme and its substrate. Noncovalent attraction allows a spatial fit between the antigen and a defender that is specific to that antigen. The *cell-mediated immune response* depends on WBCs known as *T cells*. The *antibody-mediated immune response* depends on **antibodies** (or **immunoglobulins**) produced by the WBCs known as *B cells*.



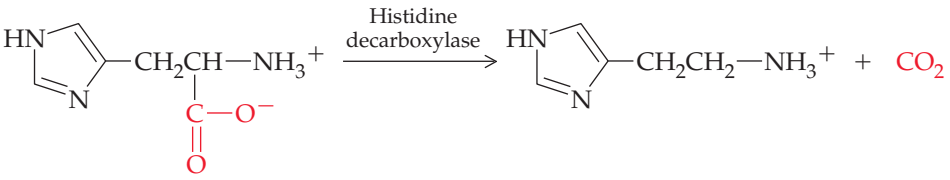
▲ **Figure 29.7**
The immune response.
The attack on antigens occurs by cell-mediated and antibody-mediated immune responses.

Both inflammation and the immune responses require normal numbers of WBCs to be effective (5–10 million WBCs per milliliter). If the WBC count falls below 1000 per milliliter of blood, any infection can be life-threatening. The devastating results of WBC destruction in acquired immunodeficiency syndrome (AIDS) is an example of this condition.

Inflammatory Response

Inflammation Result of the inflammatory response; includes swelling, redness, warmth, and pain.

Cell damage due to infection or injury initiates **inflammation,** a nonspecific defense mechanism that produces swelling, redness, warmth, and pain. For example, the swollen, painful, red bump that develops around a splinter in your finger is an inflammation (generally known as a *wheal-and-flare reaction*). Chemical messengers released at the injured site direct the inflammatory response. One such messenger is histamine, which is synthesized from the amino acid histidine and is stored in cells throughout the body. Histamine release is also triggered by an allergic response.



Histidine Histamine

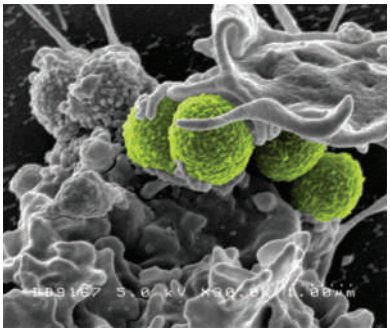
Histamine sets off dilation of capillaries and increases the permeability of capillary walls. The resulting increased blood flow into the damaged area reddens and warms the skin, and swelling occurs as plasma carrying blood-clotting factors and defensive proteins enters the intercellular space. At the same time, WBCs cross capillary walls to attack invaders.

Bacteria or other antigens at the inflammation site are destroyed by WBCs known as *phagocytes,* which engulf invading cells and destroy them by enzyme-catalyzed hydrolysis reactions. Phagocytes also emit chemical messengers that help to direct the inflammatory response. An inflammation caused by a wound will heal completely only after all infectious agents have been removed, with dead cells and other debris absorbed into the lymph system.

Cell-Mediated Immune Response

The cell-mediated immune response is under the control of several kinds of *T lymphocytes* or *T cells.* The cell-mediated immune response principally guards against abnormal cells and bacteria or viruses entering the normal cells; it also guards against the invasion of some cancer cells and causes the rejection of transplanted organs.

A complex series of events begins when a T cell recognizes an antigenic cell. The result of these events is production of *cytotoxic,* or *killer,* T cells that can destroy the invader (e.g., by releasing a toxic protein that kills the antigenic invader by perforating cell membranes) and *helper* T cells, which enhance the body's defenses against the invader. Thousands of *memory* T cells are also produced; they remain on guard and will immediately generate the appropriate killer T cells if the same pathogen reappears.



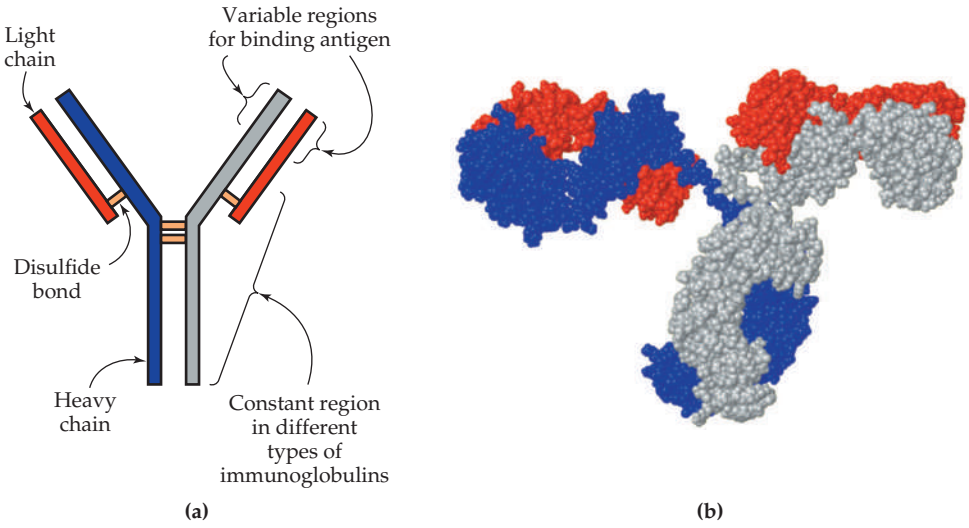
▲ A lymphocyte reaches out to snare several *Staphylococcus aureus* bacteria (highlighted in green).

Antibody-Mediated Immune Response

The WBCs known as *B lymphocytes* or *B cells,* with the assistance of T cells, are responsible for the antibody-mediated immune response. Unlike T cells, which identify only antigenic cells, B cells identify antigens adrift in body fluids. A B cell is activated when it first binds to an antigen and then encounters a helper T cell that recognizes the same antigen. This activation can take place anywhere in the body, but it often occurs in lymph nodes, tonsils, or the spleen, which have large concentrations of lymphocytes.

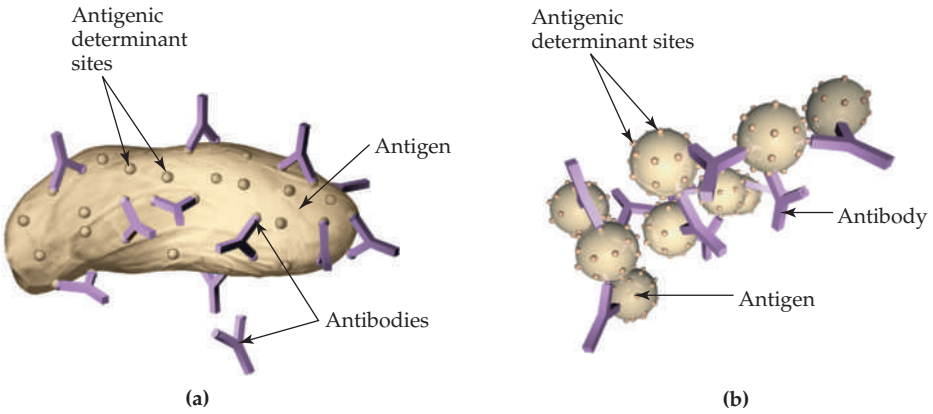
Once activated, B cells divide to form plasma cells that secrete antibodies specific to the antigen. The antibodies are immunoglobulins. The body contains up to 10,000

different immunoglobulins at any given time, and we have the capacity to make more than 100 million others. The immunoglobulins are glycoproteins composed of two "heavy" polypeptide chains and two "light" polypeptide chains joined by disulfide bonds, as shown in Figure 29.8. The variable regions are sequences of amino acids that will bind a specific antigen. Once synthesized, antibodies spread out to find their antigens.



▶ Figure 29.8
Structure of an immunoglobulin, which is an antibody.
(a) The regions of an immunoglobulin. The disulfide bridges that hold the chains together are shown in orange. (b) Molecular model of an immunoglobulin; the heavy chains are gray and blue and both light chains are red.

Formation of an antigen–antibody complex (Figure 29.9) inactivates the antigen by one of several methods. The complex may, for example, attract phagocytes, or it may block the mechanism by which the invader connects with a target cell.



▶ Figure 29.9
Antigen–antibody complexes.
(a) Antigens bind to antigenic-determinant sites on the surface of, for example, a bacterium. (b) Because each antibody has two binding sites, the interaction of many antigens and antibodies creates a large immune complex.

Activated B-cell division also yields memory cells that remain on guard and quickly produce more plasma cells if the same antigen reappears. The long-lived B and T memory cells are responsible for long-term immunity to diseases after the first illness or after a vaccination.

Several classes of immunoglobulins have been identified. *Immunoglobulin G antibodies* (known as *gamma globulins*), for example, protect against viruses and bacteria. Allergies and asthma are caused by an oversupply of *immunoglobulin E*. Numerous disorders result from the mistaken identification of normal body constituents as foreign and the overproduction of antibodies to combat them. These **autoimmune diseases** include attack on connective tissue at joints in rheumatoid arthritis, attack on pancreatic islet cells in some forms of diabetes mellitus, and a generalized attack on nucleic acids and blood components in systemic lupus erythematosus.

Autoimmune disease Disorder in which the immune system identifies normal body components as antigens and produces antibodies to them.

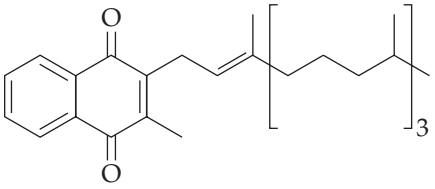
29.5 Blood Clotting

Learning Objective:

- List the steps involved in blood clotting.

A blood clot consists of blood cells trapped in a mesh of the insoluble fibrous protein known as **fibrin.** Clot formation is a multiple-step process requiring participation of 12 clotting factors; calcium ion is one of the clotting factors. Others, most of which are glycoproteins, are synthesized in the liver by pathways that require vitamin K as a coenzyme. Therefore, a deficiency of vitamin K, the presence of a competitive inhibitor of vitamin K, or a deficiency of a clotting factor can cause excessive bleeding, sometimes from even minor tissue damage. Hemophilia is a disorder caused by an inherited genetic defect that results in the absence of one or more of the clotting factors. Hemophilia occurs in 1 in 10,000 individuals, with 80–90% of people with hemophilia being male.

Fibrin Insoluble protein that forms the fiber framework of a blood clot.



Vitamin K
(Phylloquinone)

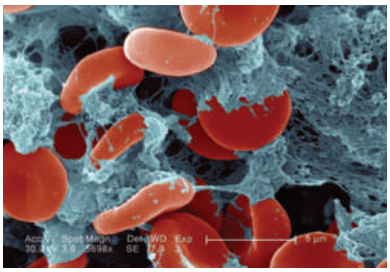
The body's mechanism for halting blood loss from even the tiniest capillary is referred to as **hemostasis.** The first events in hemostasis are (1) constriction of surrounding blood vessels and (2) formation of a plug composed of the blood cells known as *platelets* at the site of tissue damage.

Hemostasis The stopping of bleeding.

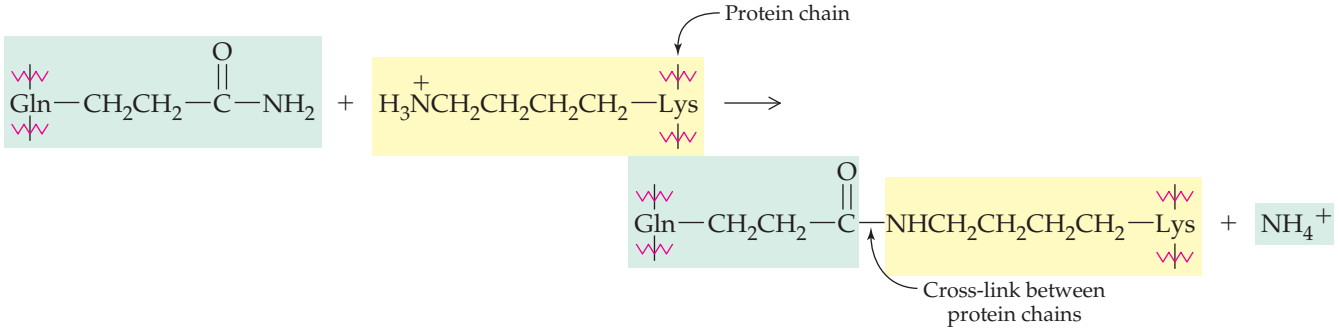
Next, a **blood clot** is formed in a process that is triggered by two pathways: (1) The *intrinsic pathway* begins when blood makes contact with the negatively charged surface of the fibrous protein collagen, which is exposed at the site of tissue damage. Clotting is activated in exactly the same manner when blood is placed in a glass tube, because the surface of the glass has a negative charge. (2) The *extrinsic pathway* begins when damaged tissue releases an integral membrane glycoprotein known as *tissue factor.*

Blood clot A network of fibrin fibers and trapped blood cells that forms at the site of blood loss.

The result of either pathway is a cascade of reactions that is initiated when an inactive clotting factor (a zymogen, Section 19.8) is converted to its active form by cleavage of specific polypeptide sequences on its surface. Commonly, the newly activated enzyme then catalyzes the activation of the next factor in the cascade. The two pathways merge and, in the final step of the common pathway, the enzyme *thrombin* catalyzes cleavage of small polypeptides from the soluble plasma protein fibrinogen. Negatively charged groups in these polypeptides make fibrinogen soluble and keep the molecules apart. Once these polypeptides are removed, the resulting insoluble fibrin molecules immediately associate with each other by noncovalent interactions. Then they are bound into fibers by formation of amide cross-links between lysine and glutamine side chains in a reaction catalyzed by another of the clotting factors.

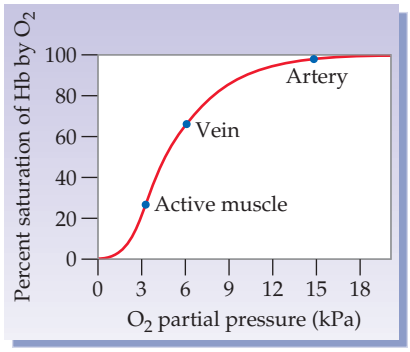


▲ Colorized electron micrograph of a blood clot. RBCs can be seen enmeshed in the fibrin network.



Once the clot has done its job of preventing blood loss and binding together damaged surfaces as they heal, the clot is broken down by hydrolysis of its peptide bonds.

▲ **Figure 29.10**
A pulse oximetry sensor for continuous monitoring of blood oxygen.
One side of the sensor contains two light-emitting diodes (LEDs), one that emits in the visible red range (better absorbed by dark-red deoxygenated blood) and one that emits in the infrared range (better absorbed by oxygenated blood, which is bright red). On the opposite side of the sensor, a photodetector measures the light that passes through and sends the signal to an instrument that computes the percent oxygen saturation of the blood and also records the pulse. Normal oxygen saturation is 95–100%. Below 85%, tissues are at risk, and below 70% is typically life-threatening.



▲ **Figure 29.11**
Oxygen saturation of hemoglobin at normal physiological conditions.
Oxygen pressure is about 15×10^3 Pa in arteries and 3×10^3 Pa in active muscles. Note the large release of oxygen as the partial pressure drops from 6×10^3 Pa to 3×10^3 Pa.

29.6 Red Blood Cells and Blood Gases

Learning Objective:

- Explain the relationships among O_2 and CO_2 transport and acid-base balance.

RBCs, or erythrocytes, have one major purpose: to transport blood gases. Erythrocytes in mammals have no nuclei or ribosomes and cannot replicate themselves. In addition, they have no mitochondria or glycogen and must obtain glucose from the surrounding plasma. Their enormous number—about 250 million in a single drop of blood—and their large surface area provide for rapid exchange of gases throughout the body. Because they are small and flexible, erythrocytes can squeeze through the tiniest capillaries one at a time.

Of the protein in an erythrocyte, 95% is hemoglobin, the transporter of oxygen and carbon dioxide. Hemoglobin (Hb) is composed of four polypeptide chains with the quaternary structure shown earlier in Figure 18.5. Each protein chain has a central heme molecule in a crevice in its nonpolar interior, and each of the four hemes can combine with one O_2 molecule.

Oxygen Transport

The iron(II) ion, Fe^{2+}, sits in the center of each heme molecule and is the site to which O_2 binds through one of oxygen's unshared electron pairs. In contrast to the cytochromes of the respiratory chain, where iron cycles between Fe^{2+} and Fe^{3+}, heme iron must remain in the reduced Fe^{2+} state to maintain its oxygen-carrying ability. Hemoglobin (Hb) carrying four oxygens (oxyhemoglobin) is bright red. Hemoglobin that has lost one or more oxygens (deoxyhemoglobin) is dark red-purple, which accounts for the darker color of venous blood. Dried blood is brown, because exposure to atmospheric oxygen has oxidized the iron (think of rust). The color of arterial blood carrying oxygen is used in a clinically valuable method for monitoring oxygenation (known as *pulse oximetry,* Figure 29.10).

At normal physiological conditions, the percentage of heme molecules that carry oxygen, known as the *percent saturation,* is dependent on the partial pressure of oxygen in surrounding tissues (Figure 29.11). The shape of the curve indicates that binding of oxygen to heme is allosteric in nature (see Section 19.7). Each O_2 that binds causes changes in the hemoglobin quaternary structure that enhance binding of the next O_2, and releasing each oxygen enhances release of the next. As a result, oxygen is more readily released to tissue where the partial pressure of oxygen is low. The average oxygen partial pressure in peripheral tissue is 6×10^3 Pa, a pressure at which Hb remains 75% saturated by oxygen, leaving a large amount of O_2 in reserve for emergencies. Note, however, the rapid drop in the curve between 6×10^3 Pa and 3×10^3 Pa, which is the oxygen pressure in tissue where metabolism is occurring rapidly.

Carbon Dioxide Transport, Acidosis, and Alkalosis

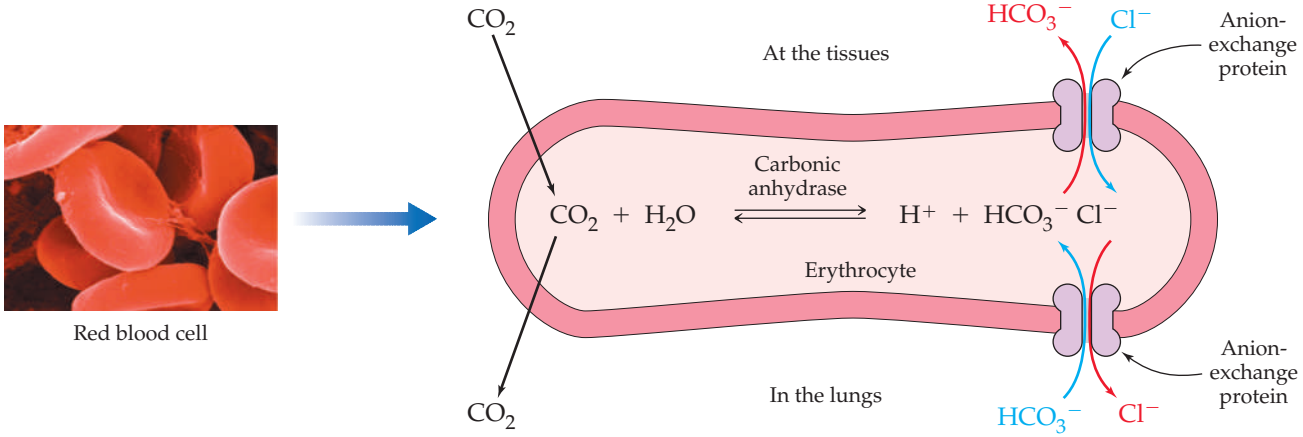
Oxygen and carbon dioxide are the "blood gases" transported by erythrocytes. By way of the hydrogen carbonate ion/carbon dioxide buffer, the intimate relationships among H^+ and HCO_3^- concentrations and O_2 and CO_2 partial pressures are essential to maintaining electrolyte and acid-base balance.

$$\underbrace{CO_2(aq) + H_2O(l)}_{\text{Controlled by the lungs}} \rightleftharpoons H_2CO_3(aq) \rightleftharpoons \underbrace{HCO_3^-(aq) + H^+(aq)}_{\text{Controlled by the kidneys}}$$

In a clinical setting, "monitoring blood gases" usually refers to measuring the pH of blood as well as the gas concentrations. Carbon dioxide from metabolism in peripheral cells diffuses into interstitial fluid and then into capillaries, where it is transported in the blood three ways: (1) as dissolved $CO_2(aq)$, (2) bonded to Hb, or (3) as HCO_3^- in solution. About 7% of the CO_2 produced dissolves in blood plasma. The rest enters erythrocytes, where some of it binds to the protein portion of hemoglobin by reaction with the nonionized amino acid $-NH_2$ groups present.

$$Hb{-}NH_2 + CO_2 \rightleftharpoons Hb{-}NHCOO^- + H^+$$

Most of the CO_2 is rapidly converted to hydrogen carbonate ion within erythrocytes, which contain a large concentration of carbonic anhydrase. The resulting water-soluble HCO_3^- ion can leave the erythrocyte and travel in the blood to the lungs, where it will be converted back to CO_2 for exhalation. To maintain electrolyte balance, a Cl^- ion enters the erythrocyte for every HCO_3^- ion that leaves, and the process is reversed when the blood reaches the lungs.



A cell-membrane protein controls this ion exchange, which is passive, as the ions move from higher to lower concentrations.

Without some compensating change, the result of hemoglobin reacting with CO_2 and the action of carbonic anhydrase would be an unacceptably large increase in acidity. To cope with this, hemoglobin responds by reversibly binding hydrogen ions.

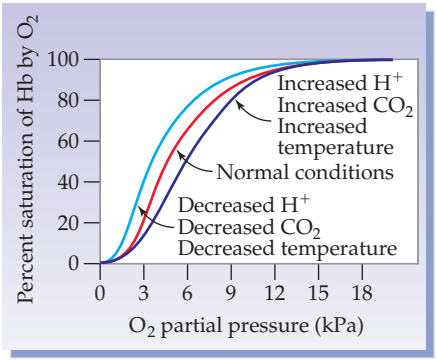
$$Hb \cdot 4O_2 + 2H^+ \rightleftharpoons Hb \cdot 2H^+ + 4O_2$$

The release of oxygen is enhanced by allosteric effects when the hydrogen ion concentration increases, and oxygen is held more firmly when the hydrogen ion concentration decreases.

The changes in the oxygen saturation curve with CO_2 and H^+ concentrations and with temperature are shown in Figure 29.12. The curve shifts to the right, indicating decreased affinity of Hb for O_2, when the H^+ and CO_2 concentrations increase and when the temperature increases. These are exactly the conditions in muscles that are working hard and need more oxygen. The curve shifts to the left, indicating increased affinity of Hb for oxygen, under the opposite conditions of decreased H^+ and CO_2 concentrations and lower temperature.

Homeostasis requires a blood pH between 7.35 and 7.45. A pH outside this range results in either **acidosis** or **alkalosis.**

Acidosis	Normal	Alkalosis
Blood pH Below 7.35	Blood pH 7.35–7.45	Blood pH Above 7.45



▲ **Figure 29.12**
Changes in oxygen affinity of hemoglobin with changing conditions.
The normal curve of Figure 29.11 is shown in red here.

Acidosis The abnormal condition associated with a blood plasma pH below 7.35; may be respiratory or metabolic.

Alkalosis The abnormal condition associated with a blood plasma pH above 7.45; may be respiratory or metabolic.

The wide variety of conditions that cause acidosis or alkalosis can be divided between respiratory malfunctions and metabolic malfunctions. Table 29.4 gives examples of each. *Respiratory* disruption of acid-base balance can result when carbon dioxide generation by metabolism and carbon dioxide removal at the lungs are out of balance. *Metabolic* disruption of acid-base balance can result from abnormally high acid generation or failure of buffer systems and kidney function to regulate hydrogen carbonate concentration.

Table 29.4 Causes of Acidosis and Alkalosis

Type of Imbalance	Causes
Respiratory acidosis	CO_2 buildup due to: Decreased respiratory activity (hypoventilation) Cardiac insufficiency (e.g., congestive failure, cardiac arrest) Deterioration of pulmonary function (e.g., asthma, emphysema, pulmonary obstruction, pneumonia)
Respiratory alkalosis	Loss of CO_2 due to: Excessive respiratory activity (hyperventilation, due, for example, to high fever, nervous condition)
Metabolic acidosis	Increased production of metabolic acids due to: Fasting or starvation Untreated diabetes Excessive exercise Decreased acid excretion in urine due to: Poisoning Renal failure Decreased plasma hydrogen carbonate concentration due to: Diarrhea
Metabolic alkalosis	Elevated plasma hydrogen carbonate concentration due to: Vomiting Diuretics Antacid overdose

KEY CONCEPT PROBLEM 29.3

Carbon dioxide dissolved in body fluids has a pronounced effect on pH.

(a) Does pH go up or down when carbon dioxide dissolves in these fluids? Does this change indicate higher or lower acidity?

(b) What does a blood gas analysis measure?

PROBLEM 29.4

Classify the following conditions as a cause of respiratory or metabolic acidosis or alkalosis (consult Table 29.4).

(a) Emphysema

(b) Kidney failure

(c) Overdose of an antacid

PROBLEM 29.5

Classify the following conditions as a cause of respiratory or metabolic acidosis or alkalosis (consult Table 29.4).

(a) Severe panic attack

(b) Congestive heart failure

(c) Running a marathon

29.7 The Kidney and Urine Formation

Learning Objective:

- Describe the transfer of water and solutes during urine formation.

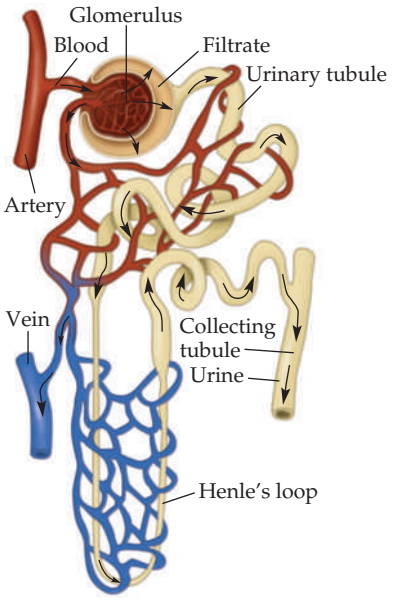
The kidneys bear the major responsibility for maintaining a constant internal environment in the body. By managing the elimination of appropriate amounts of water, electrolytes, hydrogen ions, and nitrogen-containing wastes, the kidneys respond to changes in health, diet, and physical activity.

About 25% of the blood pumped from the heart goes directly to the kidneys, where the functional units are the *nephrons* (Figure 29.13). Each kidney contains over a million of them. Blood enters a nephron at a *glomerulus* (at the top in Figure 29.13), a tangle of capillaries surrounded by a fluid-filled space. **Filtration,** the first of three essential kidney functions, occurs here. The pressure of blood pumped into the glomerulus directly from the heart is high enough to push plasma and all its solutes except large proteins across the capillary membrane into the surrounding fluid, the **glomerular filtrate.** The filtrate flows from the capsule into the tubule that makes up the rest of the nephron, and the blood enters the network of capillaries intertwined with the tubule.

About 125 mL of filtrate per minute enters the kidneys, and they produce 180 L of filtrate per day. This filtrate contains not only waste products but also many solutes the body cannot afford to lose, such as glucose and electrolytes. Since we excrete only about 1.4 L of urine each day, you can see that another important function of the kidneys is **reabsorption**—the recapture of water and essential solutes by moving them out of the tubule.

Reabsorption alone, however, is not sufficient to provide the kind of control over urine composition that is needed. More of certain solutes must be excreted than are present in the filtrate. This situation is dealt with by **secretion**—the transfer of solutes *into* the kidney tubule.

Reabsorption and secretion require the transfer of solutes and water among the filtrate, the interstitial fluid surrounding the tubule, and blood in the capillaries. Table 29.5 lists some of the substances reabsorbed or secreted. Solutes cross the tubule and capillary membranes by passive diffusion in response to concentration or ionic charge differences or by active transport. Water moves in response to differences in the osmolarity of the fluids on the two sides of the membranes. Solute and water movement is also controlled by hormone-directed variations in the permeability of the tubule membrane.



▲ **Figure 29.13**
Structure of a nephron.
Water moves out of the urinary tubule and the collecting tubule. The concentration of solutes in urine is established as they move both in and out along the tubules.

Filtration (kidney) Filtration of blood plasma through a glomerulus and into a kidney nephron.

Glomerular filtrate Fluid that enters the nephron from the glomerulus; filtered blood plasma.

Reabsorption (kidney) Movement of solutes out of filtrate in a kidney tubule.

Secretion (kidney) Movement of solutes into filtrate in a kidney tubule.

Table 29.5 Reabsorption and Secretion in Kidney Tubules

Reabsorbed	Secreted
Ions	Ions
Na^+, Cl^-, K^+, Ca^{2+}, Mg^{2+}, PO_4^{3-}, SO_4^{2-}, HCO_3^-	K^+, H^+, Ca^{2+}
Metabolites	Wastes
Glucose	Creatinine
Amino acids	Urea
Proteins	Ammonia
Vitamins	Various organic acids and bases (including uric acid)
	Miscellaneous
	Neurotransmitters
	Histamine
	Drugs (penicillin, atropine, morphine, numerous others)

29.8 Urine Composition and Function

Learning Objective:

- Describe the composition of urine.

Urine contains the products of glomerular filtration, minus the substances reabsorbed in the tubules, plus the substances secreted in the tubules. The actual concentrations of these substances in urine at any time are determined by the amount of water being excreted, which can vary significantly with water intake, exercise, temperature, and state of health. (For identical quantities of solutes, concentration *decreases* when the quantity of solvent water *increases,* and concentration *increases* when the quantity of water *decreases*.)

About 50 g of solids in solution are excreted every day—about 20 g of electrolytes and 30 g of nitrogen-containing wastes (urea and ammonia from amino acid catabolism, creatinine from breakdown of creatine phosphate in muscles, and uric acid from purine catabolism). Normal urine composition is usually reported as the quantity of each solute excreted per day, and laboratory urinalysis often requires collection of all urine excreted during a 24-hour period.

The following paragraphs briefly describe a few of the mechanisms that control the composition of urine.

Acid-Base Balance

Respiration, buffers, and excretion of hydrogen ions in urine combine to maintain acid-base balance. Metabolism normally produces an excess of hydrogen ions; a portion of these must be excreted each day to prevent acidosis. Very little free hydrogen ion exists in blood plasma, and therefore very little enters the glomerular filtrate. Instead, the H^+ to be eliminated is produced by the reaction of CO_2 with water in the cells lining the tubules of the nephrons:

$$CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H^+ + HCO_3^-$$

(H^+: To filtrate; HCO_3^-: To bloodstream)

The HCO_3^- ions return to the bloodstream, and the H^+ ions enter the filtrate. Thus, the more hydrogen ions there are to be excreted, the more hydrogen carbonate ions are returned to the bloodstream.

The urine must carry away the necessary quantity of H^+ without becoming excessively acidic. To accomplish this, the H^+ is tied up by reaction with HPO_4^{2-} absorbed at the glomerulus or by reaction with NH_3 produced in the tubule cells by deamination of glutamate:

$$H^+ + HPO_4^{2-} \longrightarrow H_2PO_4^-$$
$$H^+ + NH_3 \longrightarrow NH_4^+$$

When acidosis occurs, the kidney responds by synthesizing more ammonia, thereby increasing the quantity of H^+ eliminated.

A further outcome of H^+ production in tubule cells is the net reabsorption of the HCO_3^- that entered the filtrate at the glomerulus. The body cannot afford to lose its primary buffering ion, HCO_3^-. If HCO_3^- were to be lost, the body would have to produce more; the result would be production of additional acid from carbon dioxide by reaction with water. Instead, H^+ secreted into the filtrate combines with HCO_3^- in the filtrate to produce CO_2 and water:

$$H^+ + HCO_3^- \longrightarrow CO_2 + H_2O$$

(H^+ + HCO_3^-: In the filtrate; CO_2: To bloodstream)

Upon returning to the bloodstream, the CO_2 is reconverted to HCO_3^-.

CHEMISTRY IN ACTION

What's in Your Blood Test?

Along with your annual physical, your doctor will almost certainly order that routine blood work be done either before or right after they see you. If you have ever looked at the lab orders, you are sure to have come across a myriad of confusing abbreviations, such as CBC, or CMP, WBC with differential, or LP. What exactly has your doctor ordered and why?

As we learned in the beginning of the chapter, because blood is one of the body fluids that touches every part of your body, including the major organs, it is the "biochemical superhighway" of the body and in it are clues to what is happening in areas that are not easily accessed by your physician. These clues come in the form of the levels of chemical species present. The quantity of a given chemical in the blood is determined either directly or indirectly using automated analyzers that rely on premixed reagents and automatic division of a fluid sample into small portions for each test. As a result, there are certain tests (or 'screens') that are commonly run. Almost all routine blood work will request a chemistry panel (either a basic (BMP) or comprehensive (CMP) metabolic panel), a complete blood count (CBC), and some sort of lipid panel (LP). Depending on age, sex, or previous medical conditions, your physician may order other tests be done as well. The following table shows the most common things being looked for in a blood test and why. Normal ranges have been left out because some are dependent on the laboratory doing the test, some on age and sex, while others are still being revised.

Most Common Blood Tests Run during a Typical Annual Physical

Test	Classification	What Test Tells You
Serum glucose[1]	General test	Abnormal levels can be a sign of diabetes or prediabetes; requires fasting for 8–12 hours prior.
Calcium[2] Serum calcium[2]	General test Protein tests	Abnormal calcium levels in the blood may be a sign of kidney problems, bone disease, thyroid disease, cancer, malnutrition, or another disorder.
Sodium[1] Potassium[1] Chloride[1] Carbon dioxide[1] (CO_2)	Electrolyte tests	Abnormal electrolyte levels may be a sign of dehydration, kidney disease, liver disease, heart failure, high blood pressure, or other disorders.
Human serum albumin[2]	Protein tests	Produced in the liver, it is the most abundant protein in blood plasma. Low levels can indicate liver disease, kidney damage, or malnutrition. Elevated levels can indicate dehydration.
Bilirubin	Liver function	A breakdown product of old blood cells; found in bile. High levels can indicate liver or gall bladder disease.
RBC count Mean corpuscular volume (MCV or MPV)	CBC	RBCs carry oxygen from your lungs to the rest of your body. Abnormal RBC levels may be a sign of anemia, dehydration, bleeding, or another disorder. MCV is a measure of the average size of the RBCs and abnormal MCV levels may be a sign of anemia.
WBC count WBC with differential	CBC	WBCs are part of your immune system, which fights infections and diseases. Abnormal WBC levels may be a sign of infection, blood cancer, or an immune system disorder.
Hemoglobin (Hgb)	CBC	An iron-rich protein in RBCs that carries oxygen. Abnormal levels may be a sign of anemia or other blood disorders. Excess glucose due to diabetes can raise the level of hemoglobin A1c.
Total cholesterol	Lipid panel	Measures all of the cholesterol in all the lipoprotein particles. High levels correlate to higher risk of heart attack and stroke.
High-density lipoprotein cholesterol (HDL-C)	Lipid panel	Measures the cholesterol in HDL particles; often called "good cholesterol" because it removes excess cholesterol and carries it to the liver for removal. High levels correlate to lower risk of heart attack and stroke.
Low-density lipoprotein cholesterol (LDL-C)	Lipid panel	Calculates the cholesterol in LDL particles; often called "bad cholesterol" because it deposits excess cholesterol in walls of blood vessels, which can contribute to atherosclerosis. High levels correlate to higher risk of heart attack and stroke.
Triglycerides	Lipid panel	Measures all the triglycerides in all the lipoprotein particles; most is in the very low-density lipoproteins (VLDL). High levels correlate to higher risk of heart attack and stroke.

[1]*Done in BMP and CMP;* [2]*Done in CMP only*

It is important to note that the actual numbers obtained, and where they fall within currently accepted normal ranges, is crucial. It is also key to note that these typical blood tests act simply as first indicators; for example, your doctor may look at your blood glucose level and note that it is too high; this does not mean that you have diabetes, but it does suggest further testing. You need to talk to your doctor after your blood test and have them explain to you what each value means, and if out of range, what can be done to bring it back into range. Your annual blood test can be your first step in preventing disease.

CIA Problem 29.5 Which tests might indicate a patient was suffering from dehydration? Or anemia?

CIA Problem 29.6 Why do blood tests play such an important part in assessing the overall health of a patient?

CIA Problem 29.7 One of the more advanced blood tests used to screen for lipids is the Vertical Auto Profile (VAP) test. Using the internet, determine what this test is and why it believed to be a better indicator of cardiovascular health than a standard lipid panel.

In summary, acid-base reactions in the kidneys have the following results:

- Secreted H^+ is eliminated in the urine as NH_4^+ or $H_2PO_4^-$.
- Secreted H^+ combines with filtered HCO_3^-, producing CO_2 that returns to the bloodstream and again is converted to HCO_3^-.

Fluid and Na^+ Balance

The amount of water reabsorbed is dependent on the osmolarity of the fluid passing through the kidneys, the ADH–controlled permeability of the collecting duct membrane, and the amount of Na^+ actively reabsorbed. Increased sodium reabsorption means higher interstitial osmolarity, greater water reabsorption, and decreased urine volume. In the opposite condition of decreased sodium reabsorption, less water is reabsorbed and urine volume increases. "Loop diuretic" drugs such as furosemide (trademarked as Lasix), which is used in treating hypertension and congestive heart failure, act by inhibiting the active transport of Na^+ out of the region of the urinary tubule called Henle's loop. Caffeine acts as a diuretic in a similar way.

The reabsorption of Na^+ is normally under the control of the steroid hormone aldosterone. The arrival of chemical messengers signaling a decrease in total blood plasma volume accelerates the secretion of aldosterone. The result is increased Na^+ reabsorption in the kidney tubules accompanied by increased water reabsorption.

SUMMARY REVISITING THE LEARNING OBJECTIVES

- **Describe the major categories of body fluids, their general composition, and the exchange of solutes between them.** Body fluids are either intracellular or extracellular. *Extracellular fluid* includes *blood plasma* (the fluid part of blood) and *interstitial fluid. Blood serum* is the fluid remaining after blood has clotted. Solutes in body fluids include blood gases, electrolytes, metabolites, and proteins. Solutes are carried throughout the body in blood and lymph. Exchange of solutes between blood and interstitial fluid occurs at the network of blood and lymph capillaries in peripheral tissues. Exchange of solutes between interstitial fluid and intracellular fluid occurs by passage across cell membranes *(see Problems 6, 13–15, 18, 19, 23, 26, 27, and 55–59)*.
- **Discuss how fluid balance is maintained.** To maintain physiological homeostasis, the daily intake of water must roughly equal that of the daily output of water; this is approximately 2500 mL per day for an average adult. If output is greater than intake (as in the case of endurance athletes), body mass will be lost; 4% or greater body mass loss is considered to be dangerous. Output of water and electrolytes are very closely controlled by hormones. A shortage of water causes secretion of ADH. In the kidney, ADH causes a decrease in the water content of the urine, while thirst receptors in the hypothalamus, the heart, and blood vessels trigger increased water intake *(see Problems 6, 12, 20, 21, 23, 26–29, 53, 57, and 61)*.
- **Describe the composition and functions of blood.** The principal functions of blood are (1) transport of solutes and blood gases, (2) regulation, such as regulation of heat and acid-base balance, and (3) defense, which includes the *immune response* and *blood clotting.* In addition to plasma and proteins, blood is composed of RBCs *(erythrocytes),* which transport blood gases; WBCs *(leukocytes),* for defense functions; and *platelets*, which participate in blood clotting (Table 29.3) *(see Problems 7, 8, 15–17, 22, 25–28, and 61)*.
- **Explain the roles of the blood components that participate in inflammation and the immune response.** The presence of an *antigen* (a substance foreign to the body) initiates (1) the inflammatory response, (2) the cell-mediated immune response, and (3) the antibody-mediated immune response. The *inflammatory response* is initiated by histamine and accompanied by the destruction of invaders by *phagocytes.* The *cell-mediated response* is effected by *T cells* that can, for example, release a toxic protein that kills invaders. The *antibody-mediated response* is effected by *B cells*, which generate *antibodies (immunoglobulins),* proteins that complex with antigens and destroy them *(see Problems 8–11, 18, 19, and 29–36)*.
- **List the steps involved in blood clotting.** A blood clot is a multistep process that is triggered either by an intrinsic pathway that begins when blood makes contact with the protein collagen or by an extrinsic pathway that begins when damaged tissue releases a membrane glycoprotein known as tissue factor. The result of either pathway is a cascade of reactions in which a series of zymogens are activated, ultimately resulting in the formation of a clot composed of the insoluble fibrous protein *fibrin* and platelets *(see Problems 7, 37–40, and 56)*.
- **Explain the relationships among O_2 and CO_2 transport and acid-base balance.** Oxygen is transported attached to Fe^{2+} ions in hemoglobin. The percent saturation of hemoglobin with oxygen (Figure 29.12) is governed by the partial pressure of oxygen in surrounding tissues and allosteric variations in hemoglobin structure. Carbon dioxide is transported in blood as a solute, attached to hemoglobin, or in solution as hydrogen carbonate ion. In peripheral tissues, carbon dioxide diffuses into RBCs, where it is converted to hydrogen carbonate ion. Acid-base balance is controlled as hydrogen ions generated by hydrogen carbonate formation are bound by hemoglobin. At the lungs, oxygen enters the cells, and hydrogen carbonate and hydrogen ions leave. A blood pH outside the normal range of 7.35–7.45 can be caused by respiratory or

metabolic imbalance, resulting in the potentially serious conditions of *acidosis* or *alkalosis (see Problems 12, 41–52, and 60).*

- **Describe the transfer of water and solutes during urine formation.** The first essential kidney function is *filtration,* in which plasma and most of its solute cross capillary membranes and enter the *glomerular filtrate.* Water and essential solutes are then reabsorbed, whereas additional solutes for elimination are secreted into the filtrate *(see Problems 12, 20, 53, 54, and 60).*
- **Describe the composition of urine.** Urine is composed of the products of filtration, minus the substances reabsorbed, plus any secreted substances. It is composed of water, nitrogen-containing wastes, and electrolytes (including $H_2PO_4^-$ and NH_4^+) that are excreted to help maintain acid-base balance. The balance between water and Na^+ excreted or absorbed is governed by the osmolarity of fluid in the kidney, the hormone aldosterone, and various chemical messengers *(see Problems 12, 20, 53, 57, and 60).*

KEY WORDS

Acidosis, *p. 895*
Alkalosis, *p. 895*
Antibody (immunoglobulin), *p. 890*
Antigen, *p. 890*
Autoimmune disease, *p. 892*
Blood clot, *p. 893*
Blood plasma, *p. 883*
Blood serum, *p. 887*
Erythrocytes, *p. 887*
Extracellular fluid, *p. 883*
Fibrin, *p. 893*
Filtration (kidney), *p. 897*
Glomerular filtrate, *p. 897*
Hemostasis, *p. 893*
Immune response, *p. 890*
Inflammation, *p. 891*
Inflammatory response, *p. 890*
Interstitial fluid, *p. 883*
Intracellular fluid, *p. 883*
Leukocytes, *p. 887*
Osmolarity, *p. 883*
Reabsorption (kidney), *p. 897*
Secretion (kidney), *p. 897*
Whole blood, *p. 887*

UNDERSTANDING KEY CONCEPTS

29.6 Body fluids occupy two different compartments, either inside the cells or outside the cells.

(a) What are body fluids found inside the cell called?

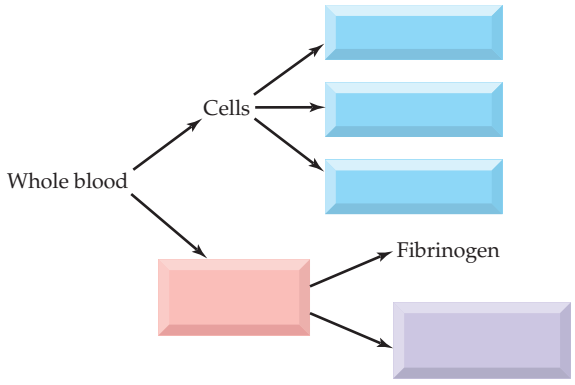
(b) What are body fluids found outside the cell called?

(c) What are the two major subclasses of fluids found outside the cells?

(d) What major electrolytes are found inside the cells?

(e) What major electrolytes are found outside the cells?

29.7 In the diagram shown here, fill in the blanks with the names of the principal components of whole blood.



29.8 Fill in the blanks to identify some of the major functions of blood

(a) Blood carries _____ from lungs to tissues.

(b) Blood carries _____ from the tissues to lungs.

(c) Blood transports _____ from the digestive system to the tissues.

(d) Blood carries _____ from the tissues to the site of excretion.

(e) Blood transports _____ from the endocrine glands to their site of binding.

(f) Blood transports defensive agents such as _____ to destroy foreign material and to prevent blood loss.

29.9 List four symptoms of inflammation.

29.10 Explain how the chemical messenger histamine is biosynthesized and how it elicits each symptom of inflammation.

29.11 What type of WBCs are involved in a cell-mediated immune response? In an antibody-mediated immune response? (see Figure 29.7).

29.12 How does the composition of urine help to maintain a healthy physiological acid-base balance?

ADDITIONAL PROBLEMS

BODY FLUIDS

29.13 What are the three principal body fluids and the approximate percentage of total body water accounted for by each?

29.14 What characteristics are needed for a substance to be soluble in body fluids?

29.15 Give an example of a substance found in tissues that is not soluble in blood. How are components that are not normally soluble in blood transported?

29.16 What effects do the differences in pressure between arterial capillaries, interstitial fluids, and venous capillaries have on solutes crossing cell membranes?

29.17 How does blood pressure compare with the interstitial fluid pressure in arterial capillaries? With the interstitial fluid pressure in venous capillaries?

29.18 What is the purpose of the lymphatic system?

29.19 Where in the body does the lymph enter the bloodstream?

29.20 What is vasopressin?

29.21 What happens when excess secretion of ADH occurs? State two causes of this.

29.22 What is the difference between blood plasma and blood serum?

29.23 At what percent of body mass loss is collapse very likely to occur?

29.24 What are the three main types of cells found in blood?

29.25 What is the major function of each of the three types of blood cells?

29.26 What are electrolytes?

29.27 What are the major cations found in interstitial fluid?

29.28 What are the major cations found in intracellular fluid?

29.29 What is an antigen?

29.30 The recognition of an antigen can elicit three types of responses. What are they?

29.31 How are specific immune responses similar to the enzyme–substrate interaction (Section 19.4)?

29.32 What class of plasma proteins is involved in the antibody-mediated immune response?

29.33 What kinds of cells are associated with the antibody-directed immune response, and how do they work?

29.34 In the cell-mediated immune response, there are three types of T cells produced. What are they, and what is the function of each?

29.35 T cells are often discussed in conjunction with the disease AIDS, in which a virus destroys these cells. How do T cells work to combat disease?

29.36 What are memory cells, and what is their role in the immune response?

29.37 What is a blood clot? What is it composed of?

29.38 What vitamin and what mineral are specifically associated with the clotting process?

29.39 Describe the intrinsic pathway in blood clotting.

29.40 Why, do you suppose, are many of the enzymes involved in blood clotting secreted by the body as zymogens?

29.41 How many O_2 molecules can be bound by each hemoglobin tetramer?

29.42 What must be the charge of the iron in hemoglobin for it to perform its function?

29.43 What color is deoxyhemoglobin? Why?

29.44 How does the degree of saturation of hemoglobin vary with the partial pressure of O_2 in the tissues?

29.45 Oxygen has an allosteric interaction with hemoglobin. What are the results of this interaction as oxygen a) binds to and b) is released from hemoglobin?

29.46 What are the three ways of transporting CO_2 in the body?

29.47 Use Figure 29.11 to estimate the partial pressure of O_2 at which hemoglobin is 50% saturated with oxygen under normal conditions. Dry air at sea level is about 21% oxygen. What would be the percentage saturation of your hemoglobin under these conditions?

29.48 When an actively metabolizing tissue produces CO_2, the H^+ concentration of blood increases. Explain how this happens using a chemical equation.

29.49 Do the following conditions cause hemoglobin to release more O_2 to the tissues or to absorb more O_2?

(a) Raising the temperature

(b) Increased production of CO_2

(c) Increasing the H^+ concentration

29.50 What are the two types of acidosis? How do they differ? (Hint: See Table 29.4.)

29.51 Ketoacidosis is a condition that can arise in an individual with diabetes due to excessive production of ketone bodies. Is this condition classified as metabolic acidosis or respiratory acidosis? Explain.

29.52 What are the two types of alkalosis? How do they differ? (Hint: See Table 29.4.)

29.53 Kidneys are often referred to as filters that purify the blood. What other two essential functions do the kidneys perform to help maintain homeostasis?

29.54 Write the reactions by which HPO_4^{2-} and HCO_3^- absorb excess H^+ from the urine before elimination.

CONCEPTUAL PROBLEMS

29.55 What is the chemical basis for ethanol's solubility in blood?

29.56 Nursing mothers are able to impart some immunity to their infants. Why do you think this is so?

29.57 Many people find they retain water after eating salty food, evidenced by swollen fingers and ankles. Explain this phenomenon in terms of how the kidneys operate.

29.58 How does active transport differ from osmosis?

29.59 When is active transport necessary to move substances through cell membranes?

29.60 Discuss the importance of the CO_2/HCO_3^- equilibrium in blood and in urine.

29.61 We have discussed homeostasis throughout this text. But what is *hemostasis*? Is it related to homeostasis?

29.62 When people panic, cry, or have a high fever, they often begin to hyperventilate. Hyperventilation is abnormally fast or deep respiration, which results in the loss of carbon dioxide from the blood. Explain how hyperventilation changes the blood chemistry. Why can breathing into a paper bag alleviate hyperventilation?

GROUP PROBLEMS

29.63 Have each member of your group choose an energy drink. Search the internet and determine what ingredients are present, and what each does. Compare your results; what do you find they have in common? What are their major differences?

29.64 Referring to Table 16.2, which compounds would you expect to cross the BBB the easiest? Which would be the hardest to cross? Have each member of the group choose a compound and provide a chemical rationale for their answer.

29.65 Certain common medications you might take require a doctor to monitor your liver function. Search the internet to find a list of these. Have each member of the group choose a drug and provide what it is used for.

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APPENDIX A

Scientific Notation

What Is Scientific Notation?

The numbers that you encounter in chemistry are often either very large or very small. For example, there are about 33,000,000,000,000,000,000,000 H_2O molecules in 1.0 mL of water, and the distance between the H and O atoms in an H_2O molecule is 0.000 000 000 095 7 m. These quantities are more conveniently written in *scientific notation* as 3.3×10^{22} molecules and 9.57×10^{-11} m, respectively. In scientific notation (also known as *exponential notation*), a quantity is represented as a number between 1 and 10 multiplied by a power of 10. In this kind of expression, the small raised number to the right of the 10 is the exponent.

Number	Exponential Form	Exponent
1,000,000	1×10^6	6
100,000	1×10^5	5
10,000	1×10^4	4
1,000	1×10^3	3
100	1×10^2	2
10	1×10^1	1
1		
0.1	1×10^{-1}	−1
0.01	1×10^{-2}	−2
0.001	1×10^{-3}	−3
0.000 1	1×10^{-4}	−4
0.000 01	1×10^{-5}	−5
0.000 001	1×10^{-6}	−6
0.000 000 1	1×10^{-7}	−7

Numbers greater than 1 have *positive* exponents, which tell how many times a number must be *multiplied* by 10 to obtain the correct value. For example, the expression 5.2×10^3 means that 5.2 must be multiplied by 10 three times:

$$5.2 \times 10^3 = 5.2 \times 10 \times 10 \times 10 = 5.2 \times 1000 = 5200$$

Note that doing this means moving the decimal point three places to the right:

5200.
123

The value of a positive exponent indicates *how many places to the right the decimal point must be moved* to give the correct number in ordinary decimal notation.

Numbers less than 1 have *negative* exponents, which tell how many times a number must be *divided* by 10 (or multiplied by one-tenth) to obtain the correct value. Thus, the expression 3.7×10^{-2} means that 3.7 must be divided by 10 two times:

$$3.7 \times 10^{-2} = \frac{3.7}{10 \times 10} = \frac{3.7}{100} = 0.037$$

Note that doing this means moving the decimal point two places to the left:

0.037
21

The value of a negative exponent indicates *how many places to the left the decimal point must be moved* to give the correct number in ordinary decimal notation.

Representing Numbers in Scientific Notation

How do you convert a number from ordinary notation to scientific notation? If the number is greater than or equal to 10, shift the decimal point to the *left* by n places until you obtain a number between 1 and 10. Then, multiply the result by 10^n. For example, the number 8137.6 is written in scientific notation as 8.1376×10^3:

$$8137.6 = 8.1376 \times 10^3$$

Number of places decimal point was shifted to the left.

Shift decimal point to the left by 3 places to get a number between 1 and 10.

When you shift the decimal point to the left by three places, you are in effect dividing the number by $10 \times 10 \times 10 = 1000 = 10^3$. Therefore, you must multiply the result by 10^3 so that the value of the number is unchanged.

To convert a number less than 1 to scientific notation, shift the decimal point to the *right* by n places until you obtain a number between 1 and 10. Then, multiply the result by 10^{-n}. For example, the number 0.012 is written in scientific notation as 1.2×10^{-2}:

$$0.012 = 1.2 \times 10^{-2}$$

Number of places decimal point was shifted to the right.

Shift decimal point to the right by 2 places to get a number between 1 and 10.

When you shift the decimal point to the right by two places, you are in effect multiplying the number by $10 \times 10 = 100 = 10^2$. Therefore, you must multiply the result by 10^{-2} so that the value of the number is unchanged $(10^2 \times 10^{-2} = 10^\circ = 1)$.

The following table gives some additional examples. To convert from scientific notation to ordinary notation, simply reverse the preceding process. Thus, to write the number 5.84×10^4 in ordinary notation, drop the factor of 10^4 and move the decimal point 4 places to the *right* $(5.84 \times 10^4 = 58{,}400)$. To write the number 3.5×10^{-1} in ordinary notation, drop the factor of 10^{-1} and move the decimal point 1 place to the *left* $(3.5 \times 10^{-1} = 0.35)$. Note that you don't need scientific notation for numbers between 1 and 10 because $10^0 = 1$.

Number	Scientific Notation
58,400	5.84×10^4
0.35	3.5×10^{-1}
7.296	$7.296 \times 10^0 = 7.296 \times 1$

Mathematical Operations with Scientific Notation

Addition and Subtraction in Scientific Notation

To add or subtract two numbers expressed in scientific notation, both numbers must have the same exponent. Thus, to add 7.16×10^3 and 1.32×10^2, first write the latter number as 0.132×10^3 and then add:

$$\begin{array}{r} 7.16 \times 10^3 \\ +0.132 \times 10^3 \\ \hline 7.29 \times 10^3 \end{array}$$

The answer has three significant figures. (Significant figures are discussed in Section 1.8.) Alternatively, you can write the first number as 71.6×10^2 and then add:

$$\begin{array}{r} 7.16 \times 10^2 \\ +\ 1.32 \times 10^2 \\ \hline 72.9 \times 10^2 = 7.29 \times 10^3 \end{array}$$

Subtraction of these two numbers is carried out in the same manner.

$$\begin{array}{r} 7.16 \times 10^3 \\ -0.132 \times 10^3 \\ \hline 7.03 \times 10^3 \end{array} \quad \text{or} \quad \begin{array}{r} 7.16 \times 10^2 \\ -1.32 \times 10^2 \\ \hline 70.3 \times 10^2 = 7.03 \times 10^3 \end{array}$$

Multiplication in Scientific Notation

To multiply two numbers expressed in scientific notation, multiply the factors in front of the powers of 10 and then add the exponents. For example,

$$(2.5 \times 10^4)(4.7 \times 10^7) = (2.5)(4.7) \times 10^{4+7} = 12 \times 10^{11} = 1.2 \times 10^{12}$$
$$(3.46 \times 10^5)(2.2 \times 10^{-2}) = (3.46)(2.2) \times 10^{5+(-2)} = 7.6 \times 10^3$$

Both answers have two significant figures.

Division in Scientific Notation

To divide two numbers expressed in scientific notation, divide the factors in front of the powers of 10 and then subtract the exponent in the denominator from the exponent in the numerator. For example,

$$\frac{3 \times 10^6}{7.2 \times 10^2} = \frac{3}{7.2} \times 10^{6-2} = 0.4 \times 10^4 = 4 \times 10^3 \text{ (1 significant figure)}$$
$$\frac{7.50 \times 10^{-5}}{2.5 \times 10^{-7}} = \frac{7.50}{2.5} \times 10^{-5-(-7)} = 3.0 \times 10^2 \text{ (2 significant figures)}$$

Scientific Notation and Electronic Calculators

With a scientific calculator you can carry out calculations in scientific notation. You should consult the instruction manual for your particular calculator to learn how to enter and manipulate numbers expressed in an exponential format. On most calculators, you enter the number $A \times 10^n$ by (i) entering the number A, (ii) pressing a key labeled EXP or EE, and (iii) entering the exponent n. If the exponent is negative, you press a key labeled $+/-$ before entering the value of n. (Note that you do not enter the number 10.) The calculator displays the number $A \times 10^n$ with the number A on the left followed by some space and then the exponent n. For example,

$$4.625 \times 10^2 \quad \text{is displayed as} \quad 4.625\ 02$$

To add, subtract, multiply, or divide exponential numbers, use the same sequence of keystrokes as you would in working with ordinary numbers. When you add or subtract on a calculator, the numbers need not have the same exponent; the calculator automatically takes account of the different exponents. Remember, though, that the calculator often gives more digits in the answer than the allowed number of significant figures. It's sometimes helpful to outline the calculation on paper, as in the preceding examples, to keep track of the number of significant figures.

PROBLEM A.1

Perform the following calculations, expressing the results in scientific notation with the correct number of significant figures. (You don't need a calculator for these.)

(a) $(1.50 \times 10^4) + (5.04 \times 10^3)$
(b) $(2.5 \times 10^{-2}) - (5.0 \times 10^{-3})$
(c) $(6.3 \times 10^{15}) \times (10.1 \times 10^3)$
(d) $(2.5 \times 10^{-3}) \times (3.2 \times 10^{-4})$
(e) $(8.4 \times 10^4) \div (3.0 \times 10^6)$
(f) $(5.530 \times 10^{-2}) \div (2.5 \times 10^{-5})$

ANSWERS

(a) 2.00×10^4 **(b)** 2.0×10^{-2} **(c)** 6.4×10^{19}
(d) 8.0×10^{-7} **(e)** 2.8×10^{-2} **(f)** 2.2×10^3

PROBLEM A.2

Perform the following calculations, expressing the results in scientific notation with the correct number of significant figures. (Use a calculator for these.)

(a) $(9.72 \times 10^{-1}) + (3.4823 \times 10^2)$
(b) $(3.772 \times 10^3) - (2.891 \times 10^4)$
(c) $(1.956 \times 10^3) \div (6.02 \times 10^{23})$
(d) $3.2811 \times (9.45 \times 10^{21})$
(e) $(1.0015 \times 10^3) \div (5.202 \times 10^{-9})$
(f) $(6.56 \times 10^{-6}) \times (9.238 \times 10^{-4})$

ANSWERS

(a) 3.4920×10^2 **(b)** -2.514×10^4 **(c)** 3.25×10^{-21}
(d) 3.10×10^{22} **(e)** 1.925×10^{11} **(f)** 6.06×10^{-9}

APPENDIX B

Conversion Factors

Length SI Unit: Meter (m)

1 meter = 0.001 kilometer (km)
= 100 centimeters (cm)
= 1.0936 yards (yd)

1 centimeter = 10 millimeters (mm)
= 0.3937 inch (in.)

1 nanometer = 1×10^{-9} meter

1 Angstrom (Å) = 1×10^{-10} meter

1 inch = 2.54 centimeters

1 mile = 1.6094 kilometers

Volume SI Unit: Cubic meter (m^3)

1 cubic meter = 1000 liters (L)

1 liter = 1000 cubic centimeters (cm^3)
= 1000 milliliters (mL)
= 1.056710 quarts (qt)

1 cubic inch = 16.4 cubic centimeters

Temperature SI Unit: Kelvin (K)

0 K = −273.15 °C
= −459.67 °F

$°F = (9/5)°C + 32°; °F = (1.8 \times °C) + 32°$

$$°C = (5/9)(°F - 32°); °C = \frac{(°F - 32°)}{1.8}$$

$K = °C + 273.15°$

Mass SI Unit: Kilogram (kg)

1 kilogram = 1000 grams (g)
= 2.205 pounds (lb)

1 gram = 1000 milligrams (mg)
= 0.03527 ounce (oz)

1 pound = 453.6 grams

1 atomic mass unit = 1.66054×10^{-24} gram

Pressure SI Unit: Pascal (Pa)

1 pascal = 9.869×10^{-6} atmosphere

1 atmosphere = 101,325 pascals
= 760 mmHg (Torr)
= 14.70 lb/in^2 (psi)

Energy SI Unit: Joule (J)

1 joule = 0.23901 calorie (cal)

1 calorie = 4.184 joules

1 Calorie (nutritional unit) = 1000 calories
= 1 kcal

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Answers to Selected Problems

Short answers are given for in-chapter problems, Understanding Key Concepts problems, and even-numbered end-of-chapter problems.

Chapter 1

1.1 solid **1.2** mixture (heterogeneous): **(a), (d);** pure (element): **(b), (c)** **1.3** physical: **(a);** chemical: **(b), (c), (d)** **1.4** chemical change; on the left: pure substance; on the right: mixture **1.5** **(a)** 2 **(b)** 1 **(c)** 6 **(d)** 5 **(e)** 4 **(f)** 3 **1.6** **(a)** 1 nitrogen atom, 3 hydrogen atoms **(b)** 1 sodium atom, 1 hydrogen atom, carbon atom, 3 oxygen atoms **(c)** 8 carbon atoms, 18 hydrogen atoms **(d)** 6 carbon atoms, 8 hydrogen atoms, 6 oxygen atoms **1.7** **(a)** 0.01 m **(b)** 0.1 g **(c)** 1000 m **(d)** 0.000 001 s **(e)** 0.000 000 001 g **1.8** **(a)** 3 **(b)** 4 **(c)** 5 **(d)** exact **1.9** 32.3 °C; three significant figures **1.10** **(a)** 5.8×10^{-2} g **(b)** 4.6792×10^{4} m **(c)** 6.072×10^{-3} cm **(d)** 3.453×10^{2} kg **1.11** **(a)** 48,850 mg **(b)** 0.000 008 3 m **(c)** 0.0400 m **1.12** **(a)** 6.3000×10^{5} **(b)** 1.30×10^{3} **(c)** 7.942×10^{11} **1.13** **(a)** 2.30 g **(b)** 188.38 mL **(c)** 0.009 L **(d)** 1.000 kg **1.14** **(a)** 50.9 mL **(b)** 0.078 g **(c)** 11.9 m **(d)** 51 mg **(e)** 103 **1.15** **(a)** 454 g **(b)** 2.5 L **(c)** 105 qt **1.16** 795 mL **1.17** 2.5 mL **1.18** **(a)** 10.6 mg/kg **(b)** 36 mg/kg **1.19** 331.0 K **1.20** 312.15 K **1.21** 7,700 cal **1.22** 0.85 J/K·mol **1.23** float; density = 0.637 g/cm^3 **1.24** 8.392 mL **1.25** more dense **1.26** gases: helium (He), neon (Ne), argon (Ar), krypton (Kr), xenon (Xe), radon (Rn); coinage metals: copper (Cu), silver (Ag), gold (Au) **1.27** Red: vanadium, sources: magnetite, fossil fuels, and bauxite, uses: steel alloys, emeralds, superconducting magnet, and ceramics; Green: boron, sources: borate minerals, including borax and kernite, uses: laundry aid, silly putty, glass, semiconductors, and insecticides; Blue: bromine, sources: Earth's crust and sea water, uses: flame retardant, gasoline additive, and pesticides **1.28** Americium **1.29** **(a)** 0.978 **(b)** three **(c)** less dense **1.30** The smaller cylinder is more precise because the gradations are smaller. **1.31** 3 1/8 in.; 8.0 cm **1.32** start: 0.11 mL stop: 0.25 mL volume: 0.14 mL **1.33** higher in chloroform **1.34** Physical change doesn't alter the identity of the substance; a chemical change alters the chemical identity **1.36** physical: **(a), (d);** chemical **(b), (c), (e)** **1.38** Changes in state: melting, boiling, condensation, and freezing. Melting: a solid is heated to a liquid. Boiling: a liquid is heated to a gas. Condensation: a gas is cooled to a liquid. Freezing: a liquid is cooled to a solid. **1.40** No, as butane is a liquid at 269 K **1.42** **(a)** gasoline—(i) and (iii) **(b)** iodine—(ii) and (v) **(c)** water—(iii) and (vi) **(d)** air—(i) and (iv) **(e)** blood—(i) and (iii) **(f)** sodium hydrogen carbonate—(ii) and (vi) **(g)** gaseous ammonia—(iv) and (vi) **(h)** silicon—(ii) and (v) **1.44** **(a)** reactants: sodium (solid), water (liquid); products: hydrogen (gas), sodium hydroxide (aqueous) **(b)** compounds: water, sodium hydroxide; element: sodium, hydrogen **1.46** **(a)** I, use: preventing goiter **(b)** Cr, use: harden steel **(c)** Tc, use: biomedical imaging **(d)** As, use: pesticides **(e)** Ba, uses: paint and biomedical imaging **1.48** **(a)** Br **(b)** Mn **(c)** C **(d)** K **1.50** Carbon, hydrogen, nitrogen, and oxygen; 10 atoms **1.52** $C_{13}H_{18}O_2$ **1.54** A physical quantity consists of a number and a unit. **1.56** **(a)** cubic centimeter **(b)** decimeter **(c)** millimeter **(d)** nanoliter **(e)** milligram **(f)** cubic meter **1.58** 10^{9} pg, 3.5×10^{4} pg **1.60** **(a)** 9.457×10^{3} **(b)** 7×10^{-5} **(c)** 2.000×10^{10} **(d)** 1.2345×10^{-2} **(e)** 6.5238×10^{2} **1.62** **(a)** 6 **(b)** 3 **(c)** 3 **(d)** 4 **(e)** 1 to 5 **(f)** 2 or 3 **1.64** **(a)** 12,760 km, 13,000 km, 12,756.3 km **(b)** $1.275\,627 \times 10^{4}$ km **1.66** **(a)** 12.1 g **(b)** 96.19 cm **(c)** 263 mL **(d)** 20.9 mg **1.68** **(a)** 0.3614 cg **(b)** 0.0120 mL **(c)** 0.0144 mm **(d)** 60.3 ng **(e)** 1.745 dL **(f)** 1.5×10^{3} cm **1.70** **(a)** 97.8 kg **(b)** 0.133 mL **(c)** 0.46 ng **(d)** 2.99 mm **1.72** **(a)** 62.1 mi/hr **(b)** 27.8 m/s **1.74** **(a)** 6×10^{-4} cm **(b)** 2×10^{3} cells/cm; **1.76** 10 g **1.78** 6×10^{10} cells **1.80** **(a)** 2240 J = 2.24 kJ **(b)** 536 cal = 0.537 kcal **1.82** 0.092 cal/g · °C **1.84** Hg: 75 °C; Fe: 40.8 °C **1.86** 0.179 g/cm^3 **1.88** 11.4 g/cm^3 **1.90** 159 mL **1.92** freezing point = 491.67 °R; boiling point = 671.67 °R **1.94** 3.12 in; 7.92 cm; Discrepancies are due to rounding errors and changes in significant figures. **1.96** **(a)** 3.5×10^{5} cal $(1.46 \times 10^{6}$ J); **(b)** 9.84 °C **1.98** 3.9×10^{-2} g/dL iron, 8.3×10^{-3} g/dL calcium, 2.24×10^{-1} g/dL cholesterol **1.100** 7.8×10^{6} mL/day **1.102** 0.13 g **1.104** 4.4 g; 0.0097 lb **1.106** 2200 mL **1.108** 2.2 tablespoons **1.110** iron **1.112** At the crossover point, °F = °C.

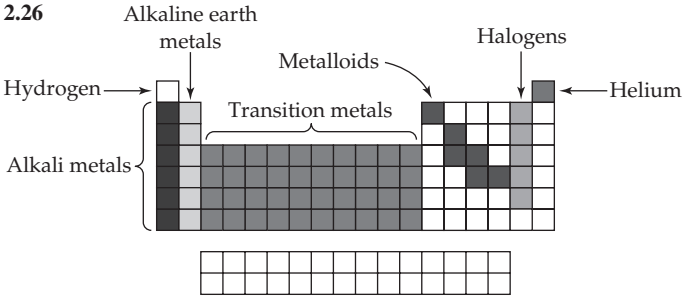
$$°F = \left(\frac{1.8\ °F}{°C} \times °C\right) + 32\ °F \quad \text{If } °C = °F,\ °F = 1.8\ °F + 32°.$$

The crossover temperature is °F = °C = −40°. **1.114** $C_2H_3Cl_3O_2$—four different elements; carbon—two, hydrogen—three, chlorine—three, oxygen—two **1.116** 1.26×10^{11} L; production of fertilizers

Chapter 2

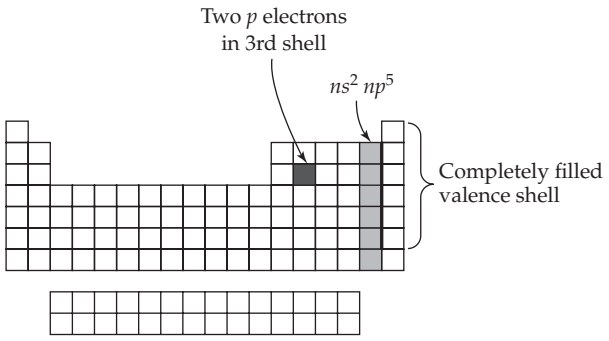
2.1 **(a)** Re **(b)** Sr **(c)** Te **2.2** The answers agree. **2.3** **(a)** $^{79}_{35}$Br, $^{81}_{35}$Br **(b)** 79.986 amu; slight difference with the periodic table at 79.904 amu **2.4** $^{35}_{17}$Cl, $^{37}_{17}$Cl **2.5** group 3A, period 3 **2.6** silver, calcium **2.7** nitrogen (2), phosphorus (3), arsenic (4), antimony (5), bismuth (6) **2.8** The metalloids are along the black zigzag line, beginning in column 3A. They are found between the metals and the nonmetals. **2.9** **(a)** Titanium, transition metal groups **(b)** Tellurium, main group **(c)** Selenium, main group **(d)** Scandium, transition metal groups **(e)** Astatine, main group, halogens **(f)** Argon, main group, noble gas **2.10** **(a)** nonmetal, main group, noble gas **(b)** metal, main group **(c)** nonmetal, main group **(d)** metal, transition element **2.11** **(a)** Li, Na, K, Rb **(b)** F, O, C, Li **(c)** F, Cl, Br, I **2.12** **(a)** Rb, K, Na, Li **(b)** F, O, Li, C **(c)** F, Cl, Br, I **2.13** **(a)** Na-23, Group 1A, third period, metal; **(b)** O-18, Group 6A, sixth period, nonmetal **2.14** 12, magnesium **2.15** sulfur; main group (6A); nonmetal; last electron found in a 3*p* orbital. **2.16** **(a)** $1s^2\,2s^2\,2p^2$ **(b)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^3$ **(c)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^5$ **(d)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^1$ **2.17** $4p^3$, all are unpaired **2.18** gallium **2.19** **(a)** $1s^2\,2s^2\,2p^5$; [He] $2s^2\,2p^5$ **(b)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^1$; [Ne] $3s^2\,3p^1$ **(c)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^2\,3d^{10}\,4p^3$; [Ar] $4s^2\,3d^{10}\,4p^3$ **2.20** group 2A **2.21** group 7A; shell 1 = 2 electrons, shell 2 = 8 electrons, shell 3 = 7 electrons; $1s^2\,2s^2\,2p^6\,3s^2\,3p^5$ **2.22** group 6A, $ns^2\,np^4$ **2.23** ·X· **2.24** :Rn: ·Pb· :Xe: ·Ra· **2.25** red = 700 − 780 nm; blue = 400 − 480 nm; blue = higher energy

2.26



2.27 red: gas (fluorine); blue: atomic number 79 (gold); green: (calcium); beryllium, magnesium, strontium, barium, and radium are similar.

2.28



2.29 selenium **2.30** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^2\,3d^{10}\,4p^3$ **2.32** Atoms of different elements differ in the number of protons and electrons they have. **2.34** **(a)** 16.0 amu **(b)** 78.9 amu **2.36** 16.0 g **2.38** 6.022×10^{23} atoms **2.40** Protons and neutrons are found in a dense central region called the nucleus. Electrons move about the nucleus in large, specifically defined regions called orbitals.

2.42

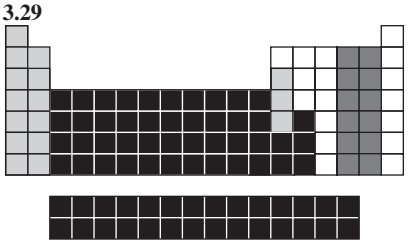
Isotope	(a) $^{27}_{13}Al$	(b) $^{28}_{14}Si$	(c) $^{11}_{5}B$	(d) $^{115}_{47}Ag$
Number of protons	13	14	5	47
Number of neutrons	14	14	6	68
Number of electrons	13	14	5	47

2.44 **(a)** fluorine—19 **(b)** neon—19 **(c)** fluorine—21 **(d)** magnesium—21 **2.46** **(a)** $^{120}_{50}Sn$ **(b)** $^{56}_{26}Fe$ **(c)** $^{226}_{88}Ra$ **2.48** 63.55 amu **2.50** Eight electrons are needed to fill the 3*s* and 3*p* subshells. **2.52** Am, metal **2.54** **(a, b)** transition metals **(c)** 3*d* **2.56** **(a)** Rb: (i), (v), (vii) **(b)** W: (i), (iv) **(c)** Ge: (iii), (v) **(d)** Kr: (ii), (v), (vi) **2.58** selenium **2.60** sodium, potassium, rubidium, cesium, francium **2.62** 2 **2.64** 2, 8, 18 **2.66** 3, 4, 5 **2.68** 10, neon **2.70** **(a)** two paired, two unpaired **(b)** four paired, one unpaired **(c)** two unpaired **2.72** 2, 1, 2, 1, 3, 3 **2.74** 2 **2.76** beryllium, 2*s*; arsenic, 4*p* **2.78** **(a)** 8 **(b)** 4 **(c)** 2 **(d)** 1 **(e)** 3 **(f)** 7 **2.80** neon, argon, krypton, xenon, radon **2.82** 119 **2.84** **(a)** 5*p* **(b)** 3*d* **(c)** 4*p* **(d)** 3*p* **2.86** Sr, metal, group 2A, period 5, 38 protons **2.88** 2, 8, 18, 18, 4; metal **2.90** **(a)** The 4*s* subshell fills before 3*d* **(b)** The 2*s* subshell fills before 2*p*. **(c)** Silicon has 14 electrons: $1s^2\,2s^2\,2p^6\,3s^2\,3p^2$ **(d)** The 3*s* electrons have opposite spins. **2.92** Electrons will fill or half-fill a *d* subshell instead of filling an *s* subshell of a higher shell. **2.94** 7*p* **2.96** **(a)** Co-60: 33 neutrons, 27 protons, 27 electrons (there are lots of possible answers for radioactive isotopes) **(b)** Os-190: 114 neutrons, 76 protons, 76 electrons **(c)** Tc-99: 56 neutrons, 43 protons, 43 electrons **2.98** **(a)** The peaks and valleys tend to correlate with the different groups of the periodic table. **(b)** Electronegativity, ionization energy, electron affinity, etc.

Chapter 3

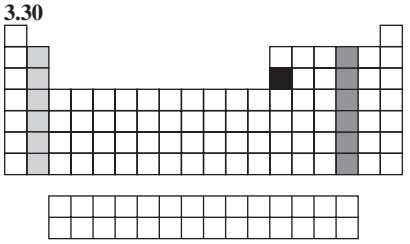
3.1 Mg^{2+} is a cation. **3.2** S^{2-} is an anion. **3.3** O^{2-} is an anion. **3.4** Potassium ($1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^1$) can gain the argon configuration by losing 1 electron. **3.5** Aluminum must lose 3 electrons to form Al^{3+}. **3.6** $X\cdot + \cdot\ddot{Y}\cdot \longrightarrow X^{2+} + :\ddot{Y}:^{2-}$ **3.7** Fe^{2+}, $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,3d^6$ **3.8** **(a)** $Se + 2\,e^- \rightarrow Se^{2-}$ **(b)** $Ba \rightarrow Ba^{2+} + 2e^-$ **(c)** $Br + e^- \rightarrow Br^-$ **3.9** 1.0 g of Na^+ = 312.5 mL; 1.0 g of Cl^- = 285.7 mL **3.10** similar but slightly smaller ionization energies **3.11** **(a)** B **(b)** Ca **(c)** Sc **3.12** **(a)** H **(b)** S **(c)** Cr **3.13** **(a)** copper(II) ion **(b)** fluoride ion **(c)** magnesium ion **(d)** sulfide ion **3.14** **(a)** Ag^+ **(b)** Fe^{2+} **(c)** Cu^+ **(d)** Te^{2-} **3.15** Na^+, sodium ion; K^+, potassium ion; Ca^{2+}, calcium ion; Cl^-, chloride ion **3.16** **(a)** nitrate ion **(b)** cyanide ion **(c)** hydroxide ion **(d)** hydrogen phosphate ion **3.17** Group 1 A: Na^+, K^+; Group 2A: Ca^{2+}, Mg^{2+}; transition metals: Fe^{2+}; halogens: Cl^- **3.18** **(a)** MgI_2 **(b)** Al_2O_3 **(c)** $Fe_3(PO_4)_2$ **(d)** $Cr_2(SO_4)_3$ **3.19** $(NH_4)_2CO_3$ **3.20** $Al_2(SO_4)_3$, $Al(CH_3CO_2)_3$ **3.21** blue: K_2S; red: $BaBr_2$; green: Al_2O_3 **3.22** silver(I) sulphide **3.23** **(a)** tin (IV) oxide **(b)** calcium cyanide **(c)** sodium carbonate **(d)** copper (I) sulfate **(e)** barium hydroxide **(f)** iron (II) nitrate **3.24** **(a)** Li_3PO_4 **(b)** $CuCO_3$ **(c)** $Al_2(SO_3)_3$ **(d)** CuF **(e)** $Fe_2(SO_4)_3$ **(f)** NH_4Cl **3.25** Ca_3N_2 **3.26** Strongest—NaCl; weakest—RbCl; smaller cations have stronger bonds **3.27** acids: **(a)**, **(d)**; bases **(b)**, **(c)** **3.28** **(a)** HCl **(b)** H_2SO_4

3.29



All of the other elements form neither anions nor cations readily.

3.30



3.31 **(a)** O^{2-} **(b)** Na^+ **(c)** Ca^{2+} **(d)** Fe^{2+} **3.32** **(a)** sodium atom (larger) **(b)** Na^+ ion (smaller) **3.33** **(a)** chlorine atom (smaller) **(b)** Cl^- anion (larger) **3.34** iron (II) chloride or ferrous chloride, $FeCl_2$; iron (III) chloride or ferric chloride, $FeCl_3$; iron (II) oxide or ferrous oxide, FeO; iron (III) oxide or ferric oxide, Fe_2O_3; lead (II) chloride, $PbCl_2$; lead (IV) chloride, $PbCl_4$; lead (II) oxide, PbO; lead (IV) oxide, PbO_2 **3.35** **(a)** ZnS **(b)** $PbBr_2$ **(c)** CrF_3 **(d)** Al_2O_3 **3.36** Cr_2O_3 chromium (III) oxide **3.38** Ion charges are determined by the element's position on the periodic table relative to the noble gases (which have an octet of electrons). **3.40** Se^{2-} **3.42** **(a)** Sr **(b)** Br **3.44** **(a)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^2\,3d^{10}\,4p^6$ **(b)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^2\,3d^{10}\,4p^6$ **(c)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6$ **(d)** $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,4s^2\,3d^{10}\,4p^6\,5s^2\,4d^{10}\,5p^6$ **(e)** $1s^2\,2s^2\,2p^6$ **3.46** **(a)** $Ca \rightarrow Ca^{2+} + 2\,e^-$ **(b)** $Au \rightarrow Au^+ + e^-$ **(c)** $F + e^- \rightarrow F^-$ **(d)** $Cr \rightarrow Cr^{3+} + 3e^-$ **3.48** true: **(d)**; false: **(a)**, **(b)**, **(c)** **3.50** **(a)** O **(b)** Li **(c)** Zn **(d)** N **3.52** none **3.54** Cr^{2+}: $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,3d^4$; Cr^{3+}: $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,3d^3$ **3.56** greater **3.58** **(a)** sulfide ion **(b)** tin (II) ion **(c)** strontium ion **(d)** magnesium ion **(e)** gold (I) ion **3.60** **(a)** Se^{2-} **(b)** O^{2-} **(c)** Ag^+ **3.62** **(a)** OH^- **(b)** HSO_4^- **(c)** $CH_3CO_2^-$ **(d)** MnO_4^- **(e)** OCl^- **(f)** NO_3^- **(g)** CO_3^{2-} **(h)** $Cr_2O_7^{2-}$ **3.64** **(a)** $NaHCO_3$ **(b)** KNO_3 **(c)** $CaCO_3$ **(d)** NH_4NO_3

3.66

	S^{2-}	Cl^-	PO_4^{3-}	CO_3^{2-}
Copper(II)	CuS	$CuCl_2$	$Cu_3(PO_4)_2$	$CuCO_3$
Ca^{2+}	CaS	$CaCl_2$	$Ca_3(PO_4)_2$	$CaCO_3$
NH_4^+	$(NH_4)_2S$	NH_4Cl	$(NH_4)_3PO_4$	$(NH_4)_2CO_3$
Ferric ion	Fe_2S_3	$FeCl_3$	$FePO_4$	$Fe_2(CO_3)_3$

3.68 copper(II) sulfide, copper(II) chloride, copper(II) phosphate, copper(II) carbonate; calcium sulfide, calcium chloride, calcium phosphate, calcium carbonate; ammonium sulfide, ammonium chloride, ammonium phosphate, ammonium carbonate; iron(III) sulfide, iron(III) chloride, iron(III) phosphate, iron(III) carbonate **3.70** **(a)** magnesium carbonate **(b)** calcium acetate **(c)** silver(I) cyanide **(d)** sodium dichromate **3.72** $Ca_3(PO_4)_2$ **3.74** An acid gives H^+ ions in water; a base gives OH^- ions. **3.76** **(a)** $H_2CO_3 \rightarrow 2H^+ + CO_3^{2-}$ **(b)** $HCN \rightarrow H^+ + CN^-$ **(c)** $Mg(OH)^2 \rightarrow Mg^{2+} + 2\,OH^-$ **(d)** $KOH \rightarrow K^+ + OH^-$ **3.78** H^- has the helium configuration, $1s^2$ **3.80** **(a)** CrO_3 **(b)** VCl_5 **(c)** MnO_2 **(d)** MoS_2 **3.82** **(a)** Cu_3PO_4 copper(I)phosphate **(b)** Na_2SO_4 sodium sulfate **(c)** MnO_2 manganese (IV) oxide **(d)** $AuCl_3$ gold (III) chloride **(e)** $Pb(CO_3)_2$ lead (IV) carbonate **(f)** Ni_2S_3 nickel (III) sulfide

3.84

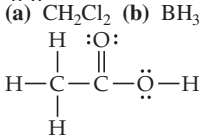
Ion	Protons	Electrons	Neutrons
(a) $^{16}O^{2-}$	8	10	8
(b) $^{89}Y^{3+}$	39	36	50
(c) $^{133}Cs^+$	55	54	78
(d) $^{81}Br^-$	35	36	46

3.86 **(a)** Mn^{4+} **(b)** Cu^+ **(c)** Ti^{4+} **3.88** Ca^{2+} (monoatomic); $C_6H_{11}O_7^-$ (polyatomic) **3.90** stannous fluoride, SnF_2

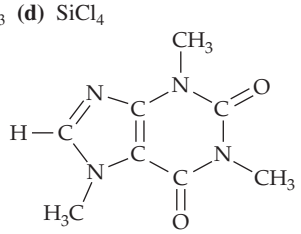
Chapter 4

4.1 $:\ddot{I}:\ddot{I}:$; xenon **4.2** **(a)** P 3, H 1 **(b)** Se 2, H 1 **(c)** H 1, Cl 1 **(d)** Si 4, F 1 **4.3** **(a)** CH_2Cl_2 **(b)** BH_3 **(c)** NI_3 **(d)** $SiCl_4$

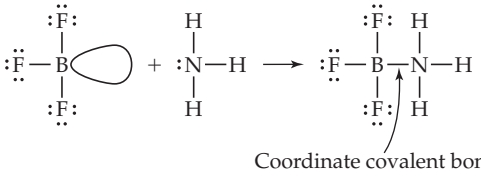
4.4



4.5

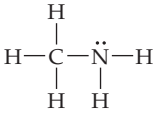


4.6

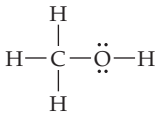


4.7 $AlCl_3$ is a covalent compound, and Al_2O_3 is ionic.

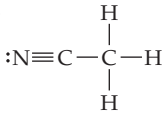
4.8



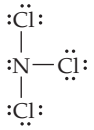
4.9 **(a)**



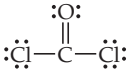
(b)



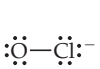
(c)



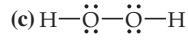
4.10 **(a)**



(b)



(c)



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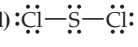
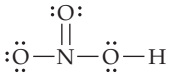
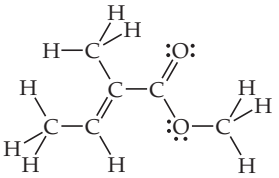


4.11

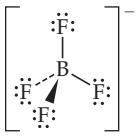


4.12 **(a)** $C_6H_{10}O_2$ **(b)**



4.13 :Ö=Ö—Ö: Oxygen normally has two bonds. Ozone is reactive as one oxygen atom has a single bond.

4.14

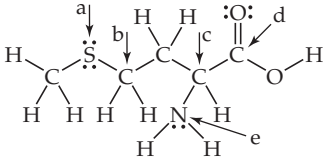


tetrahedral

4.15 chloroform, $CHCl_3$—tetrahedral; dichloroethane—planar

4.16 Both are bent.

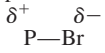
4.17



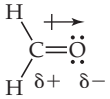
(a) bent
(b) tetrahedral
(c) tetrahedral
(d) trigonal planar
(e) pyramidal

4.18 H = P < S < N < O

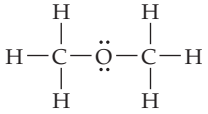
4.19 **(a)** polar covalent **(b)** ionic **(c)** nonpolar covalent **(d)** polar covalent



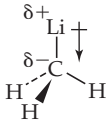
4.20



4.21 The carbons are tetrahedral; the oxygen is bent, the molecule is polar.



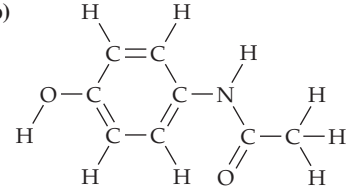
4.22



4.23 **(a)** disulfur dichloride **(b)** iodine monochloride **(c)** iodine trichloride

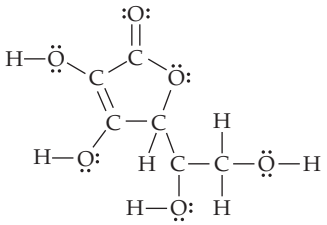
4.24 **(a)** SeF_4 **(b)** P_2O_5 **(c)** BrF_3 **4.25** **(a)** tetrahedral **(b)** pyramidal **(c)** trigonal planar **4.26** **(c)** is square planar **4.27** **(a)** $C_8H_9NO_2$

(b)

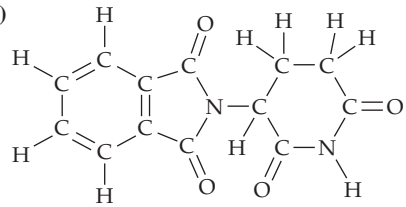


(c) All carbons are trigonal planar except the —CH_3 carbon. Nitrogen is pyramidal.

4.28

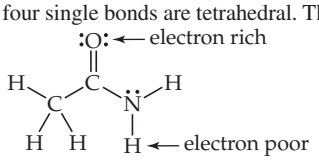


4.29 **(a)** $C_{13}H_{10}N_2O_4$ **(b)**



(c) Double-bonded carbon atoms are trigonal planar. The three carbon atoms with four single bonds are tetrahedral. The nitrogen atoms are pyramidal.

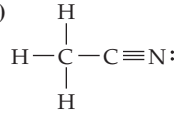
4.30



4.32 In a coordinate covalent bond, both electrons in the bond come from the same atom. **4.34** covalent bonds: **(b)**; ionic bonds: **(a)**, **(c)**, **(d)**, **(e)**

4.36 Two covalent bonds. **4.38** **(b)**, **(c)** **4.40** $SnCl_4$ **4.42** The N—O bond **4.44** **(a)** A molecular formula shows the numbers and kinds of atoms; a structural formula shows how the atoms are bonded to one another. **(b)** A structural formula shows the bonds between atoms; a condensed structure shows atoms but not bonds. **(c)** A lone pair of valence electrons is not shared in a bond; a shared pair of electrons is shared between two atoms. **4.46** **(a)** 10; triple bond **(b)** 18; double bond between N, O **(c)** 24; double bond between C, O **(d)** 20 **4.48** too many hydrogens

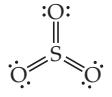
4.50 **(a)** H—Ö—N=Ö **(b)**



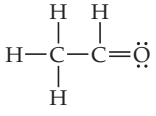
(c) H—F:

4.52 **(a)** $CH_3CH_2CH_3$ **(b)** $H_2C{=}CHCH_3$ **(c)** CH_3CH_2Cl **4.54** CH_3COOH

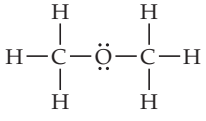
4.56 **(a)** H—Ö—N=Ö **(b)**



(c)

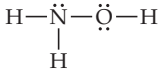


4.58

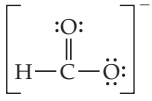


Dimethyl ether

4.60



4.62 **(a)**



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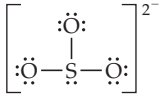

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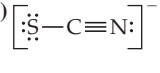
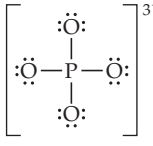
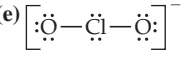


(d)

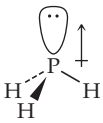
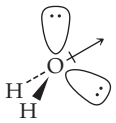


(e)



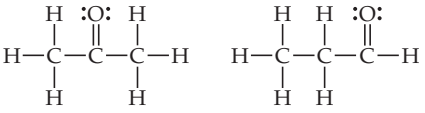
4.64 tetrahedral; pyramidal; bent **4.66** **(a)**, **(b)** tetrahedral **(c)**, **(d)** trigonal planar **(e)** pyramidal **4.68** All are trigonal planar, except for the —CH_3 carbon, which is tetrahedral. **4.70** It should have low electronegativity, like other alkali metals. **4.72** Cl > C > Cu > Ca > Cs

4.74 **(a)** $\overset{\delta^-}{O}—\overset{\delta^+}{Cl}$ **(e)** $\overset{\delta^+}{C}—\overset{\delta^-}{O}$ **4.76** $PH_3 < HCl < H_2O < CF_4$

4.78 **(a)** $H—Cl$ polar **(b)**  polar **(c)**  polar **(d)** nonpolar

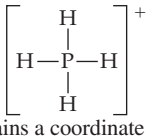
4.80 S—H bonds are nonpolar. **4.82** **(a)** selenium dioxide **(b)** xenon tetroxide **(c)** dinitrogen pentasulfide **(d)** triphosphorus tetraselenide

4.84 **(a)** $SiCl_4$ **(b)** NaH **(c)** SbF_5 **(d)** OsO_4

4.86 **(a)** 

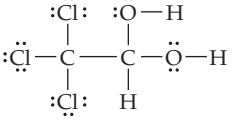
(b) The C═O carbons are trigonal planar; the other carbons are tetrahedral. **(c)** The C═O bonds are polar.

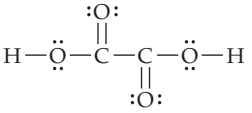
4.88 **(a)** C forms four bonds. **(b)** N forms three bonds. **(c)** S forms two bonds. **(d)** COS: C has four bonds; O and S typically have two bonds each.

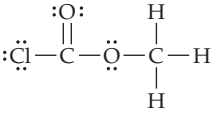
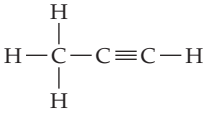
4.90 **(a)**  **(b)** tetrahedral

(c) contains a coordinate covalent bond **(d)** has 19 p and 18 e^-

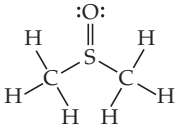
4.92 **(a)** calcium chloride **(b)** tellurium dichloride **(c)** boron trifluoride **(d)** magnesium sulfate **(e)** potassium oxide **(f)** iron(III) fluoride **(g)** phosphorus trifluoride

4.94 

4.96 

4.98 **(a)**  **(b)** 

4.100 (i) Oxygen, iodine, hydrogen; nonmetals can bond to themselves. (ii) Oxygen, phosphorus, iodine, and hydrogen; nonmetals form covalent bonds. (iii) Potassium and cesium; metals form up ionic bonds. (iv) Oxygen, phosphorus, iodine, and hydrogen; nonmetals are found in covalent and ionic bonds.

4.102 

Chapter 5

5.1 $3O_2 \rightarrow 2O_3$ **5.2** **(a)** $Ca(OH)_2 + 2HCl \rightarrow CaCl_2 + 2H_2O$ **(b)** $4Al + 3O_2 \rightarrow 2Al_2O_3$ **(c)** $2CH_3CH_3 + 7O_2 \rightarrow 4CO_2 + 6H_2O$ **(d)** $2AgNO_3 + MgCl_2 \rightarrow 2AgCl + Mg(NO_3)_2$ **5.3** $2A + B_2 \rightarrow A_2B_2$

5.4 Soluble: **(b)**, **(d)**; insoluble: **(a)**, **(c)**, **(e)** **5.5** **(a)** $NiCl_2(aq) + (NH_4)_2S(aq) \rightarrow NiS(s) + 2NH_4Cl(aq)$; precipitation **(b)** $2AgNO_3(aq) + CaBr_2(aq) \rightarrow Ca(NO_3)_2(aq) + 2AgBr(s)$

5.6 **(a)** $2CsOH(aq) + H_2SO_4(aq) \rightarrow Cs_2SO_4(aq) + 2H_2O(l)$ **(b)** $Ca(OH)_2(aq) + 2CH_3CO_2H(aq) \rightarrow Ca(CH_3CO_2)_2(aq) + 2H_2O(l)$ **(c)** $NaHCO_3(aq) + HBr(aq) \rightarrow NaBr(aq) + CO_2(g) + H_2O(l)$

5.7 **(a)** precipitation **(b)** redox **(c)** acid-base neutralization

5.8 **(a)** oxidized reactant (reducing agent): Fe; reduced reactant (oxidizing agent): Cu^{2+} **(b)** oxidized reactant (reducing agent): Mg; reduced reactant (oxidizing agent): Cl_2; **(c)** oxidized reactant (reducing agent): Al; reduced reactant (oxidizing agent): Cr_2O_3 **5.9** $2K(s) + Br_2(l) \rightarrow 2KBr(s)$; oxidizing agent: Br_2; reducing agent: K **5.10** **(a)** V(III) **(b)** Sn(IV) **(c)** Cr(VI) **(d)** Cu(II) **(e)** Ni(II) **5.11** **(a)** not redox **(b)** Na oxidized from 0 to +1; H reduced from +1 to 0 **(c)** C oxidized from 0 to +4; O reduced from 0 to −2 **(d)** C oxidized from +2 to +4; O reduced from 0 to −2 **(e)** not redox **(f)** S oxidized from +4 to +6; Mn reduced from +7 to +2 **5.12** **(b)** oxidizing agent: H_2; reducing agent: Na **(c)** oxidizing agent: O_2; reducing agent: C **(d)** oxidizing agent: O_2; reducing agent: CO **(f)** oxidizing agent: MnO_4^-; reducing agent: SO_2 **5.13** **(a)** $Zn(s) + Pb^{2+}(aq) \rightarrow Zn^{2+}(aq) + Pb(s)$ **(b)** $OH^-(aq) + H^+(aq) \rightarrow H_2O(l)$ **(c)** $2Fe^{3+}(aq) + Sn^{2+}(aq) \rightarrow 2Fe^{2+}(aq) + Sn^{4+}(aq)$

5.14 **(a)** redox **(b)** neutralization **(c)** redox **5.15** **(a)** Zn oxidized from 0 to +2; Pb reduced from +2 to 0; oxidizing agent: Pb in $Pb(NO_3)_2$; reducing agent: Zn **(c)** Sn oxidized from +2 to +4; Fe reduced from +3 to +2; oxidizing agent: Fe in $FeCl_3$; reducing agent: Sn in $SnCl_2$ **5.16** **(d)** **5.17** **(c)** **5.18** reactants: **(d)**; products: **(c)** **5.19** **(a)** box 1 **(b)** box 2 **(c)** box 3

5.20 $2Ag^+ + CO_3^{2-}$; $2Ag^+ + CrO_4^{2-}$ **5.21** **(a)** $CaCl_2$ **(b)** Na_2SO_4 **(c)** $CaSO_4$, spectator ions: Na^+ and Cl^- **5.22** In a balanced equation, the numbers and kinds of atoms are the same on both sides of the reaction arrow.

5.24 **(a)** $HCl(aq) + CaCO_3(s) \rightarrow CO_2(g) + CaCl_2(aq) + H_2O(l)$ **(b)** $2K(s) + Br_2(l) \rightarrow 2KBr(s)$ **(c)** $C_3H_8(g) + 5O_2(g) \rightarrow 3CO_2(g) + 4H_2O(l)$

5.26 **(a)** $2C_2H_6(g) + 7O_2(g) \rightarrow 4CO_2(g) + 6H_2O(g)$ **(b)** balanced **(c)** $2Mg(s) + O_2(g) \rightarrow 2MgO(s)$ **(d)** $2K(s) + 2H_2O(l) \rightarrow 2KOH(aq) + H_2(g)$

5.28 **(a)** $Hg(NO_3)_2(aq) + 2LiI(aq) \rightarrow 2LiNO_3(aq) + HgI_2(s)$ **(b)** $I_2(s) + 5Cl_2(g) \rightarrow 2ICl_5(s)$ **(c)** $4Al(s) + 3O_2(g) \rightarrow 3Al_2O_3(s)$ **(d)** $CuSO_4(aq) + 2AgNO_3(aq) \rightarrow Ag_2SO_4(s) + Cu(NO_3)_2(aq)$ **(e)** $2Mn(NO_3)_3(aq) + 3Na_2S(aq) \rightarrow Mn_2S_3(s) + 6NaNO_3(aq)$

5.30 **(a)** $2C_4H_{10}(g) + 13O_2(g) \rightarrow 8CO_2(g) + 10H_2O(l)$ **(b)** $C_2H_6O(g) + 3O_2(g) \rightarrow 2CO_2(g) + 3H_2O(l)$ **(c)** $2C_8H_{18}(g) + 25O_2(g) \rightarrow 16CO_2(g) + 18H_2O(l)$

5.32 $4HF + SiO_2 \rightarrow SiF_4 + 2H_2O$ **5.34** **(a)** redox **(b)** neutralization **(c)** precipitation **(d)** neutralization

5.36 **(a)** $Ba^{2+}(aq) + SO_4^{2-}(aq) \rightarrow BaSO_4(s)$ **(b)** $Zn(s) + 2H^+(aq) \rightarrow Zn^{2+}(aq) + H_2(g)$ **5.38** precipitation: **(a)**, **(d)**, **(e)**; redox: **(b)**, **(c)** **5.40** $Ba(NO_3)_2$

5.42 **(a)** $2NaBr(aq) + Hg_2(NO_3)_2(aq) \rightarrow Hg_2Br_2(s) + 2NaNO_3(aq)$ **(d)** $(NH_4)_2CO_3(aq) + CaCl_2(aq) \rightarrow CaCO_3(s) + 2NH_4Cl(aq)$ **(e)** $2KOH(aq) + MnBr_2(aq) \rightarrow Mn(OH)_2(s) + 2KBr(aq)$ **(f)** $3Na_2S(aq) + 2Al(NO_3)_3(aq) \rightarrow Al_2S_3(s) + 6NaNO_3(aq)$

5.44 **(a)** $2Au^{3+}(aq) + 3Sn(s) \rightarrow 3Sn^{2+}(aq) + 2Au(s)$ **(b)** $2I^-(aq) + Br_2(l) \rightarrow 2Br^-(aq) + I_2(s)$ **(c)** $2Ag^+(aq) + Fe(s) \rightarrow Fe^{2+}(aq) + 2Ag(s)$

5.46 **(a)** $Sr(OH)_2(aq) + FeSO_4(aq) \rightarrow SrSO_4(s) + Fe(OH)_2(s)$ **(b)** $S^{2-}(aq) + Zn^{2+}(aq) \rightarrow ZnS(s)$ **5.48** Most easily oxidized: metals on left side; most easily reduced: groups 6A and 7A **5.50** oxidation number increases: **(b)**, **(c)**; oxidation number decreases **(a)**, **(d)**

5.52 **(a)** Co: +3 **(b)** Fe: +2 **(c)** U: +6 **(d)** Cu: +2 **(e)** Ti: +4 **(f)** Sn: +2 **5.54** **(a)** oxidized: S; reduced: O **(b)** oxidized: Na; reduced: Cl **(c)** oxidized: Zn; reduced: Cu **(d)** oxidized: Cl; reduced: F

5.56 **(a)** $N_2O_4(l) + 2N_2H_4(l) \rightarrow 3N_2(g) + 4H_2O(g)$ **(b)** $CaH_2(s) + 2H_2O(l) \rightarrow Ca(OH)_2(aq) + 2H_2(g)$ **(c)** $2Al(s) + 6H_2O(l) \rightarrow 2Al(OH)_3(s) + 3H_2(g)$

5.58 oxidizing agents: N_2O_4, H_2O; reducing agents: N_2H_4, CaH_2, Al

5.60 $Li_2O(s) + H_2O(g) \rightarrow 2LiOH(s)$; not a redox reaction

5.62 **(a)** x neutralization **(b)** $3AgNO_3(aq) + FeCl_3(aq) \rightarrow 3AgCl(s) + Fe(NO_3)_3(aq)$; precipitation **(c)** $(NH_4)_2Cr_2O_7(s) \rightarrow Cr_2O_3(s) + 4H_2O(g) + N_2(g)$; redox **(d)** $Mn_2(CO_3)_3(s) \rightarrow Mn_2O_3(s) + 3CO_2(g)$; redox

5.64

Compound	Oxidation Number of Metal	Compound	Oxidation Number of Metal
(a) MnO_2	+4	**(b)** CrO_2	+4
Mn_2O_3	+3	CrO_3	+6
$KMnO_4$	+7	Cr_2O_3	+3

5.66 $Fe^{3+}(aq) + 3NaOH(aq) \rightarrow Fe(OH)_3(s) + 3Na^+(aq)$; $Fe^{3+}(aq) + 3OH^-(aq) \rightarrow Fe(OH)_3(s)$

5.68 $2Bi^{3+}(aq) + 3S^{2-}(aq) \rightarrow Bi_2S_3(s)$

5.70 $CO_2(g) + 2NH_3(g) \rightarrow NH_2CONH_2(s) + H_2O(l)$

5.72 **(a)** reactants: I = −1, Mn = −4; products: I = 0, Mn = +2 **(b)** reducing agent: NaI; oxidizing agent: MnO_2 **5.74** **(a)** $Mg(OH)_2$ **(b)** $Mg(OH)_2(s) + 2\,HCl(aq) \rightarrow MgCl_2(aq) + H_2O(l)$

Chapter 6

6.1 **(a)** 206.0 amu **(b)** 232.0 amu **6.2** 1.71×10^{21} molecules **6.3** 0.15 g **6.4** 111.0 amu **6.5** 0.217 mol; 4.6 g **6.6** 5.00 g weighs more **6.7** $3.0 \times 10^3 \mu$mols **6.8** **(a)** $Ni + 2HCl \rightarrow NiCl_2 + H_2$; 4.90 mol **(b)** 6.00 mol **6.9** $6CO_2 + 6H_2O \rightarrow C_6H_{12}O_6 + 6O_2$; 90.0 mol CO_2 **6.10** **(a)** 39.6 mol **(b)** 13.8 g **6.11** **(a)** 0.0272 mol **(b)** 0.0272 mol WO_3; 0.0816 mol H_2 **(c)** 6.31 g WO_3; 0.165 g H_2 **6.12** 44.7 g; 57.0% **6.13** 47.3 g **6.14** A_2 **6.15** $C_5H_{11}NO_2S$; mol. mass = 149.1 amu **6.16** **(a)** $A_2 + 3B_2 \rightarrow 2AB_3$ **(b)** 2 mol AB_3; 0.67 mol AB_3 **6.17** 10 AB ($2B_2$ left over) **6.18** Blue is the limiting reagent, yield: 73% **6.19** 22 g, 31 g **6.20** One mole of a substance is an amount equal to its formula mass in grams. One mole of a molecular compound contains 6.022×10^{23} molecules. **6.22** 1.204×10^{24} Na^+ ions; 6.022×10^{23} SO_4^{2-} ions **6.24** 2.43×10^{23} atoms Ca **6.26** **(a)** 100.1 g/mol **(b)** 60.0 g/mol **(c)** 62.0 g/mol **6.28** **(a)** 6.022×10^{23} atoms; 12.0 g **(b)** 6.022×10^{23} atoms; 12.0 g **(c)** 1.204×10^{23} atoms; 24.0 g **6.30** 2.78×10^{-3} mol aspirin **6.32** **(a)** 342.3 g/mol **(b)** 84.0 g/mol **(c)** 74.0 g/mol **(d)** 350.1 g/mol **6.34** **(a)** 26 g **(b)** 6.3 g **(c)** 5.6 g **(d)** 26 g **6.36** **(a)** $N_2(g) + O_2(g) \rightarrow 2NO(g)$ **(b)** 7.50 mol N_2 **(c)** 7.62 mol NO **(d)** 0.125 mol O_2 **6.38** **(a)** 58.3 g/mol **(b)** 0.0070 mol in one tablespoon **6.40** **(a)** $N_2H_4(g) + 3O_2(g) \rightarrow 2NO_2(g) + 2H_2O(g)$ **(b)** 15.5 mol O_2 **(c)** 496 g O_2 **6.42** **(a)** $2Mg(s) + O_2(g) \rightarrow 2MgO(s)$ **(b)** 16.5 g O_2; 41.5 g MgO **(c)** 38.0 g Mg; 63.0 g MgO **6.44** 1.97×10^3 mol CO **6.46** 19 mol Fe **6.48** 69 g B_2H_2 **6.50** **(a)** O_2 **(b)** 71.9 kg NO_2 **(c)** 82.5% **6.52** **(a)** 4.57 g NH_3 **(b)** 38 g cisplatin **6.54** 89.6% **6.56** **(a)** 0.463 g H_2 **(b)** redox reaction; H^+ is reduced (oxidizing agent); Zn is oxidized (reducing agent) **6.58** **(a)** $Cu(s) + 4H^+(aq) + 2NO_3^-(aq) \rightarrow Cu^{2+}(aq) + 2NO_2(g) + 2H_2O(l)$ **(b)** yes, 35.0 g HNO_3 can dissolve 8.82 g Cu **6.60** 0.294 m^3 ethanol **6.62** 0.406 mol NaOCl **6.64** **(a)** $3NO_2(g) + H_2O(l) \rightarrow 2HNO_3(aq) + NO(g)$ **(b)** 59.3 g HNO_3 **(c)** 73.9% **6.66** 23.9 g $AgNO_3$ **6.68** 132 kg Li_2O **6.70** **(a)** 1000 mg/day **(b)** 4.14 g calcium citrate **6.72** **(a)** $C_{24}H_{36}O_5$; 404 g/mol **(b)** 2.5×10^{-5} mol lovastatin **6.74** **(a)** recommend daily dose: 90 mg for a man and 75 mg for a woman; 500 mg/tablet **(b)** men = 555%; women = 666%

Chapter 7

7.1 **(a)** potential **(b)** kinetic **(c)** potential **(d)** kinetic **(e)** potential **(f)** kinetic **7.2** **(a)** N_2 **(b)** CO **7.3** **(a)** $\Delta H = 2720$ kJ/mol **(b)** endothermic **7.4** **(a)** endothermic **(b)** 836 kJ **(c)** 310 kJ **7.5** 380 kJ **7.6** −1270 kJ/mol; −27.6 J/g **7.7** **(a)** increase **(b)** decrease **(c)** decrease **7.8** **(a)** positive **(b)** spontaneous at all temperatures **7.9** Relatively slow. Activation energy is relatively large; ΔG is negative. **7.10** Increase the temperature, add a catalyst, and increase the concentration of reagents.

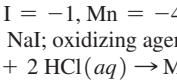
7.11 **(a)** $K = \dfrac{[NO_2]^2}{[N_2O_4]}$ **(b)** $K = \dfrac{[H_2O]^2}{[H_2S]^2[O_2]}$ **(c)** $K = \dfrac{[Br_2][F_2]^5}{[BrF_5]^2}$

7.12 **(a)** products strongly favored **(b)** reactants strongly favored **(c)** products somewhat favored **7.13** $K = 29.0$

7.14 **(a)** $K = \dfrac{[AB]^2}{[A_2][B_2]}$; $K = \dfrac{[AB]^2}{[A_2][B]^2}$ **(b)** $K = 0.11$; $K = 0.89$

7.15 reaction favored by high pressure and low temperature **7.16** **(a)** favors reactants **(b)** favors product **(c)** favors product **7.17** 0.401 mol glucose **7.18** ΔH is positive; ΔS is positive; ΔG is negative **7.19** ΔH is negative; ΔS is negative; ΔG is negative **7.20** **(a)** $2A_2 + B_2 \rightarrow 2A_2B$ **(b)** ΔH is negative; ΔS is negative; ΔG is negative **7.21** **(a)** blue curve represents faster reaction **(b)** red curve is spontaneous **7.22** **(a)** positive **(b)** nonspontaneous at low temperature; spontaneous at high temperature **7.24** Differences in bond energies between the products and reactants = *heat of reaction* or enthalpy change

7.26 **(a)** ΔH is negative. $H_2O(l) \rightarrow H_2O(s) + 6.02$ kJ **(b)** −15.1 kJ **(c)** −10.7 kJ **(d)** +6.02 kJ/mol

7.28  **(b)** 78 kcal and 330 kJ

7.30 **(a)** $2C_8H_{18} + 25O_2 \rightarrow 16CO_2 + 18H_2O +$ heat **(b)** ΔH is negative. **(c)** 2.28×10^4 kJ/1 mol C_8H_{18} **(d)** 0.0824 mol C_8H_{18}; 9.39 g C_8H_{18} **(d)** 3.40×10^3 kJ

7.32 Decreases in **(a), (b), (c), (f)**; increases in **(d), (e)**

7.34 Exothermic release heat (negative ΔH); exergonic is spontaneous (negative ΔG) **7.36** Endothermic with a large increase in entropy

7.38 **(a)** decreases **(b)** spontaneous at low temperatures until the temperature results in $\Delta H = T\Delta S$ **7.40** **(a)** negative **(b)** spontaneous at low temperatures and nonspontaneous at high temperatures, depending on the temperature **7.42** $E_{act} = +20.9$ kJ/mol **7.44** causes more collisions **7.46** also reduces the activation energy of the reverse reaction by 20.9 kJ/mol **7.48** **(a)** nonspontaneous **(b)** no, as the reaction is nonspontaneous at all temperatures **7.50** Catalysts only change the activation energy and not the equilibrium constant.

7.52 **(a)** $K = \dfrac{[H_2S]^2}{[S_2][H_2]^2}$ **(b)** $K = \dfrac{[HCl]^2}{[H_2S][Cl_2]}$ **(c)** $K = \dfrac{[BrCl]^2}{[Br_2][Cl_2]}$

(d) $K = \dfrac{[CO][H_2]}{[H_2O]}$ **7.54** **(a)** $K = \dfrac{[CO_2]^2}{[CO]^2[O_2]}$ **(b)** 1.3×10^3; products

7.56 **(a)** 0.062 mol/L **(b)** 2.1 mol/L **7.58** reactants

7.60 **(a)** exothermic **(b)** products **(c)** no effect for (1) and (5); shifts left for (2) and (3); shifts right for (4) **7.62** **(a)** reactants **(b)** products **(c)** no effect **7.64** increases **7.66** **(a)** increases **(b)** decreases **(c)** increases **(d)** no change **7.68** **(a)** exothermic **(b)** −7.7 kcal, −32 kJ **7.70** **(a)** CO removes Hb so less Hb is available to react with O_2 **(b)** shifts equilibrium to the right **7.72** **(a)** 22.6 kJ needed **(b)** 22.6 kJ released

7.74 **(a)** $2CH_3OH(l) + 3O_2(g) \rightarrow 2CO_2(g) + 4H_2O(g)$ **(b)** −1347 kJ **(c)** −1140 kJ **7.76** **(a)** −108 kJ **(b)** −18.8 kcal **7.78** Snack food: SunChips—210 Cal **(a)** Running—590 Cal/hour; biking—590 Cal/hour; swimming—510 Cal/hour **(b)** 21 minutes running or biking; 25 minutes swimming (Note: The exact number of minutes depends on the type of snack.)

7.80 **(a)** −23 kcal; −104 kJ; exothermic **(b)** increase either N_2 or H_2; remove NH_3; cool the reaction; increase pressure or decrease volume **(c)** high pressures; intermediate temperatures; removing liquefied NH_3

Chapter 8

8.1 **(a)** disfavored by ΔH; favored by ΔS **(b)** $\Delta H = -40.6$ kJ/mol; $\Delta S = -109$ J/(mol · K) **8.2** **(a)** decrease **(b)** increase **8.3** **(a), (c)** **8.4** **(a)** London forces **(b)** hydrogen bonds, dipole–dipole forces, London forces **(c)** dipole–dipole forces, London forces

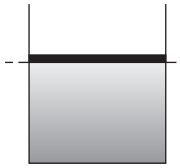
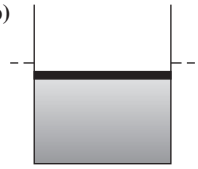
8.5 220 mmHg; 4.25 psi; 2.93×10^4 Pa **8.6** 2.2 atm; 1700 mmHg; 220,000 Pa **8.7** 749 torr; 986 atm **8.8** 1000 mmHg **8.9** 0.45 m^3

8.10 1.3×10^{-3} m^3, 1.8×10^{-2} m^3 **8.11** 637 °C; −91 °C

8.12 33 psi **8.13** 0.352 m^3 **8.14** balloon **(a)**

8.15 4.46×10^3 mol; 7.14×10^4 g CH_4; 1.96×10^5 g CO_2

8.16 5.0 atm **8.17** 1100 mol; 4400 g

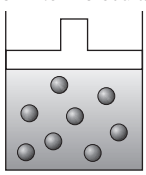
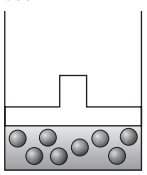
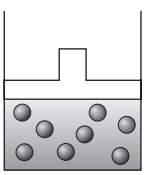
8.18 **(a)**  **(b)** 

8.19 9.4×10^5 Pa He; 1.9×10^4 Pa O_2; about the same.

8.20 75.4% N_2, 13.2% O_2, 5.3% CO_2, 6.2% H_2O **8.21** 4550 Pa

8.22 $P_{He} = 66{,}667$ Pa; $P_{Xe} = 33{,}333$ Pa **8.23** 8.06 kJ, 59.9 kJ

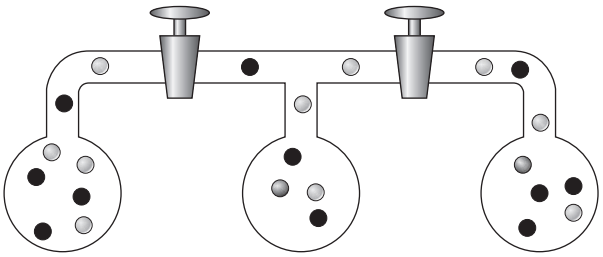
8.24 102 kJ **8.25** ether, isopropanol, ammonia, and water; increases with strength of intermolecular forces

8.26 **(a)**  **(b)**  **(c)** 

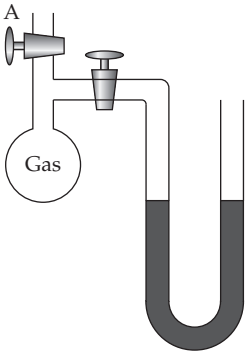
(a) volume increases by 50% **(b)** volume decreases by 50% **(c)** volume unchanged

8.27 **(b)**; **(c)** **8.28** **(c)**

8.29

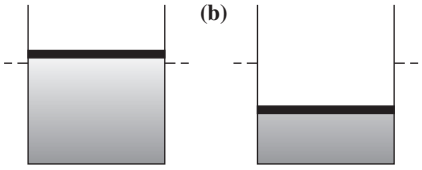


8.30 A

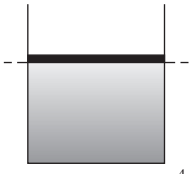


8.31 **(a)** 10 °C **(b)** 75 °C **(c)** 4.2 kJ/mol **(d)** 31.4 kJ/mol

8.32 **(a)** **(b)**



(c)

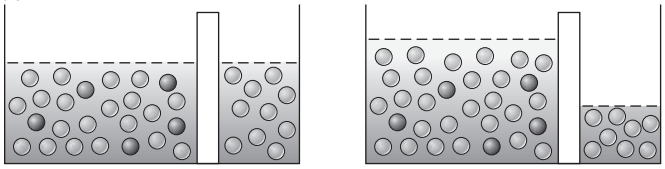


8.33 red = 4.8 × 10^4 Pa; yellow = 1.6 × 10^4 Pa; total pressure = 9.6 × 10^4 Pa **8.34** **(a)** all molecules **(b)** molecules with polar covalent bonds **(c)** molecules with —OH or —NH bonds and HF **8.36** Ethanol forms hydrogen bonds. **8.38** One atmosphere is equal to exactly 760 mmHg. **8.40** (1) A gas consists of tiny particles moving at random with no forces between them. (2) The amount of space occupied by the gas particles is small. (3) The average kinetic energy of the gas particles is proportional to the Kelvin temperature. (4) Collisions between particles are elastic. **8.42** **(a)** 760 mmHg **(b)** 1310 mmHg **(c)** 5.7 × 10^3 mm Hg **(d)** 711 mmHg **(e)** 0.314 mmHg **8.44** 930 mmHg; 1.22 atm **8.46** V varies inversely with P when n and T are constant. **8.48** 101 mL **8.50** 1.75 L **8.52** V varies directly with T when n and P are constant. **8.54** 364 K = 91 °C **8.56** 0.220 × 10^{-6} m^3 **8.58** P varies directly with T when n and V are constant. **8.60** 1.2 × 10^5 Pa **8.62** 493 K = 220 °C **8.64** 68.4 mL **8.66** **(a)** P increases by factor of 4 **(b)** P decreases by factor of 4 **8.68** Because gas particles are so far apart and have no interactions, their chemical identity is unimportant. **8.70** 2.7 × 10^{22} molecules/L; 1.4 g **8.72** 11.8 g **8.74** 15 kg **8.76** $PV = nRT$ **8.78** Cl_2 has fewer molecules but weighs more. **8.80** 370 atm; 3.75 × 10^7 Pa **8.82** 2.2 × 10^4 mmHg; 2.9 × 10^6 Pa **8.84** 22.3 L **8.86** the pressure contribution of one component in a mixture of gases **8.88** 93 mmHg **8.90** the partial pressure of the vapor above the liquid **8.92** Increased pressure raises a liquid's boiling point; decreased pressure lowers it. **8.94** **(a)** 122 kJ **(b)** 724 kJ **8.96** Atoms in a crystalline solid have a regular, orderly arrangement. **8.98** 20.2 kJ **8.100** As temperature increases, molecular collisions become more violent. **8.102** 0.13 mol; 4.0 L **8.104** 590 g/day **8.106** 0.611 mol; 16.4 g/mol **8.108** 6 × 10^{15} L; 1 × 10^8 atoms/L **8.110** **(a)** $2C_8H_{18} + 25O_2 \rightarrow 16CO_2 + 18H_2O$ **(b)** 1.1 × 10^{11} kg CO_2 **(c)** 5.6 × 10^{13} L CO_2 **8.112** **(a)** 3.5 atm **(b)** 0.7 atm O_2; 2.8 atm N_2 **8.114** **(a)** As pressure increases, the ice melts slightly, allowing for ice skating. **(b)** No, as pressure increases, CO_2 stays as a solid. (This assumes that the temperature is low enough to keep CO_2 as a solid.) **8.115** Atmospheric CO_2 levels would remain constant.

Chapter 9

9.1 **(a)** heterogeneous mixture **(b)** homogeneous solution **(c)** homogeneous colloid **(d)** homogeneous solution **9.2** **(c)**, **(d)** **9.3** unsaturated; Cooling would reduce the solubility of KBr, causing some to precipitate from solution. **9.4** 5.6 g/100 mL **9.5** 6.8 × 10^{-5} g/100 mL **9.6** 231 g **9.7** Place 38 mL acetic acid in flask and dilute to 500.0 mL. **9.8** 0.0086% (m/v) **9.9** **(a)** 20 g **(b)** 60 mL H_2O **9.10** 1.6 ppm **9.11** Pb: 0.015 ppm, 0.0015 mg; Cu: 1.3 ppm, 0.13 mg **9.12** 0.927 M **9.13** **(a)** 0.061 mol **(b)** 0.67 mol **9.14** 0.48 g **9.15** **(a)** 0.0078 mol **(b)** 0.39 g **9.16** 39.1 mL **9.17** 750 L **9.18** **(a)** 39.1 g; 39.1 mg **(b)** 79.9 g; 79.9 mg **(c)** 12.2 g; 12.2 mg **(d)** 48.0 g; 48.0 mg **(e)** 9.0 g; 9.0 mg **(f)** 31.7 g; 31.7 mg **9.19** 9.0 mg **9.20** **(a)** 2.0 mol ions; **(b)** 2.0 °C **9.21** weak electrolyte **9.22** **(a)** Red curve is a pure solvent; blue curve is a solution. **(b)** solvent bp = 62 °C; solution bp = 69 °C **(c)** 2 M **9.23** −1.9 °C **9.24** 3 ions/mol **9.25** **(a)** 0.70 osmol **(b)** 0.30 osmol **9.26** **(a)** 0.090 M Na^+; 0.020 M K^+; 0.110 M Cl^-; 0.11 M glucose **(b)** 0.33 osmol

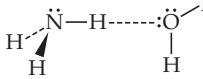
9.27



Before equilibrium At equilibrium

9.28 HCl completely dissociates into ions; acetic acid dissociates only slightly. **9.29** upper curve: HF; lower curve: HBr **9.30** **(a)** **9.31** **(d)** **9.32** homogeneous: mixing is uniform; heterogeneous: mixing is nonuniform **9.34** polarity **9.36** **(b)**, **(d)** **9.38** **(a)** 15.3 g/100 mL **(b)** 14.6 mols NH_3 in 1 L **9.40** Concentrated solutions can be saturated or not; saturated solutions can be concentrated or not. **9.42** Molarity is the number of moles of solute per liter of solution. **9.44** **(a)** 157.5 mL **(b)** 3.596 M **9.46** Dissolve 1.5 g NaCl in water to a final volume of 250 mL. **9.48** **(a)** 7.7% (m/v) **(b)** 3.9% (m/v) **9.50** **(a)** 0.054 mol **(b)** 0.25 mol **9.52** 230 mL, 1600 mL **9.54** 10 ppm **9.56** **(a)** 3.6 g **(b)** 15 g **(c)** 120 g **9.58** 0.38 mL **9.60** **(a)** 4.80 × 10^{-3} mol **(b)** 240 mL **9.62** 333 mL **9.64** 5.0% (m/v) NaCl **9.66** 375 mL **9.68** NaCl—strong electrolyte; glucose—nonelectrolyte **9.70** 19 mEq/L **9.72** **(a)** 5.0 g **(b)** 2.9 g **(c)** 9.56 g **(d)** 21 g **9.74** 5 mg **9.76** 0.300 M KCl **9.78** 100.65 °C **9.80** NaCl has the same osmolarity; distilled water has a lower osmolarity **9.82** neither solution, as they have the same osmotic pressure **9.84** ~2.0 g **9.86** 0.25 g $CaCl_2$; 4.6 mEq Ca^{2+} **9.88** **(a)** 1.30 × 10^{-4} mol **(b)** 0.00520 M or 5.20 mM **(c)** 66 mL **9.90** 1.9 ppm

9.92



(b) 3.05 mol/L

9.94 **(a)** 46.7 mL **(b)** 1.63 g **9.96** **(a)** CO_2 is the most soluble, and then O_2, N_2, and the least soluble is CO. **(b)** Increased pressures of air or oxygen will force N_2 and CO out of the body. **9.98** **(a)** NaCl: 0.147 M; KCl: 0.0040 M; $CaCl_2$: 0.0030 M **(b)** 0.31 osmol; essentially isotonic; cells are unharmed **9.100** **(a)** $CaCO_3(s) + CO_2(aq) + H_2O(l) \rightarrow Ca(HCO_3)_2(aq)$; Calcium carbonate is insoluble, but its solubility increases in water that is saturated in dissolved CO_2 due to the formation of soluble hydrogen carbonate. **(b)** At higher temperatures, the solubility of CO_2 decreases, which shifts the equilibrium in (a) to the left, resulting in the formation of the calcium carbonate (scale).

Chapter 10

10.1 **(a)**, **(b)** **10.2** **(a)**, **(c)** **10.3** **(a)** H_2S **(b)** HPO_4^{2-} **(c)** HCO_3^- **(d)** NH_3 **10.4** acids: HF, H_2S; bases: HS^-, F^-; conjugate acid-base pairs: H_2S and HS^-, HF and F^- **10.5** **(a)** NH_4^+ **(b)** H_2S0_4 **(c)** H_2C0_3 **10.6** **(a)** F^- **(b)** OH^- **10.7** $HPO_4^{2-} + OH^- \rightleftharpoons H_2O + PO_4^{3-}$; conjugate acid-base pairs: H_2O and OH^-, HPO_4^{2-} and PO_4^{3-}; forward reaction is favored **10.8** $HF + NH_3 \rightleftharpoons F^- + NH_4^+$; conjugate acid-base pairs: HF and F^-, NH_3 and NH_4^+; favored in forward direction **10.9** The $—NH_3^+$ hydrogens are most acidic. **10.10** benzoate **10.11** **(a)** basic, $[OH^-] = 3.2 \times 10^{-3}\ M$ **(b)** acidic, $[OH^-] = 2.5 \times 10^{-12}\ M$ **10.12** **(a)** 11.51 **(b)** 2.40

10.13 **(a)** $[H_3O^+] = 1 \times 10^{-13}\,M$; $[OH^-] = 0.1\,M$ **(b)** $[H_3O^+] = 1 \times 10^{-3}\,M$; $[OH^-] = 1 \times 10^{-11}\,M$ **(c)** $[H_3O^+] = 1 \times 10^{-8}\,M$; $[OH^-]\ 1 \times 10^{-6}\,M$ **(b)** is most acidic; **(a)** is most basic **10.14** 0.010 M HNO_2; weaker acid **10.15** **(a)** acidic; $[H_3O^-] = 3 \times 10^{-7}\,M$; $[OH^-] = 3 \times 10^{-8}\,M$ **(b)** basic; $[H_3O^+] = 1 \times 10^{-8}\,M$; $[OH^-] = 1 \times 10^{-6}\,M$ **(c)** acidic; $[H_3O^+] = 2 \times 10^{-4}\,M$; $[OH^-] = 5 \times 10^{-11}\,M$ **(d)** acidic; $[H_3O^+] = 3 \times 10^{-4}\,M$; $[OH^-] = 3 \times 10^{-11}\,M$; order $b < a < c < d$ **10.16** **(a)** 8.28 **(b)** 5.05 **10.17** 2.60 **10.18** **(a)** 0.079 Eq **(b)** 0.338 Eq **(c)** 0.14 Eq **10.19** **(a)** 0.26 N **(b)** 1.13 N **(c)** 0.47 N

10.20 $Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O$;
$Mg(OH)_2 + 2HCl \rightarrow MgCl_2 + 2H_2O$

10.21 **(a)** $2HCO_3^-(aq) + H_2SO_4(aq) \rightarrow 2H_2O(l) + 2CO_2(g) + SO_4^{2-}$
(b) $CO_3^{2-}(aq) + 2HNO_3(aq) \rightarrow H_2O(l) + CO_2(g) + 2NO_3^-(aq)$

10.22 $H_2SO_4(aq) + 2NH_3(aq) \rightarrow (NH_4)_2SO_4(aq)$

10.23 $CH_3CH_2NH_2 + HCl \rightarrow CH_3CH_2NH_3^+\,Cl^-$ **10.24** **(a)** neutral **(b)** basic **(c)** basic **(d)** acidic **10.25** 3.38 **10.26** 9.45 **10.27** hydrogen carbonate/carbonic acid = 10/1 **10.28** 9.13 **10.29** 0.730 M **10.30** 133 mL **10.31** **(a)** $2.41 \times 10^{-3}\,M$; 4.83×10^{-3} Eq **(b)** 0.225 M **10.32** $2.23 \times 10^{-4}\,M$; pH = 3.65 **10.33** **(a)** box 2 **(b)** box 3 **(c)** box 1 **10.34** The O—H hydrogen in each is most acidic.; acetic acid **10.35** **(a)** box 1 **(b)** box 2 **(c)** box 1 **10.36** **(a)** box 3 **(b)** box 1 **10.37** 0.67 M **10.38** HBr dissociates completely into H^+ and Br^- ions. **10.40** KOH dissociates completely into K^+ and OH^- ions. **10.42** A monoprotic acid can donate one proton; a diprotic acid can donate two; HCl, H_2SO_4. **10.44** **(a), (e)** **10.46** **(a)** acid **(b)** base **(c)** neither **(d)** acid **(e)** neither **(f)** acid **10.48** **(a)** CH_2ClCO_2H **(b)** $C_5H_5NH^+$ **(c)** $HSeO_4^-$ **(d)** $(CH_3)_3NH^+$ **10.50** The equilibrium constant for the dissociation of an acid. $K_a = \dfrac{[H_3O^+][A^-]}{[HA]}$ **10.52** pH is defined as the negative logarithm of the molar H_3O^+ concentration.

10.54 $[H_3O^+] = 1.32 \times 10^{-3}$; 1.3%

10.56 $HSO_4^- < HF < HCOOH < H_2CO_3 < NH_4^+$ **10.58** 6×10^{-6}; weak acid **10.60** 2×10^{-6} to 8×10^{-8}

10.62

	10.57	10.58	10.59	10.60	10.61
pOH	6.1	8.8	7.2–10.0	6.9–8.2	12.3; 1.7

10.64

	$[OH^-]$	pOH
(a) Egg white	4×10^{-7}	6.40
(b) Apple cider	2.0×10^{-11}	10.70
(c) Ammonia	4.3×10^{-3}	2.36
(d) Vinegar	2.5×10^{-12}	11.60
Most acidic	vinegar, apple cider, egg white, ammonia	*Least acidic*

10.66 $[H_3O^+] = 1.2 \times 10^{-2}$; $[OH^-] = 8.3 \times 10^{-13}$; pH = 1.92

10.68 **(a)** $HCl(aq) + PO^{3-}(aq) \rightleftharpoons HPO_4^{2-}(aq) + Cl^-(aq)$
stronger acid, stronger base, weaker acid, weaker base
(b) $CN^-(aq) + HSO_4^-(aq) \rightleftharpoons HCN(aq) + SO_4^{2-}(aq)$
stronger base, stronger acid, weaker acid, weaker base
(c) $HClO_4(aq) + NO_2^-(aq) \rightleftharpoons HNO_2(aq) + ClO_4^-(aq)$
stronger acid, stronger base, weaker acid, weaker base
(d) $HF(aq) + CH_3O^-(aq) \rightleftharpoons CH_3OH(aq) + F^-(aq)$
stronger acid, stronger base, weaker acid, weaker base

10.70 **(a)** $LiOH(aq) + HNO_3(aq) \longrightarrow H_2O(l) + LiNO_3(aq)$
(b) $BaCO_3(aq) + 2HI(aq) \longrightarrow H_2O(l) + CO_2(g) + BaI_2(aq)$
(c) $H_3PO_4(aq) + 3KOH(aq) \longrightarrow 3H_2O(l) + K_3PO_4(aq)$
(d) $Ca(HCO_3)_2(aq) + 2HCl(aq) \longrightarrow 2H_2O(l) + 2CO_2(g) + CaCl_2(aq)$
(e) $Ba(OH)_2(aq) + H_2SO_4(aq) \longrightarrow 2H_2O(l) + BaSO_4(s)$

10.72 **(a)** acidic **(b)** neutral **(c)** basic **(d)** basic **10.74** A buffer contains a weak acid and its anion. The acid neutralizes any added base, and the anion neutralizes any added acid.

10.76 **(a)** $pH = pK_a + \log \dfrac{[CH_3CO_2^-]}{[CH_3CO_2H]} = 4.74 + \log \dfrac{[0.100]}{[0.100]} = 4.74$

(b) $CH_3CO_2^-\,Na^+ + H_3O^+ \rightarrow CH_3CO_2H + Na^+$; $CH_3CO_2H + OH^- \rightarrow CH_3CO_2^- + H_2O$ **10.78** 9.19 **10.80** 9.07 **10.82** An equivalent for an acid/base is the amount necessary to produce one mole H^+/OH^- ions.

10.84 **(a)** 1 Eq/mol **(b)** 3 Eq/mol **(c)** 1 Eq/mol **(d)** 2 Eq/mol

10.86 25 mL; 50 mL **10.88** **(a)** 0.50 Eq **(b)** 0.084 Eq **(c)** 0.25 Eq

10.90 0.13 M; 0.26 N **10.92** 0.22 M **10.94** 0.0750 M

10.96 pH = 7 (neutral) as both reactions involve a strong acid and a strong base **10.98** **(a)** 0.613 mol **(b)** pH = −0.39 **10.100** 250 mg

10.102 Both have the same amount of acid; HCl has higher $[H_3O^+]$ and lower pH. **10.104** 0.70 N; 0.35 M **10.106** **(a)** NH_4^+, acid; OH^-, base; NH_3, conjugate base; H_2O, conjugate acid **(b)** 5.56 g

10.108 **(a)** $Na_2O(aq) + H_2O(l) \rightarrow 2NaOH(aq)$
(b) 13.0 **(c)** 5.00 L **10.110** **(a)** ammonium carbonate, $(NH_4)_2CO_3$
(b) formation of ammonium carbonate: $2NH_3 + CO_2 \rightarrow NH_2CO_2NH_4$
$NH_2CO_2NH_4 + H_2O \rightarrow (NH_4)_2CO_3$ decomposition of ammonium carbonate into NH_3, which is the "active component":
$(NH_4)_2CO_3 \rightarrow NH_4HCO_3 + NH_3$

Chapter 11

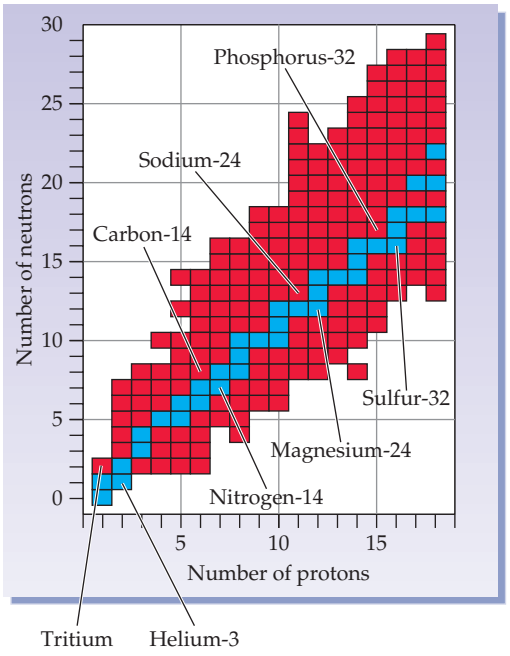
11.1 $^{218}_{84}Po$ **11.2** $^{226}_{88}Ra$ **11.3** $^{89}_{38}Sr \rightarrow {}^{0}_{-1}e + {}^{89}_{39}Y$

11.4 **(a)** $^{3}_{1}H \rightarrow {}^{0}_{-1}e + {}^{3}_{2}He$ **(b)** $^{210}_{82}Pb \rightarrow {}^{0}_{-1}e + {}^{210}_{83}Bi$ **(c)** $^{20}_{9}F \rightarrow {}^{0}_{-1}e + {}^{20}_{10}Ne$

11.5 **(a)** $^{38}_{20}Ca \rightarrow {}^{0}_{1}e + {}^{38}_{19}K$ **(b)** $^{118}_{54}Xe \rightarrow {}^{0}_{1}e + {}^{118}_{53}I$
(c) $^{79}_{37}Rb \rightarrow {}^{0}_{1}e + {}^{79}_{36}Kr$ **11.6** **(a)** $^{62}_{30}Zn + {}^{0}_{-1}e \rightarrow {}^{62}_{29}Cu$
(b) $^{110}_{50}Sn + {}^{0}_{-1}e \rightarrow {}^{110}_{49}In$ **(c)** $^{86}_{36}Kr + {}^{0}_{-1}e \rightarrow {}^{81}_{35}Br$

11.7 $^{120}_{49}In \rightarrow {}^{0}_{-1}e + {}^{120}_{50}Sn$ **11.8** 13% **11.9** 5.0 L

11.10 **(a), (b)**



(b) $^{3}_{1}H \rightarrow {}^{0}_{-1}e + {}^{3}_{2}He$; $^{14}_{6}C \rightarrow {}^{0}_{-1}e + {}^{14}_{7}N$; $^{24}_{11}Na \rightarrow {}^{0}_{-1}e + {}^{24}_{12}Mg$; $^{32}_{15}P \rightarrow {}^{0}_{-1}e + {}^{32}_{16}S$ **11.11** 3 days **11.12** 13 m **11.13** 175 μCi

11.14 0.002 rem; 12,500 X-rays **11.15** $^{237}_{93}Np$

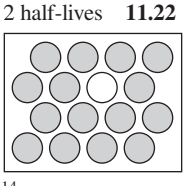
11.16 $^{241}_{95}Am + {}^{4}_{2}He \rightarrow 2\,{}^{1}_{0}n + {}^{243}_{97}Bk$ **11.17** $^{40}_{18}Ar + {}^{1}_{1}H \rightarrow {}^{1}_{0}n + {}^{40}_{19}K$

11.18 $^{235}_{92}U + {}^{1}_{0}n \rightarrow 2\,{}^{1}_{0}n + {}^{137}_{52}Te + {}^{97}_{40}Zr$

11.19 $^{238}_{92}U + {}^{1}_{0}n \rightarrow {}^{239}_{92}U \rightarrow {}^{0}_{-1}e + {}^{239}_{93}Np \rightarrow {}^{0}_{-1}e + {}^{239}_{94}Pu$ **11.20** $^{3}_{2}He$

11.21 2 half-lives **11.22** $^{28}_{12}Mg \rightarrow {}^{0}_{-1}e + {}^{28}_{13}Al$

11.23



Aluminum—28
Magnesium—28

11.24 $^{14}_{6}C$; unstable **11.25** The shorter arrows represent β emission; longer arrows represent α emission.

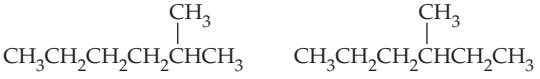
11.26 $^{241}_{94}Pu \rightarrow {}^{241}_{95}Am \rightarrow {}^{237}_{93}Np \rightarrow {}^{233}_{91}Pa \rightarrow {}^{233}_{92}U$

11.27 $^{148}_{69}Tm \rightarrow {}^{0}_{1}e \rightarrow {}^{148}_{68}Er$ or $^{148}_{69}Tm + {}^{0}_{-1}e \rightarrow {}^{148}_{68}Er$ **11.28** 3.5 years

11.29 Inconsistent with nuclear decay because time between 100% → 50% (5 days) is different than time between 50% → 25% (8 days). **11.30** It emits radiation by decay of an unstable nucleus. **11.32** A nuclear reaction changes the identity of the atoms, is unaffected by temperature or catalysts, and often releases a large amount of energy. A chemical reaction does not change the identity of the atoms, is affected by temperature and catalysts, and involves relatively small energy changes. **11.34** by breaking bonds in DNA **11.36** A neutron decays to a proton and an electron. **11.38** The number of nucleons and the number of charges is the same on both sides. **11.40** α emission: Z decreases by 2 and A decreases by 4; β emission: Z increases by 1 and A is unchanged **11.42** Radioactive decay of an unstable nucleus occurs spontaneously. In fission, radioactive decay is induced by bombardment of and reaction of a nucleus with neutrons. **11.44** **(a)** $^{35}_{17}Cl$ **(b)** $^{24}_{11}Na$ **(c)** $^{90}_{39}Y$ **11.46** **(a)** $^{109}_{47}Ag$ **(b)** $^{10}_{5}B$ **11.48** **(a)** $4^{1}_{0}n$ **(b)** $^{146}_{57}La$ **11.50** $^{198}_{80}Hg + {}^{1}_{0}n \rightarrow {}^{198}_{79}Au + {}^{1}_{1}H$; a proton **11.52** $^{228}_{90}Th$ **11.54** Half of a sample decays in that time. **11.56** **(a)** 2.3 half-lives **(b)** 0.0063 g **11.58** 0.8 ng; 2×10^{-3} ng **11.60** The inside walls of a Geiger counter tube are negatively charged, and a wire in the center is positively charged. Radiation ionizes argon gas inside the tube, which creates a conducting path for current between the wall and the wire.
11.62 In a scintillation counter, a phosphor emits a flash of light when struck by radiation, and the flashes are counted. **11.64** more than 0.25 Sv **11.66** 1.9 mL **11.68** **(a)** 4.7 rem **(b)** 1.9 rem **11.70** no filter—α radiation; plastic—β radiation; foil—γ radiation; based on penetrating power of decay particles **11.72** Nuclear decay is an intrinsic property of a nucleus and is not affected by external conditions or chemical conversion of the compound containing the radioactive nucleus. **11.74** 112 cpm
11.76 **(a)** β emission **(b)** Mo-98 **11.78** **(a)** $^{238}_{94}Pu \rightarrow {}^{4}_{2}He + {}^{234}_{92}U$ **(b)** for radiation shielding **11.80** Their cells divide rapidly. **11.82** advantages: few harmful by-products, fuel is inexpensive; disadvantage: needs a high temperature **11.84** **(a)** $^{253}_{99}Es + {}^{4}_{2}He \rightarrow {}^{256}_{101}Md + {}^{1}_{0}n$ **(b)** $^{250}_{98}Cf + {}^{11}_{5}B \rightarrow {}^{257}_{103}Lr + 4^{1}_{0}n$ **11.86** six α particles and four β particles **11.88** 3; 4 **11.90** **(a)** A stable isotope of boron is attached to compounds that seek out tumors in the body. **(b)** Protons strike either Be-7 or Li-7 within a small nuclear reactor. This results in a neutron beam that is externally directed toward the patient's tumor. **(c)** $^{10}_{5}B + {}^{1}_{0}n \rightarrow {}^{11}_{5}B$; $^{11}_{5}B \rightarrow {}^{4}_{2}He + {}^{7}_{3}Li + E$; Both the alpha particle and lithium ions are produced in the area of the tumor and due to their limited penetration depth (approximately the diameter of one cell), they deposit their energy directly into the tumor cells.

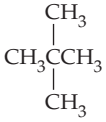
Chapter 12

12.1 **(a)** 2 alcohols **(b)** 2 carboxylic acids **(c)** alcohol, carboxylic acid **(d)** aromatic ring, amine, carboxylic acid **12.2** **(a)** CH_3CH_2CHO **(b)** CH_3COCH_3 **(c)** $CH_3CH_2CO_2H$
12.3 **(a)** $CH_3CH_2CH_2CH_2CH_2CH_2CH_3$ **(b)** $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$
12.4



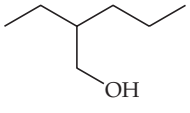
12.5 **(a)** $CH_3CH_2CH_2CH_2CH_3$ Pentane **(b)** $CH_3CHCH_2CH_3$ 2-Methylbutane

(c)

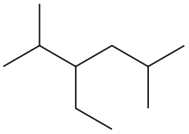


2,2-Dimethylpropane

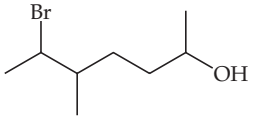
12.6 **(a)**



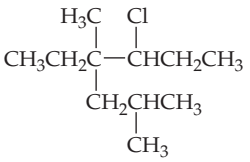
(b)



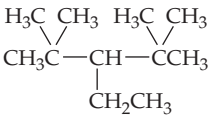
(c)



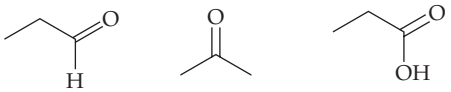
12.7 **(a)**



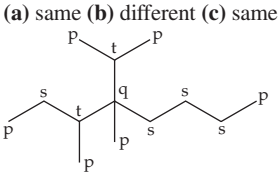
(b)



12.8 **(a)** CH_3CH_2O **(b)** CH_3COCH_3 **(c)** $CH_3CH_2CO_2H$

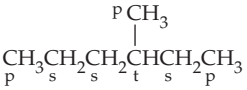


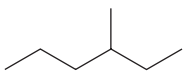
12.9 Structures **(a)** and **(c)** are identical and are isomers of **(b)**.
12.10 **(a)** same **(b)** different **(c)** same
12.11



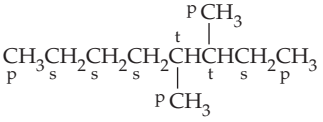
p = primary
s = secondary
t = tertiary
q = quaternary

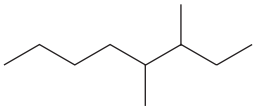
12.12 **(a)** 3-methylheptane **(b)** 4-isopropylheptane
12.13 **(a)**



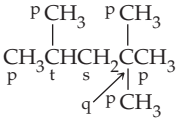


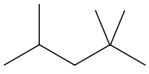
(b)



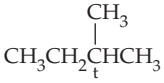


(c)



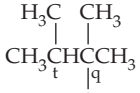


12.14 **(a)**



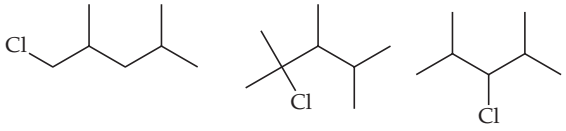
2-Methylbutane

(b)

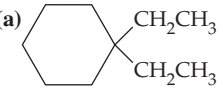


2,3,3-Trimethylbutane

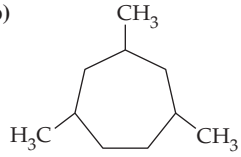
12.15 **(a)** 2,2-dimethylpentane **(b)** 2,3,3-trimethylpentane
12.16 $CH_4 + 2\,O_2 \rightarrow CO_2 + 2\,H_2O$
12.17



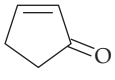
12.18 **(a)** 1-ethyl-4-methylcyclohexane **(b)** 1-ethyl-3-isopropylcyclopentane
12.19 **(a)**



(b)



12.20 **(a)** numbering of methyl groups; 1,3,4-trimethylcyclohexane **(b)** wrong parent; cyclopentylcyclohexane **(c)** combine like substituents; 1,3-diethyl-2-methylcyclopentane **12.21** propylcyclohexane
12.22 **(a)**

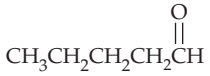


(b)

12.23 **(a)** double bond, ketone, ether **(b)** double bond, amine, carboxylic acid **12.24** **(a)** 2,3-dimethylpentane **(b)** 2,5-dimethylhexane
12.25 **(a)** 1,1-dimethylcyclopentane **(b)** isopropylcyclobutane

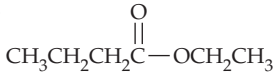
12.26 The methyl groups are on the same side of the ring in one structure and on opposite sides in the other. **12.28** groups of atoms that have a characteristic reactivity; chemistry of compounds is determined by their functional groups **12.30** A polar covalent bond is a covalent bond in which electrons are shared unequally. **12.32** **(a)** (i) amine; (ii) amide; (iii) ester; (iv) aldehyde **(b)** (v) ketone; (vi) aromatic ring; (vii) alcohol; (viii) carboxylic acid

12.34 **(a)**



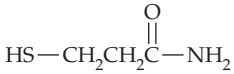
Aldehyde

(b)



Ester

(c)



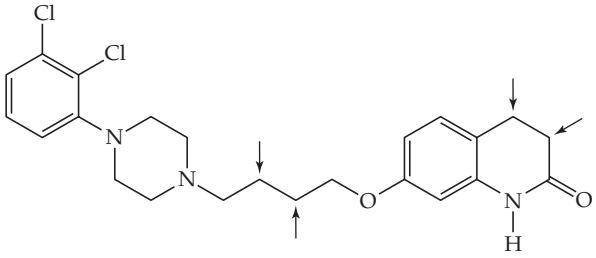
Amide, thiol

Note: There are other possibilities for (a)–(c).

12.36 They must have the same molecular formula but different structures.

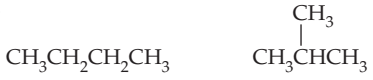
12.38 **(a), (b)** A primary carbon is bonded to one other carbon; a secondary carbon is bonded to two other carbons; a tertiary carbon is bonded to three other carbons; and a quaternary carbon is bonded to four other carbons.

(c)

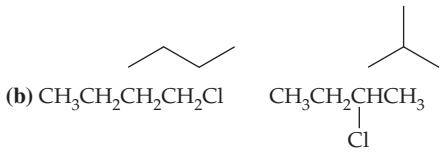


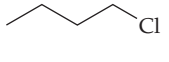
12.40 **(a)** 2,3-dimethylbutane **(b)** 1,2-dimethylcyclohexane, 1,3-dimethylcyclohexane, 1,4-dimethylcyclohexane

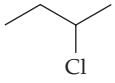
12.42 **(a)**

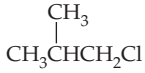


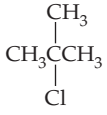
(b)











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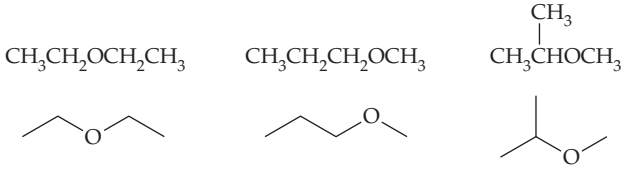
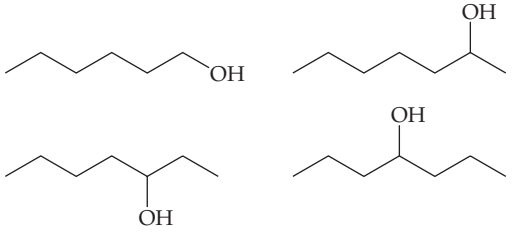
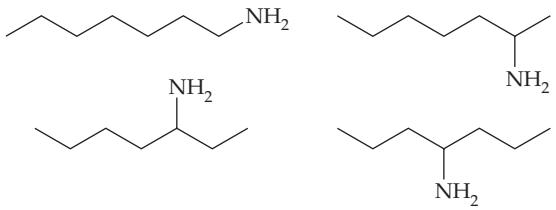


12.44 **(a)**

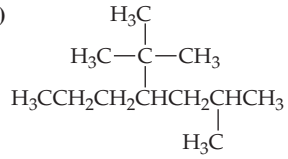


(b)



12.46 identical: **(a)**; isomers: **(b)**, **(d)**, **(e)**; unrelated: **(c)** **12.48** All have a carbon with five bonds. **12.50** **(a)** 4-ethyl-3-methyloctane **(b)** 5-isopropyl-3-methyloctane **(c)** 2,2,6-trimethylheptane **(d)** 4-isopropyl-4-methyloctane **(e)** 2,2,4,4-tetramethylpentane **(f)** 4,4-diethyl-2-methylhexane **(g)** 2,2-dimethyldecane

12.52 **(a)**



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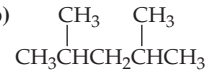

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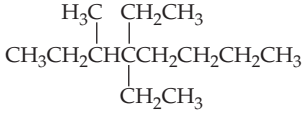

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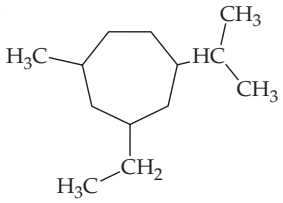
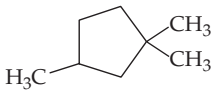


(e)

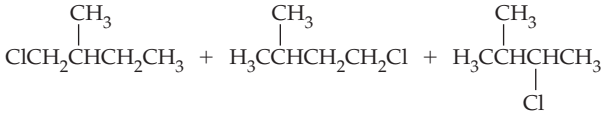


12.54 **(a)** 1-ethyl-3-methylcyclobutane **(b)** 1,1,3,3-tetramethylcyclopentane **(c)** 1-ethyl-3-propylcyclohexane **(d)** 4-butyl-1,1,2,2-tetramethylcyclopentane

12.56 **(a)** 2,2-dimethylpentane **(b)** 2,4-dimethylpentane **(c)** isobutylcyclobutane **12.58** heptane, 2-methylhexane, 3-methylhexane, 2,2-dimethylpentane, 2,3-dimethylpentane, 2,4-dimethylpentane, 3,3-dimethylpentane, 3-ethylpentane, 2,2,3-trimethylbutane

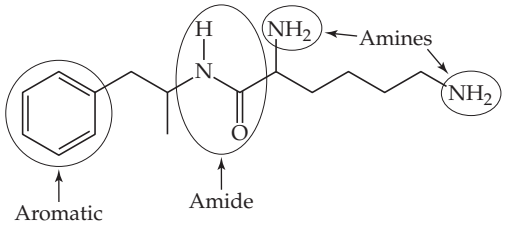
12.60 $C_3H_8 + 5\ O_2 \rightarrow 3\ CO_2 + 4\ H_2O$

12.62



12.64 **(a)** ketone, alkene, alcohol **(b)** amide, carboxylic acid, sulfide, amine

(c)

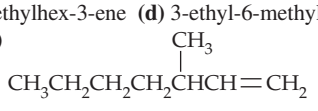


Therapeutic properties: treats ADHD in adults and children aged 6 years or older; treats moderate to serve binge eating disorder in adults **12.66** two tertiary carbons **12.68** Nonpolar solvents dissolve nonpolar substances. **12.70** pentane; greater London forces, due to its rod-like shape **12.72** **(a)** and **(d)** **12.74** Remove eye make-up, remove chewing gum from wood, shine patent-leather shoes, soften dry skin, lengthen the life of your perfume, soothe shoe blisters, remove a stuck ring, relieve razor burn, protect a new tattoo, soothe pets cracked paw pads, remove candle wax, loosen a stiff bike chain, etc. **12.76** No, isomers cannot be converted without breaking bonds.

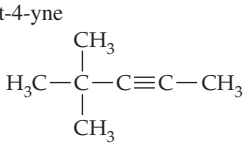
Chapter 13

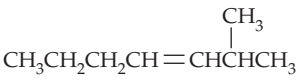
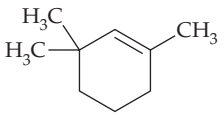
13.1 **(a)** 2-methylhept-3-ene **(b)** 2-methyl-1,5-hexadiene **(c)** 3-methylhex-3-ene **(d)** 3-ethyl-6-methyloct-4-yne

13.2 **(a)**

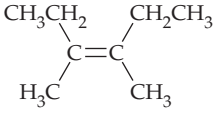


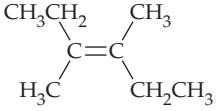
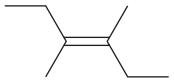
(b)

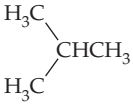
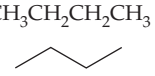


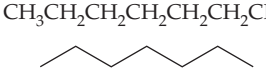
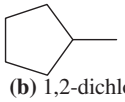
(c)  **(d)** 

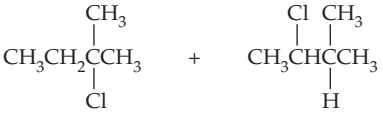
13.3 **(a)** 2,3-dimethylpent-1-ene **(b)** 2,3-dimethylhex-2-ene
13.4 **(a)** and **(c)**
13.5

cis-3,4-Dimethylhex-3-ene  

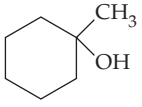
trans-3,4-Dimethylhex-3-ene  

13.6 **(a)** *cis*-4-methylhex-2-ene **(b)** *trans*-5,6-dimethylhept-3-ene
13.7 **(a)** substitution **(b)** addition **(c)** elimination **13.8** **(a)** addition **(b)** elimination
13.9 **(a)**   **(b)** 

(c)  **(d)** 

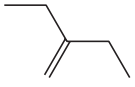
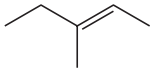
13.10 **(a)** 1,2-dibromo-2-methylpropane **(b)** 1,2-dichloropentane
(c) 4,5-dichloro-2,4-dimethylheptane **(d)** 1,2-dibromocyclopentane
13.11 

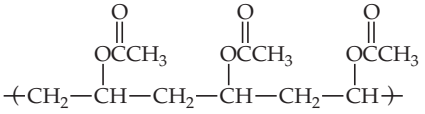
Major Minor

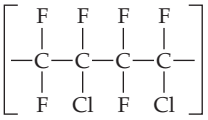
13.12 **(a)** 1-chloro-1-methylcyclopentane **(b)** 2-bromobutane **(c)** 2-chloro-2,4-dimethylpentane **13.13** **(a)** Major product; H bonds to double-bond carbon with more H atoms **(b)** Minor product; H bonds to double-bond carbon with less H atoms to form this product **13.14** 2-bromo-2,4-dimethylhexane
13.15 **(a), (b)** 

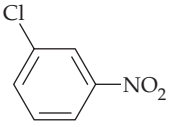
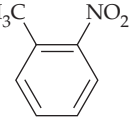
Major product for both

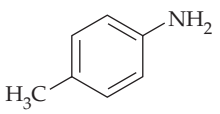
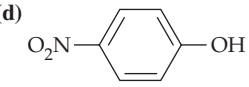
(c) 

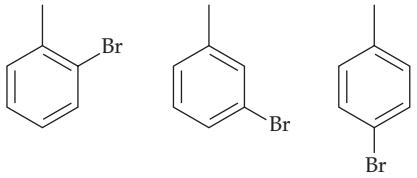
13.16 **(a)**  **(b)** 

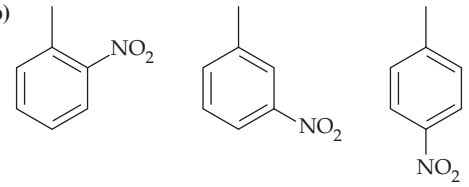
Both formed in roughly equal amounts.
13.17 

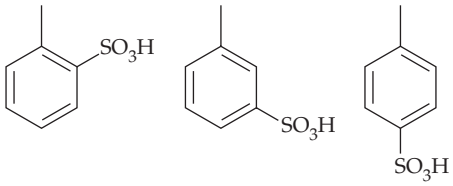
13.18 

13.19 **(a)** 3-ethylphenol or *m*-ethylphenol **(b)** 3-chlorotoluene or *m*-chlorotoluene **(c)** 1-ethyl-3-isopropylbenzene
13.20 **(a)**  **(b)** 

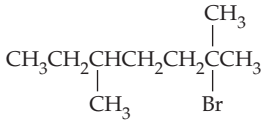
(c)  **(d)** 

13.21 **(a)** *o*-isopropylphenol **(b)** *p*-bromoaniline
13.22 **(a)** 

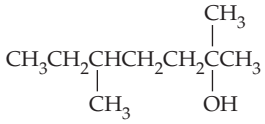
(b) 

(c) 

13.23 *o*-, *m*-, and *p*-bromophenol
13.24 **(a)** 2,5-dimethylhept-2-ene

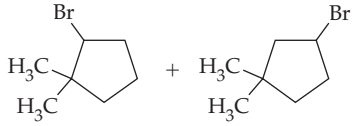


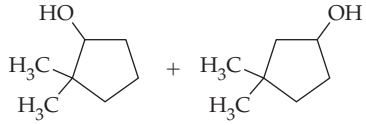
Major product

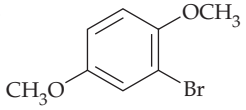
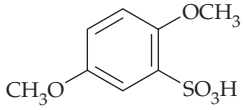


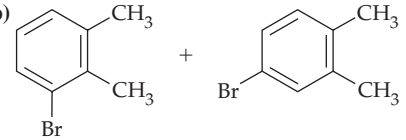
Major product

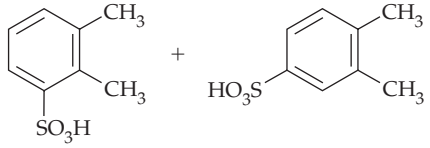
(b) 3,3-dimethylcyclopentene

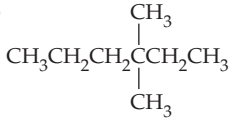




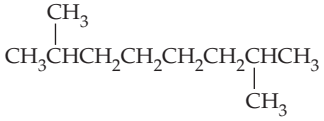
13.25 **(a)** 4,4-dimethylhex-1-yne **(b)** 2,7-dimethyloct-4-yne
13.26 **(a)** *m*-isopropylphenol **(b)** *o*-bromobenzoic acid
13.27 **(a)**  

(b) 



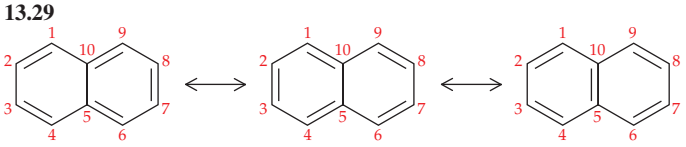
13.28 **(a)** 

3,3-dimethylhexane

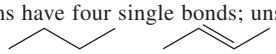
(b) 

2,7-dimethyloctane

13.29

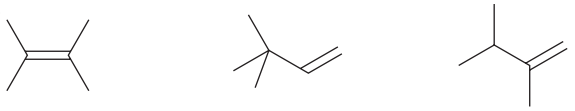


13.30 **(a)** saturated: carbon atoms have four single bonds; unsaturated: carbon–carbon multiple bonds **(b)**



13.32 alkene: *–ene*: alkyne: *–yne*: aromatic: *–benzene*

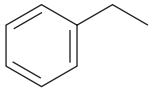
13.34 **(a)**



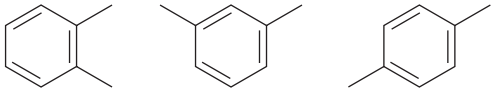
(b)

$CH_3CH_2CH_2C{\equiv}CH$ $CH_3CH_2C{\equiv}CCH_3$ $CH_3CHC{=}CH$ (CH_3 above)

(c)

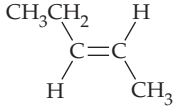


(d)

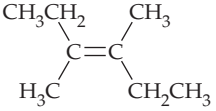


13.36 **(a)** pent-2-ene **(b)** 2,5-dimethylhex-3-yne **(c)** 3,4-diethylhex-3-ene **(d)** 2,4-dimethylhexa-2,4-diene **(e)** 3,6-dimethylcyclohexene **(f)** 4-ethyl-1,2-dimethylcyclopentene

13.38 **(a)**



(b)



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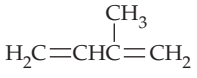
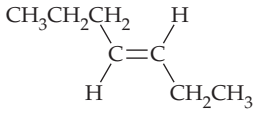
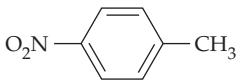


(d)



(e)



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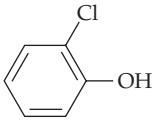
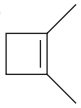
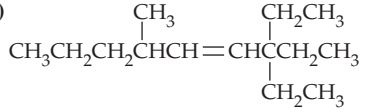


(g)

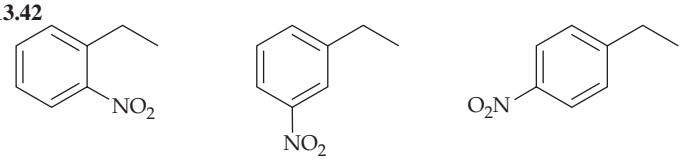


(h)



13.40 hex-1-yne, hex-2-yne, hex-3-yne, 3-methylpent-1-yne, 4-methylpent-1-yne, 4-methylpent-2-yne, 3,3-dimethylbut-1-yne

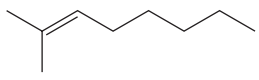
13.42



o-Ethylnitrobenzene *m*-Ethylnitrobenzene *p*-Ethylnitrobenzene

13.44 Each double bond carbon must be bonded to two different groups.

13.46 **(a)**



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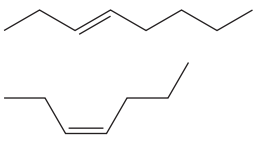
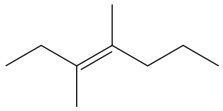
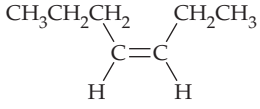


(c)



13.48 **(a)**



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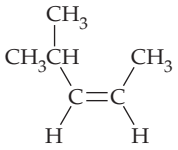

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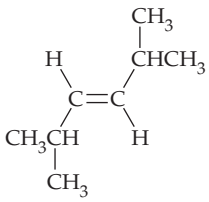
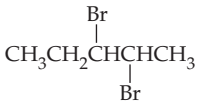


13.50 **(a)** identical **(b)** identical **13.52** substitution: two reactants exchange parts to give two products; addition: two reactants add to give one product **13.54** rearrangement **13.56** **(a)** substitution **(b)** rearrangement

13.58 **(a)** $CH_3CH_2CH_2CH_3$ **(b)**



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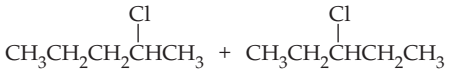
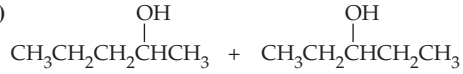
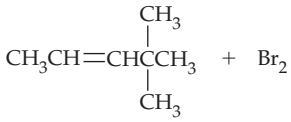


(d)



13.60 **(a)**

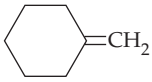


(b) $CH_3CH{=}CH_2 + H_2$

(c) $CH_3CH{=}CHCH_3$ or $H_2C{=}CHCH_2CH_3$ + HBr

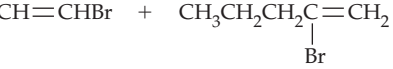
(d)

$+ H_2O$ **(e)**



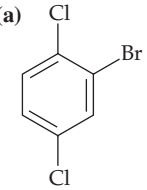
$+ Cl_2$

13.62

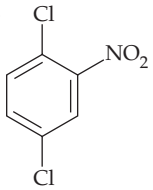


13.64 $H_2C{=}CCl_2$

13.66 **(a)**



(b)



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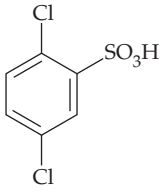

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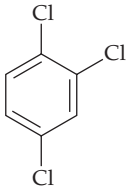
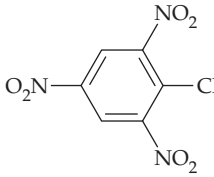


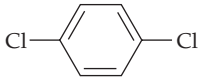
13.68



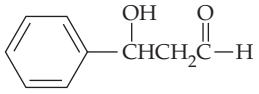
TNT

13.70 **(a)** 5-methylhex-2-ene **(b)** 4-methylhept-2-yne **(c)** 2,3-dimethylbut-1-ene **(d)** 1,2,4-trinitrobenzene **(e)** 3,4-dimethylcyclohexene **(f)** 3-methylpenta-1,3-diene **13.72** Br_2 reacts only with cyclohexene.

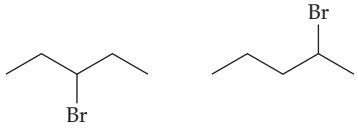
13.74



13.76

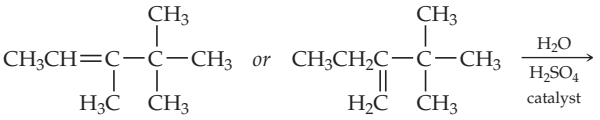


13.78

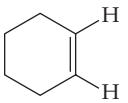


Both ends of the double bond have the same number of hydrogens, and both products can form.

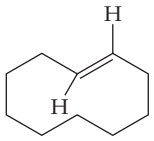
13.80



13.82 A trans double bond is too strained to exist in a small ring like cyclohexene, but a large ring is more flexible and can include a trans double bond:

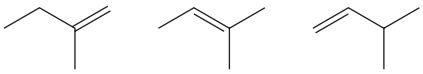


The double bond must be cis in this six-membered ring.



The double bond can be trans in this ten-membered ring.

13.84

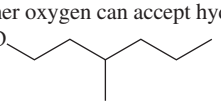


Chapter 14

14.1 **(a)** alcohol **(b)** alcohol **(c)** phenol **(d)** alcohol **(e)** ether **(f)** ether

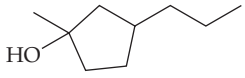
14.2 The ether oxygen can accept hydrogen bonds from water.

14.3 **(a)**



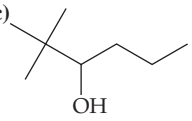
Primary alcohol

(b)



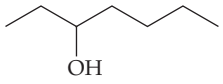
Tertiary alcohol

(c)



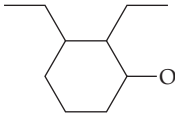
Secondary alcohol

(d)



Secondary alcohol

(e)

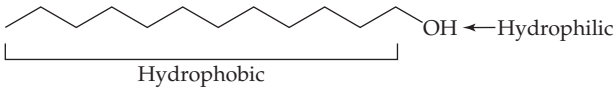


Secondary alcohol

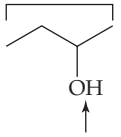
14.4 **(a)** 2-methylpropan-2-ol (*tert*-butyl alcohol), tertiary **(b)** 3-methylpentan-2-ol, secondary **(c)** 5-chloro-2-ethylhexan-1-ol, primary **(d)** 1,2-cyclopentanediol, secondary **14.5** See 14.3 and 14.4. **14.6** highest **(d)**, **(b)**, **(a)**, **(c)** lowest

14.7

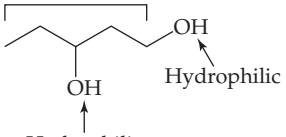
(a)



(b) Hydrophobic



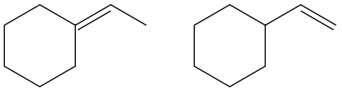
(c) Hydrophobic



water soluble **(b)** and **(c)**; insoluble **(a)**

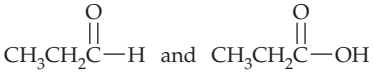
14.8 **(a)** propene **(b)** cyclohexene **(c)** 4-methylpent-1-ene (minor) and 4-methylpent-2-ene (major) **14.9** **(a)** 2-methylbutan-2-ol or 3-methylbutan-2-ol **(b)** 1,2-dimethylcyclopentanol **(c)** 1,2-diphenylethanol

14.10

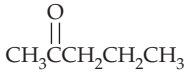


Major product Minor product

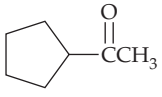
14.11 **(a)**



(b)

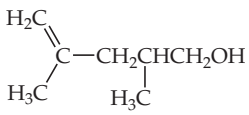


(c)



14.12 **(a)** propan-2-ol **(b)** cycloheptanol **(c)** 3-methylbutan-1-ol

14.13 **(a)**



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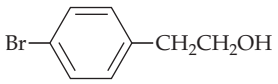
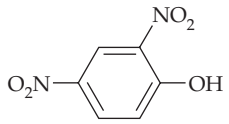
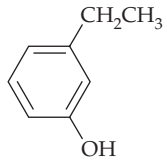


14.14 **(a)**



(b)

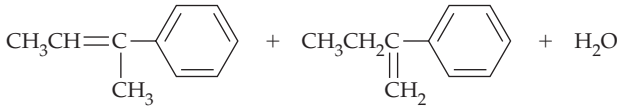


14.15 **(a)** 2,4-dibromophenol **(b)** 3-iodo-2-methylphenol

14.16 **(a)** 1,2-dimethoxypropane **(b)** *p*-methoxynitrobenzene (*p*-nitroanisole) **(c)** *tert*-butyl methyl ether **14.17** **(a)** $CH_3CH_2CH_2S—SCH_2CH_2CH_3$ **(b)** $(CH_3)_2CHCH_2CH_2S—SCH_2CH_2CH(CH_3)_2$ **14.18** **(a)** 1-chloro-1-ethylcyclopentane **(b)** 3-bromo-5-methylheptane **14.19** 2-Aminobutane has a carbon with four different groups bonded to it. **14.20** chiral: **(b)**, **(c)**

14.21 **(a)** 5-methylhexan-3-ol **(b)** *m*-methoxytoluene **(c)** 3-methylcyclohexanol

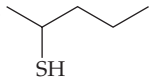
14.22



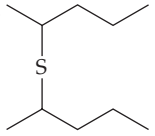
Major Minor

14.23 $(CH_3)_2CHCH_2CH_2CHO$, $(CH_3)_2CHCH_2CH_2CO_2H$

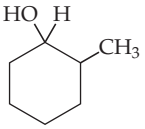
14.24 **(a)**



(b)



14.25 **(a)**



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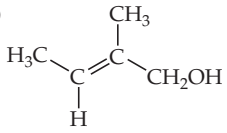

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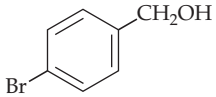
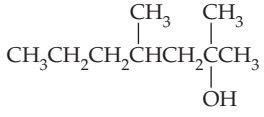


14.26 Alcohols have an —OH group bonded to an alkane-like carbon atom; ethers have an oxygen atom bonded to two carbon atoms; and phenols have an —OH group bonded to a carbon of an aromatic ring.

14.28 Alcohols form hydrogen bonds. **14.30** alcohol, ether, ketone, carbon–carbon double bond **14.32** **(a)** 2-methylpropan-2-ol (*tert*-butyl alcohol) **(b)** 2-methylpropan-1-ol **(c)** butane-1,2,4-triol **(d)** 2-methyl-2-phenylpropan-1-ol **(e)** 3-methylcyclohexanol **(f)** 3-ethyl-3-methylhexan-2-ol

14.34 **(a)**



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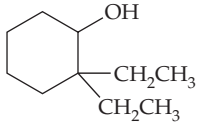

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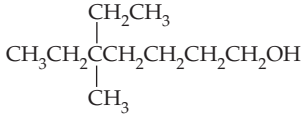

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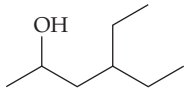
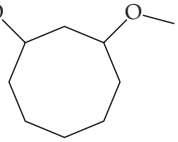


(e)



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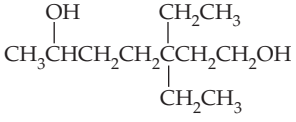
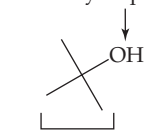


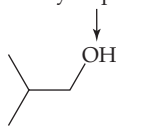
14.36 **Part (a):** **(a)** tertiary **(b)** primary **(c)** primary, secondary **(d)** primary **(e)** secondary **(f)** secondary

Part (b): **(a)**



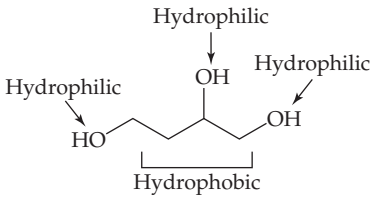
Water insoluble

(b)



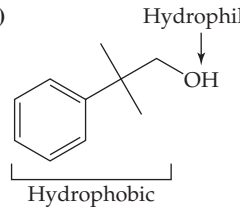
Water insoluble

(c)



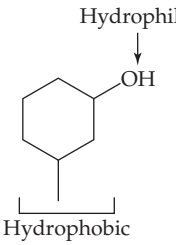
Water soluble

(d)



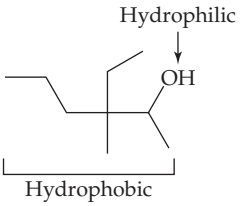
Water insoluble

(e)



Water insoluble

(f)

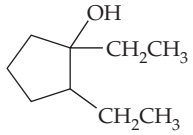


Water insoluble

14.38 lowest **(a)** < **(c)** < **(b)** highest, due to molar mass and/or ability to hydrogen bond **14.40** a ketone **14.42** a carboxylic acid

14.44 Phenols dissolve in aqueous NaOH; alcohols don't.

14.46 (a)



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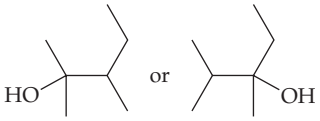

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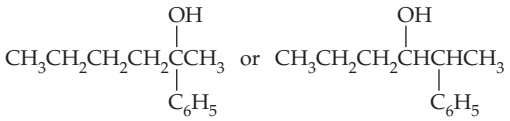

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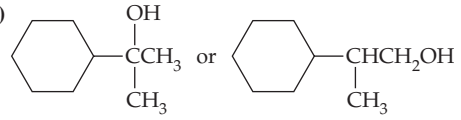
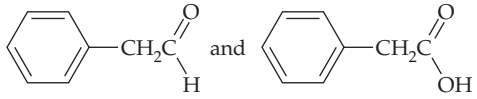
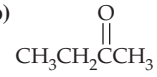


(e) $HOCH_2CH_2CH_2CH_2CH_2OH$

14.48 (a)



(b)



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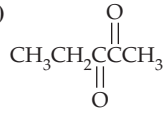
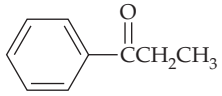


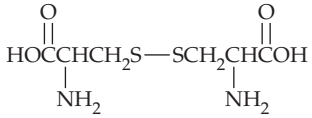
(d) NR **(e)** NR

(f)



14.50 odor

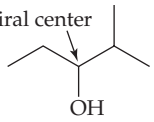
14.52



14.54 Alcohols can form hydrogen bonds; thiols and alkyl chlorides can't.

14.56 (a) right- or left-handedness with two different mirror images **(b)** superimposable mirror images with no handedness **(c)** a carbon atom bonded to four different groups **(d)** mirror-image forms of a chiral molecule

14.58 (a)



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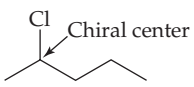

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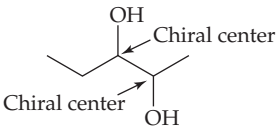

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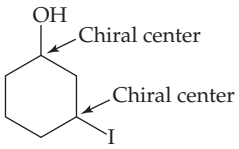
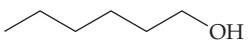
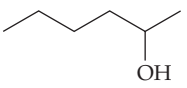


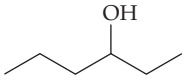
14.60



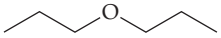
Hexan-1-ol



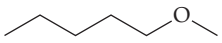
Hexan-2-ol



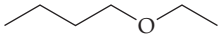
Hexan-3-ol



Dipropyl ether



Methyl pentyl ether

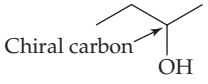


Butyl ethyl ether

14.62 Alcohols become less soluble as their nonpolar part becomes larger.

14.64 An antiseptic kills microorganisms on living tissue; a disinfectant is used on nonliving matter. **14.66** achiral: **(a), (d)**
chiral:

(b)



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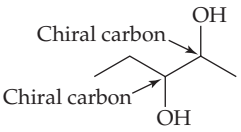

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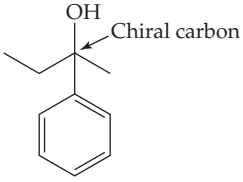

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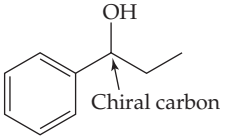
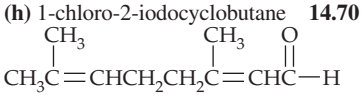
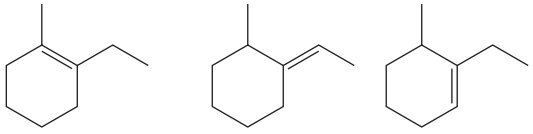


14.68 (a) *p*-dibromobenzene **(b)** 1,2-dibromobut-1-ene **(c)** *m*-propylanisole **(d)** 1,1-dibromocyclopentane **(e)** 2,4-dimethylpentane-2,4-diol **(f)** 4-methylheptane-2,4,5-triol **(g)** 4-bromo-6,6-dimethylhept-2-yne **(h)** 1-chloro-2-iodocyclobutane **14.70** 3,7-dimethyl-2,6-octadiene-1-ol



14.72 $C_2H_6O + 3\,O_2 \rightarrow 2\,CO_2 + 3\,H_2O$

14.74

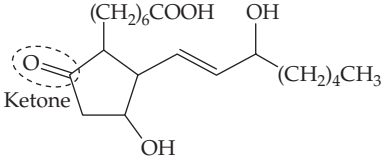


Major product Minor products

*It is possible to have more than one minor product depending on the amount of substitution.

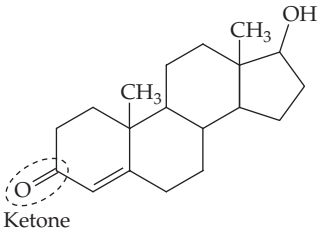
Chapter 15

15.1 (a)



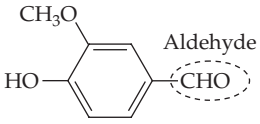
Prostaglandin E_1

(b)



Testosterone

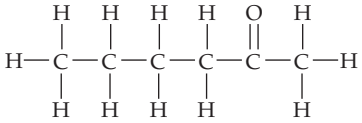
(c)

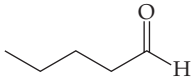


Vanillin

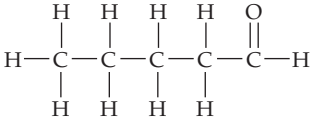
(d) $C_4H_9COCH_3$ Ketone **(e)** C_4H_9CHO Aldehyde

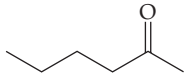
15.2 (d)





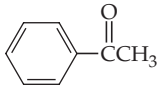
(e)



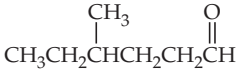


15.3 (a)

(b)



(c)



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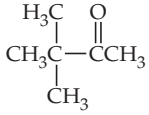
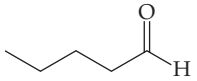
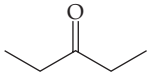


15.4 **(a)** pentanal **(b)** pentan-3-one **(c)** 4-methylhexanal **(d)** heptan-4-one

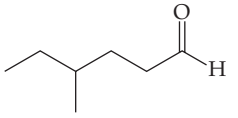
(a)



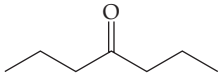
(b)



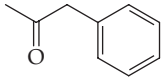
(c)



(d)

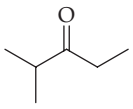


15.5 (a)



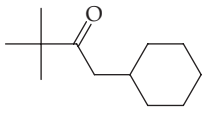
Methyl benzyl ketone

(b)



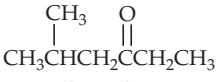
Ethyl isopropyl ketone

(c)



Tert-butyl cyclohexyl ketone

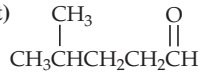
15.6 (left)



$C_7H_{14}O$

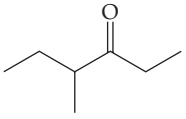
5-Methylhexan-3-one
(A ketone)

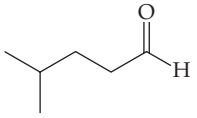
(right)



$C_6H_{12}O$

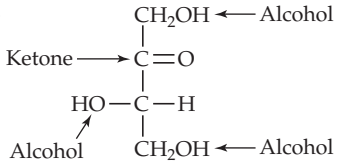
4-Methylpentanal
(An aldehyde)



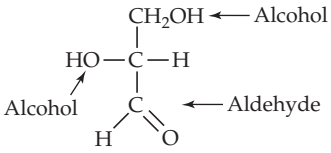


15.7 **(a)** polar, insoluble **(b)** polar, soluble **(c)** nonpolar, insoluble **(d)** polar, insoluble **15.8** Alcohols form hydrogen bonds, which raise their boiling points. Aldehydes and ketones have higher boiling points than alkanes because they are polar.

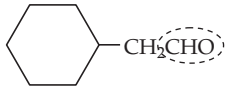
15.9 (a)



(b)

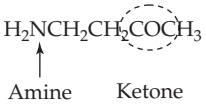


(c)



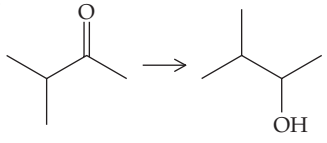
Aldehyde

(d)

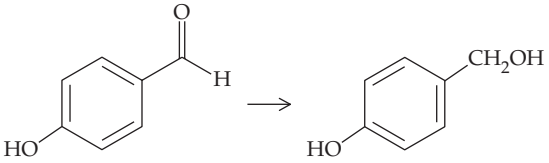


15.10 **(a)** (i) positive, (ii) positive **(b)** (i) negative, (ii) negative **(c)** (i) positive, (ii) positive **(d)** (i) negative, (ii) positive

15.11 (a)



(b)



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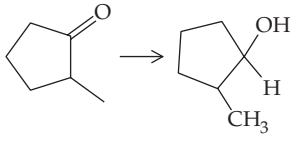
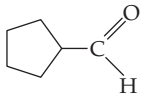


15.12 (a)



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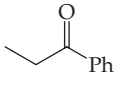

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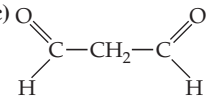
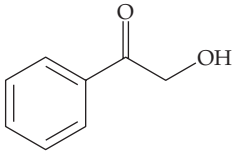


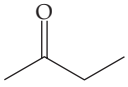
15.13 **(a)** hemiacetal **(b)** neither **(c)** neither **(d)** hemiacetal

15.14 **(a)** Ketal;

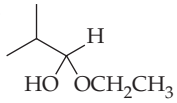


(b) Acetal;

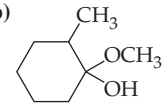
(c) Ketal;



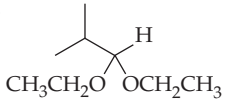
15.15 (a)



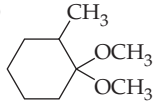
(b)



15.16 (a)

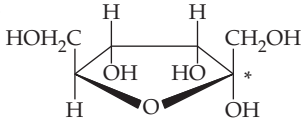


(b)



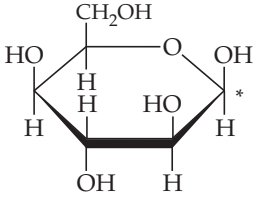
15.17 **(a)** hemiacetal **(b)** acetal **(c)** ketal **(d)** hemiketal

15.18 (a)



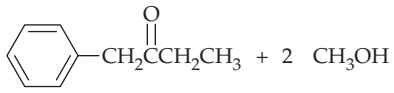
Tagatose
Hemiketal

(b)



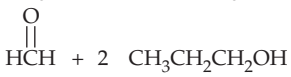
Idose
Hemiacetal

15.19 (a)



(b) $CH_3CH_2CHO + 2\ CH_3CH_2CH_2OH$

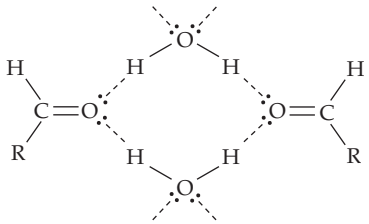
(c)



15.20 (a) Hydride adds to the carbonyl carbon, because the polar C═O carbon has a partial positive charge. **(b)** The arrow to the right represents reduction, and the arrow to the left represents oxidation.

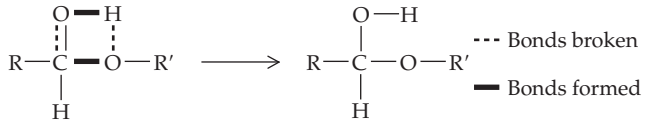
15.21 Aldehydes can be oxidized to carboxylic acids. Tollens' reagent differentiates an aldehyde from a ketone.

15.22

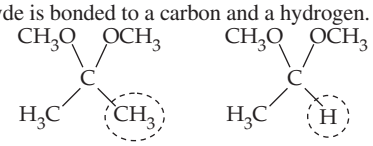


15.23 (a) Under acidic conditions, an alcohol adds to the carbonyl group of an aldehyde to form a hemiacetal, which is unstable and further reacts to form an acetal.

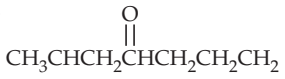
(b)



15.24 In solution, glucose exists as a cyclic hemiacetal because this structure is more stable and it protects the reactive aldehyde functional group from oxidation to the carboxylic acid. **15.25** In addition to the two oxygens, an acetal carbon of a ketone is bonded to two carbons. The acetal carbon of an aldehyde is bonded to a carbon and a hydrogen.



15.26 (a)



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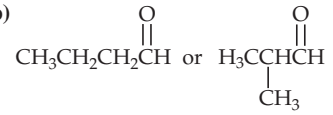

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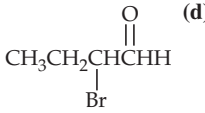

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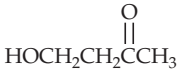
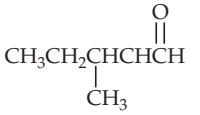
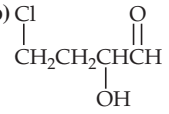


15.28 Structure **(c)** has an aldehyde group, and structures **(a), (b),** and **(f)** have ketone groups.

15.30 (a)



(b)



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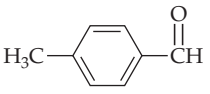

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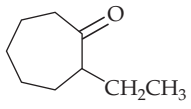

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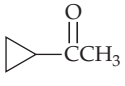

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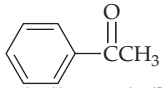
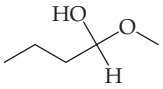


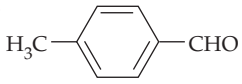
15.32 (a) 2,2-dimethylbutanal **(b)** 2-hydroxy-2-methylpentanal **(c)** 3-methylbutanal **(d)** 4-methylhexan-3-one **(e)** 3-hydroxy-2-methylcyclohexanone **15.34** For **(a),** a ketone can't occur at the end of a carbon chain. For **(b),** the methyl group receives the lowest possible number. For **(c),** numbering must start at the end of the carbon chain closer to the carbonyl group.

15.36



15.38 Tollens' reagent: (b) and (c); Benedict's reagent: (b) and (c). (a) reacts with neither

15.40 (a)



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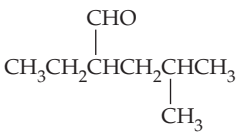
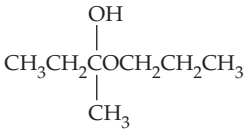


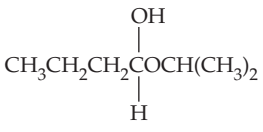
(c) $CH_3CH{=}CHCHO$

15.42 (a)



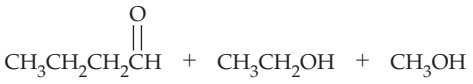
Hemiketal

(b)



Hemiacetal

(c)



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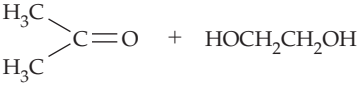
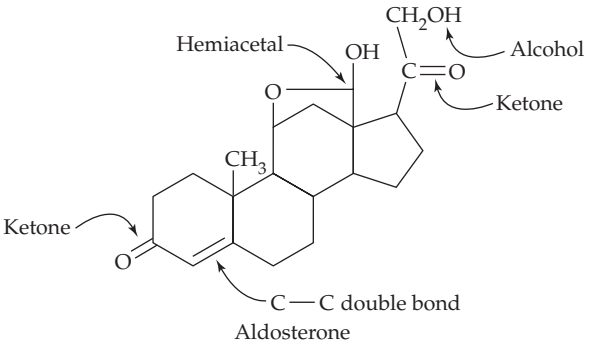


15.44

5-Hydroxyhexanal

15.46 $HOCH_2CH_2CH_2OH$ and HCHO (formaldehyde).

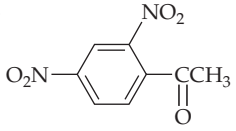
15.48



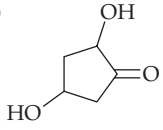
Aldosterone

15.50 *p*-methoxybenzaldehyde **15.52** Aldehydes are easily oxidized while ketones are not. **15.54 (a)** 2-methylpentan-3-one **(b)** 1,5-hexadiene **(c)** *m*-bromotoluene **(d)** 4,5,5-trimethylhexan-3-one

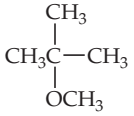
15.56 (a)



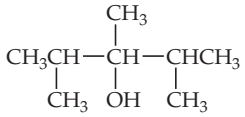
(b)



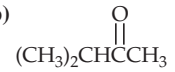
(c)



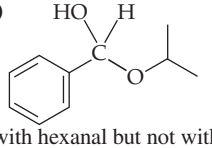
(d)



15.58 (a) $CH_3CH_2CH(CH_3)_2$ **(b)**



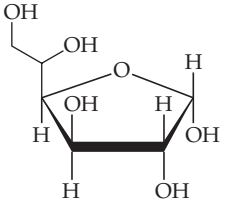
(c) $HOCH_2CH_2CH_2CH_3$ **(d)**



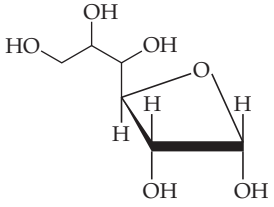
15.60 Tollens' reagent reacts with hexanal but not with hexan-3-one.

15.62 Heptan-2-one is less soluble in water because it has a longer hydrocarbon chain.

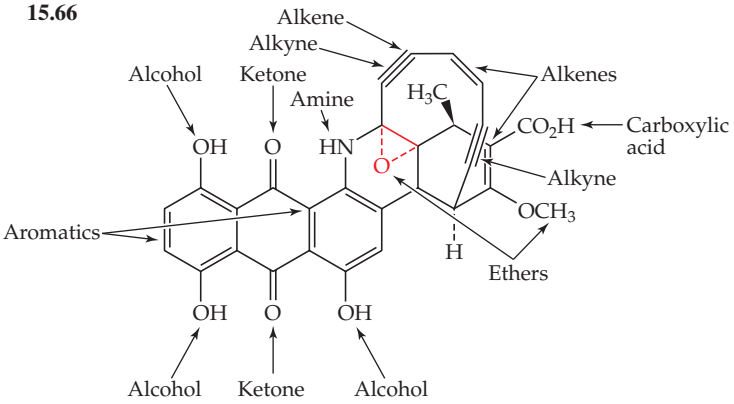
15.64 (a)



(b)



15.66



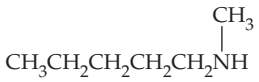
Chapter 16

16.1 **(a)** primary **(b)** secondary **(c)** primary **(d)** secondary **(e)** tertiary

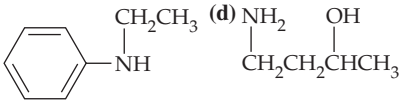
16.2 **(a)** tripropylamine **(b)** *N*-ethyl-*N*-methylcyclopentylamine **(c)** *N*-isopropylaniline

16.3 **(a)** $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2NH_2$

(b)

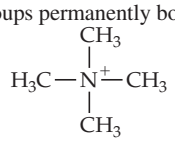


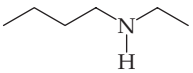
(c) **(d)**



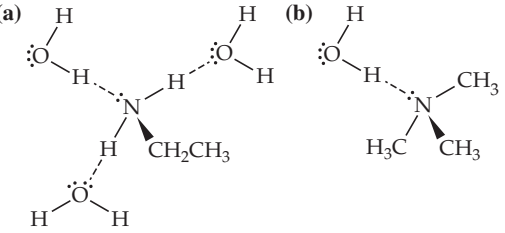
16.4 **(a)** primary **(b)** secondary **(c)** secondary **(d)** primary

16.5 The ion for carbon groups permanently bound to the nitrogen atom.



16.6 $CH_3CH_2CH_2CH_2NHCH_2CH_3$  *N*-ethylbutylamine; it is a secondary amine since the N has two carbon groups bound directly to it. **16.7** Compound **(a)** is lowest boiling (it cannot hydrogen bond with itself); **(b)** is highest boiling (strongest hydrogen bonds).

16.8 **(a)** **(b)**

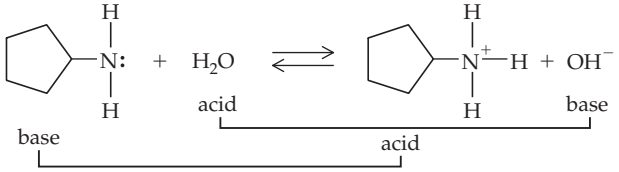


16.9 **(a)** methanamine, ethanamine, dimethylamine, trimethylamine **(b)** pyridine **(c)** aniline **16.10** **(a)** pyrimidine: $C_4H_4N_2$ **(b)** purine: $C_5H_4N_4$

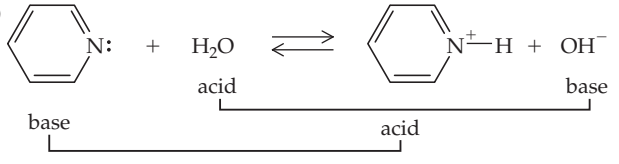
16.11 **(a)** and **(d)**

16.12

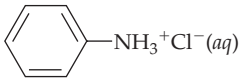
(a)



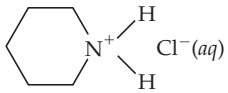
(b)



16.13 **(a)** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HNH_2CH_3^+Br^-(aq)$ **(b)**



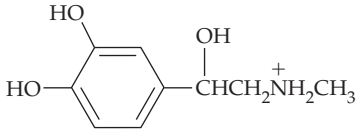
(c)



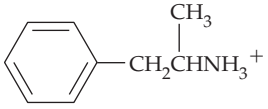
(d) $(CH_3)_3CNH_2 + H_2O(l) + Na^+(aq)$

16.14 **(a)** *N*-methylisopropylammonium bromide **(b)** anilinium chloride **(c)** piperidinium chloride **16.15** **(a)** ethanamine **(b)** triethylamine

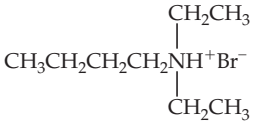
16.16 **(a)**



(b)



16.17–16.18 **(a)**



Butyldiethylammonium bromide
or N,N–Diethylbutylammonium bromide
salt of a tertiary amine

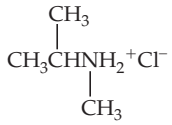
(b) $(CH_3CH_2CH_2CH_2)_4N^+OH^-$

Tetrabutylammonium hydroxide
salt of a quaternary amine

(c) $CH_3CH_2CH_2NH_3^+I^-$

Propylammonium iodide
salt of a primary amine

(d)

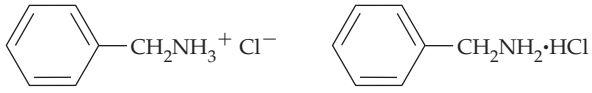


Isopropylmethylammonium chloride
salt of a secondary amine

16.19 $CH_3CH_2CH_2CH_2NH_3^+Cl^-(aq) + NaOH(aq) \rightarrow CH_3CH_2CH_2CH_2NH_2 + H_2O(l) + NaCl(aq)$

16.20 Benadryl has the general structure. In Benadryl, R = —CH_3 and R′ = R″ = C_6H_5—.

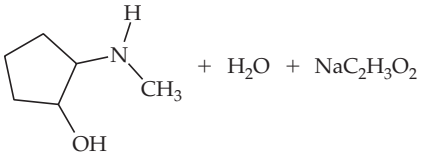
16.21



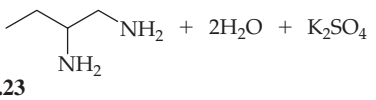
Benzylammonium chloride

16.22 **(a)** $(CH_3CH_2)_3N + H_2O + LiBr$

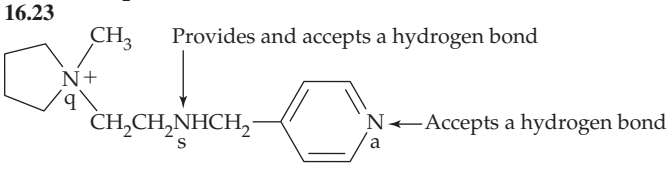
(b)



(c)

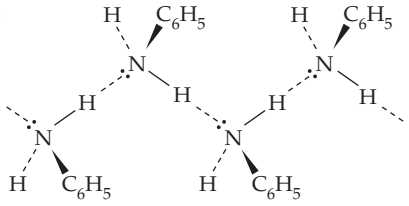


16.23

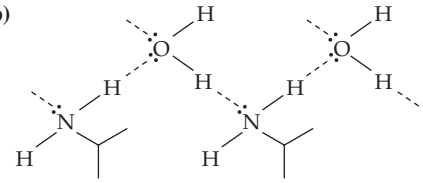


16.24 **(a)** Both amine groups can participate in hydrogen bonding. **(b)** Lysine is water-soluble because it can form hydrogen bonds with water.

16.25 (a)



(b)



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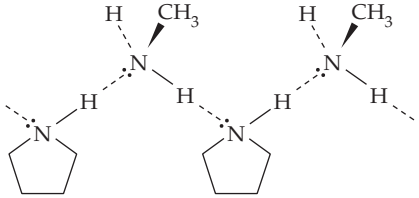
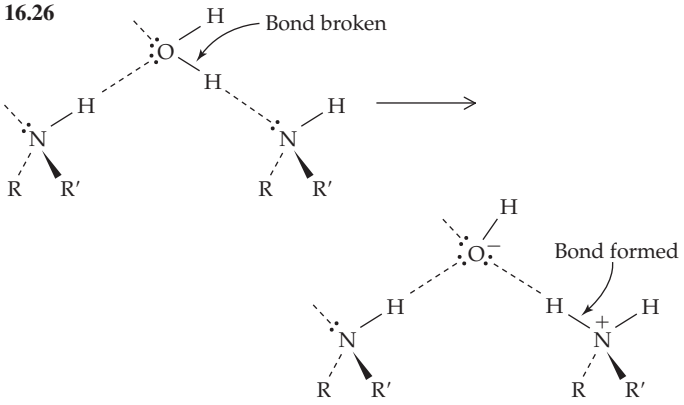
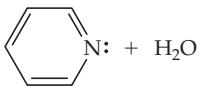


16.26



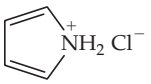
16.27 strongest base: $(CH_3)_2NH$ weakest base: $C_6H_5NH_2$

16.28 (a)

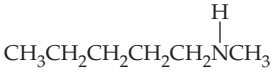


(b) $(CH_3)_2CH\overset{+}{N}H_3 + OH^-$

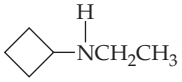
(c) $(CH_3CH_2)_3\overset{+}{N}H\ Br^-$ **(d)**



16.30 (a)



(b)



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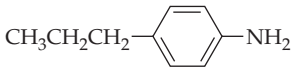
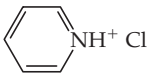


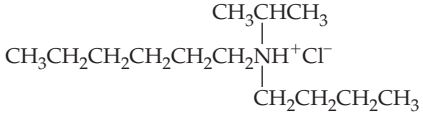
16.32 (a) *N*-ethylcyclopentylamine (secondary) **(b)** cycloheptylamine (primary) **16.34** diethylamine **16.36 (a)** *N*-methyl-2-butylammonium nitrate (salt of a secondary amine).

(b)



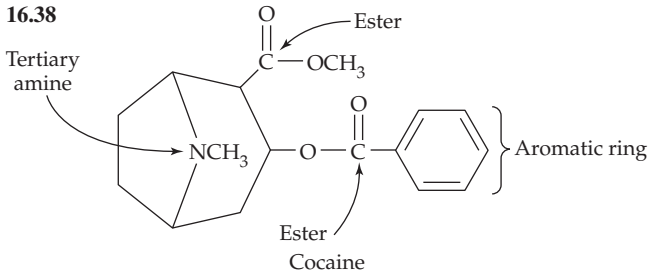
(salt of a heterocyclic amine)

(c)

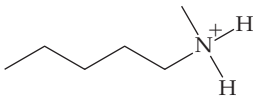


(salt of a tertiary amine)

16.38



16.40 (a)



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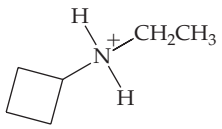

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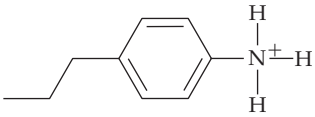
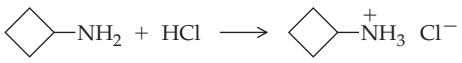


16.42 (a)



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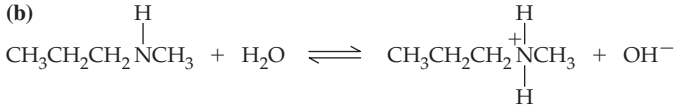

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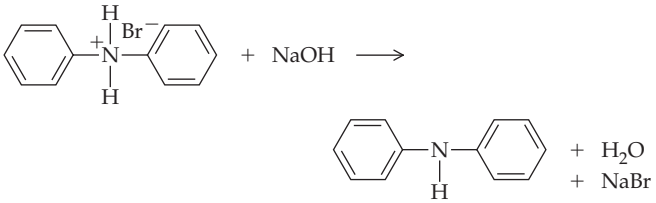
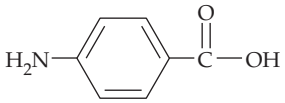


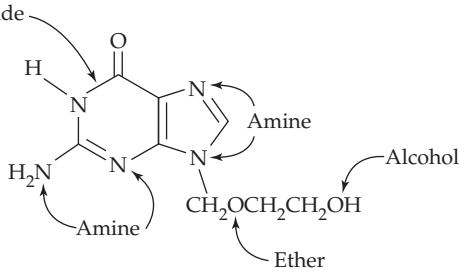
16.44 Choline doesn't react with HCl because its nitrogen isn't basic.

16.46



PABA

16.48



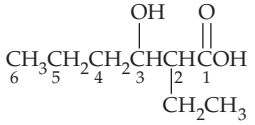
Acyclovir—related to purine

16.50 amines: foul-smelling, somewhat basic, lower boiling (weaker hydrogen bonds); Alcohols: pleasant-smelling, not basic, higher boiling (stronger hydrogen bonds) **16.52 (a)** 6-methylhept-2-ene **(b)** *p*-isopropylphenol **(c)** dibutylamine **16.54** Molecules of hexylamine can form hydrogen bonds to each other, but molecules of triethylamine can't. **16.56** The nitrogen atom is not part of the ring. **16.58 (a)** *N*-ethylcyclohexylamine **(b)** anilinium bromide **(c)** *N*-methylethylamine **16.60** Decylamine and ethanamine are both primary amines and can form hydrogen bonds but ethanamine has a smaller hydrocarbon region so it would be more soluble.

Chapter 17

17.1 carboxylic acid: **(c);** amides: **(a), (f), (h);** ester: **(d);** none: **(b), (e), (g)**

17.2 (a)



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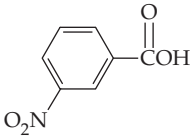
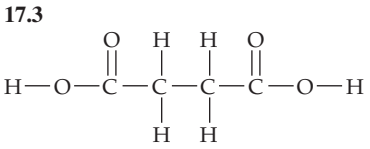
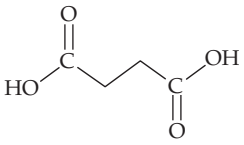
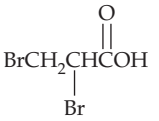


17.3





17.4



2,3-Dibromopropanoic acid

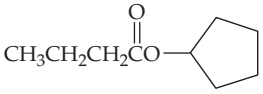
17.5 (a)

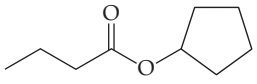
(b)

(c)

17.6 CH_3COOH is highest boiling (most H-bonding). $CH_3CH_2CH_3$ is lowest boiling (nonpolar). **17.7 (a)** C_3H_7COOH is more soluble (smaller —R group). **(b)** $(CH_3)_2CHCOOH$ is more soluble (carboxylic acid).

17.8 (a)





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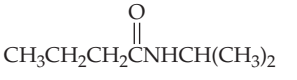
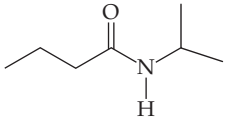
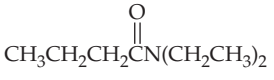
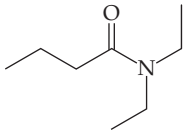




(c)

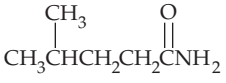




(d) cyclopentyl butyrate; *N*-isopropylbutyramide; *N*,*N*-diethylbutyramide

17.9 (a) 2-bromo-*N*-methylbutanamide **(b)** *N*-ethyl-*N*-methylbenzamide **(c)** 3-hydroxy-2-methylpropanamide

17.10 (a)



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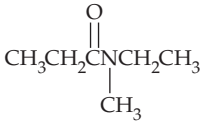
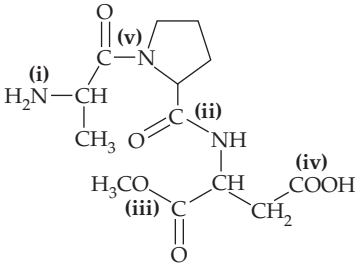
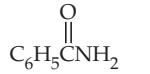


17.11

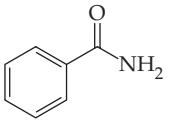


17.12 (a) (ii) **(b)** (i) **(c)** (iii) **(d)** (i) **(e)** (i) **(f)** (iii)

17.13 (a)



Amide (C_7H_7NO)



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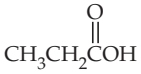
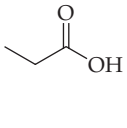
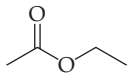


Carboxylic acid ($C_3H_6O_2$)

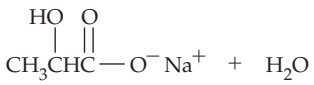


(c)

Ester ($C_4H_8O_2$)



17.14 (a)



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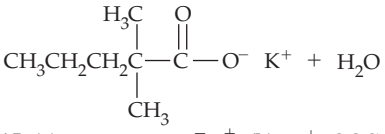
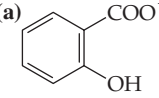


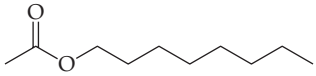
17.15 (a)



(b) $Na^+ {}^-OOCCOO^- Na^+$

17.16 CH_3COO^- $\quad$ $^-OOCCH_2CH_2CH_2COO^-$

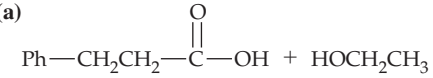
17.17



Octyl actetate (octyl methanoate)

17.18 $HCOOCH_2CH(CH_3)_2$

17.19 (a)



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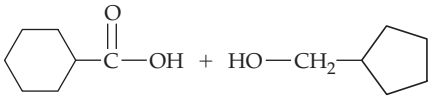
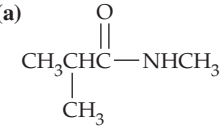


17.20 (a)



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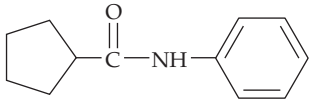
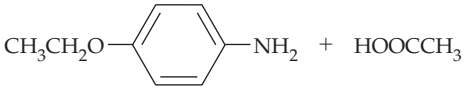
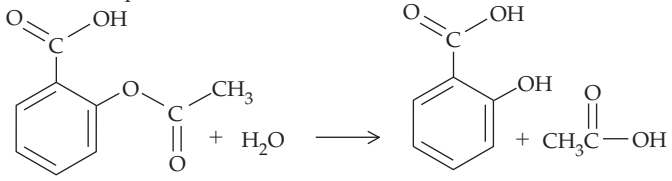


17.21 (a) ether, aromatic, amide

(b)

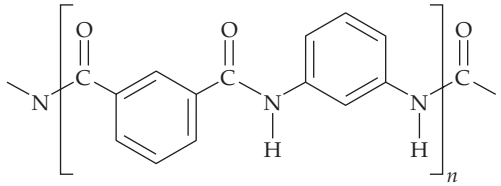


17.22 Moisture in the air hydrolyzes the ester bond, producing acetic acid as one of the products.



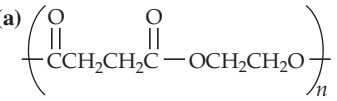
17.23 (a) benzoic acid + propan-2-ol **(b)** phenol + cyclopentanecarboxylic acid **(c)** ethanol and propanoic acid **17.24 (a)** 2-butenoic acid + methanamine **(b)** *p*-nitrobenzoic acid + dimethylamine

17.25

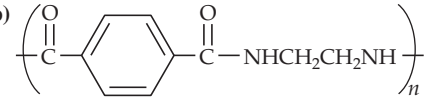


Nomex

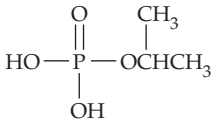
17.26 (a)



(b)

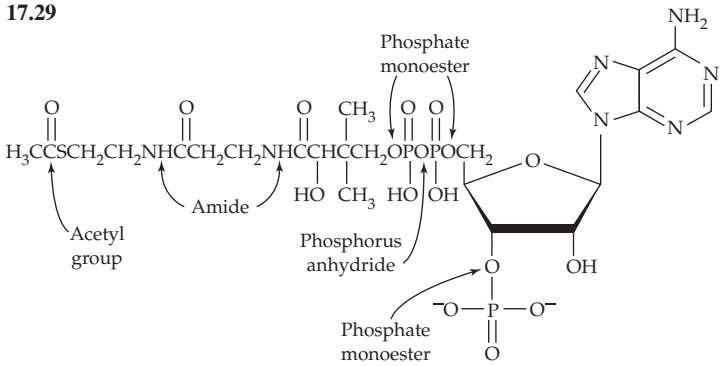


17.27

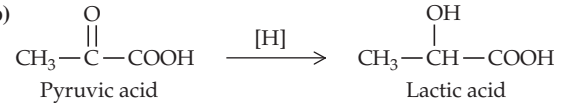


17.28 **(a)** amide + $H_2O \rightarrow CH_3COOH + NH_3$
(b) phosphate monoester + $H_2O \rightarrow CH_3CH_2OH + HOPO_3^{2-}$
(c) carboxylic acid ester + $H_2O \rightarrow CH_3CH_2COOH + HOCH_3$

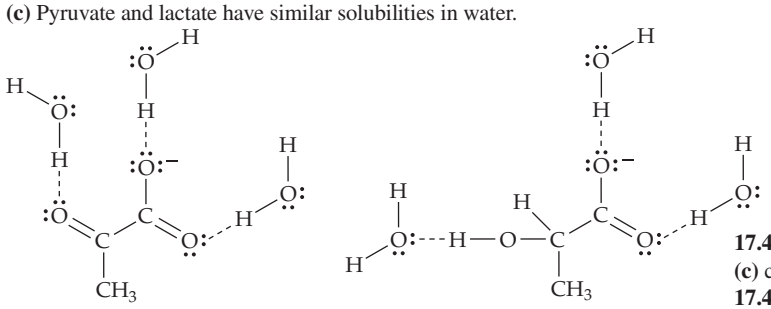
17.29



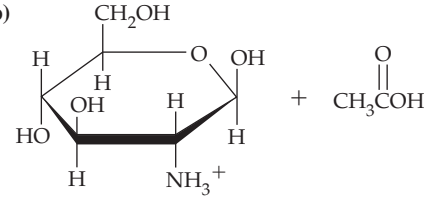
17.30 **(a)** At pH = 7.4, pyruvate and lactate are anions.
(b)



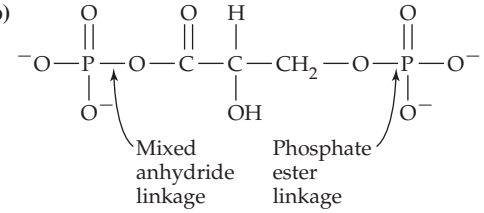
(c) Pyruvate and lactate have similar solubilities in water.



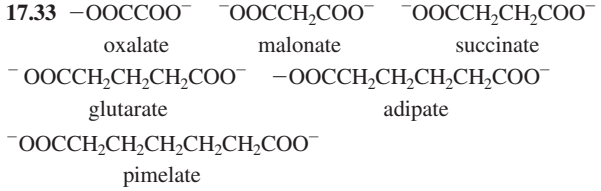
17.31 **(a)** H_2O + acid or base
(b)



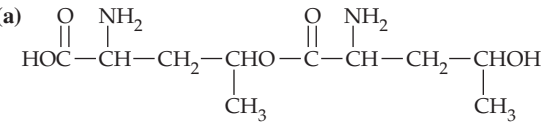
17.32 **(a)** a phosphate ester linkage
(b)



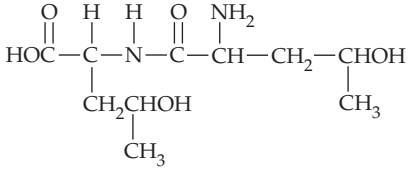
17.33



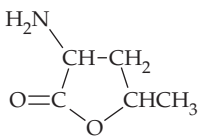
17.34 **(a)**



(b)

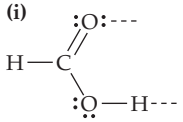


(c)



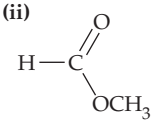
17.35 **(a)**

(i)



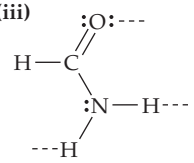
Formic acid

(ii)



Methyl formate

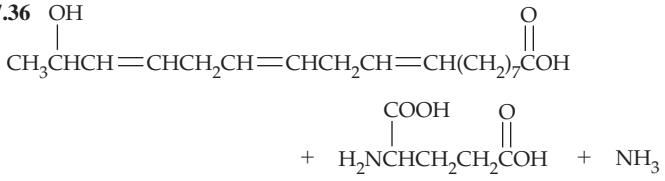
(iii)



Formamide

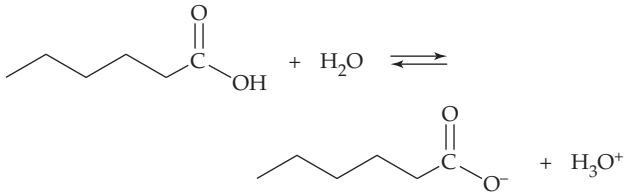
(b) Methyl acetate is lowest boiling (no hydrogen bonds); acetamide is highest boiling.

17.36

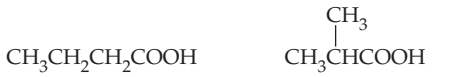


17.37 **(a)** *N*-ethyl acetamide **(b)** methyl 2-chlorocyclopentanecarboxylate **(c)** ethyl pentanoate **(d)** *N*-ethyl-*N*-methylformamide

17.38



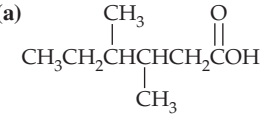
17.40



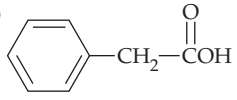
17.42 **(a)** 3-hydroxy-4-methylpentanoic acid **(b)** nonanoic acid
(c) cyclohexanecarboxylic acid **(d)** *p*-aminobenzoic acid

17.44 **(a)** potassium 3-ethylpentanoate **(b)** ammonium benzoate
(c) calcium propanoate

17.46 **(a)**



(b)



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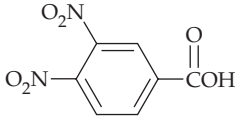

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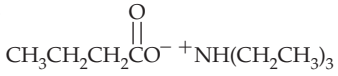
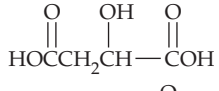
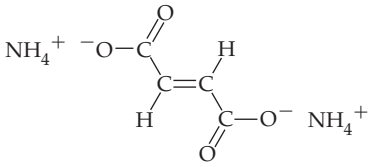


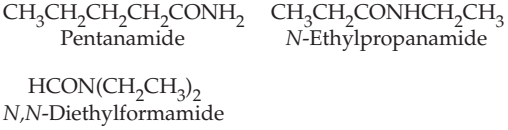
17.48



17.50



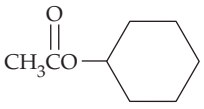
17.52 **(a)**

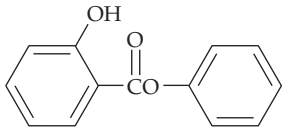


(b) $CH_3CH_2CH_2CH_2COOCH_3$ Methyl pentanoate $CH_3CH_2COOCH_2CH_2CH_3$ Propyl propanoate

$HCOOCH_2CH_2CH_2CH_2CH_3$ Pentyl formate

17.54 **(a)** 3-methylbutyl acetate **(b)** methyl 4-methylpentanoate

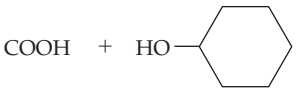
(c) 

(d) 

17.56 **(a)** $CH_3COOH + HOCH_2CH_2CH(CH_3)_2$

(b) $(CH_3)_2CHCH_2CH_2COOH + HOCH_3$

(c)



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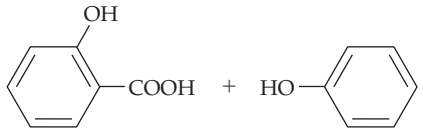
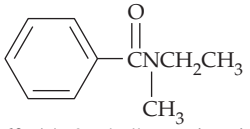
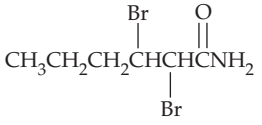


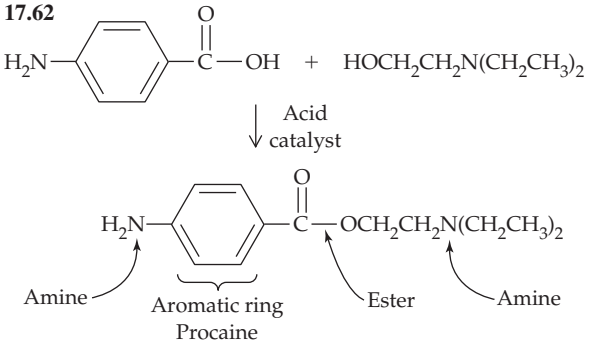
17.58 **(a)** 2-ethylbutanamide **(b)** *N*-phenylbenzamide

(c) 

(d) 

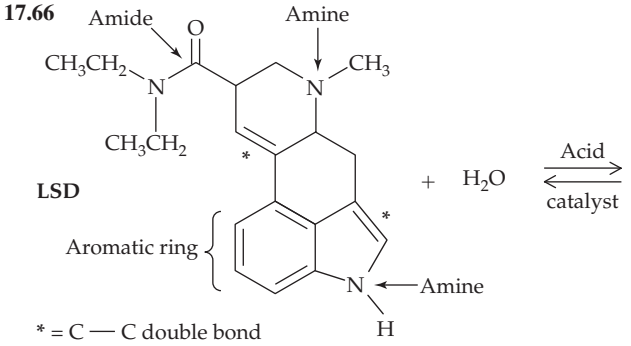
17.60 **(a)** 2-ethylbutanoic acid+ ammonia **(b)** benzoic acid+ aniline **(c)** benzoic acid + *N*-methylethylamine **(d)** 2,3-dibromohexanoic acid + ammonia

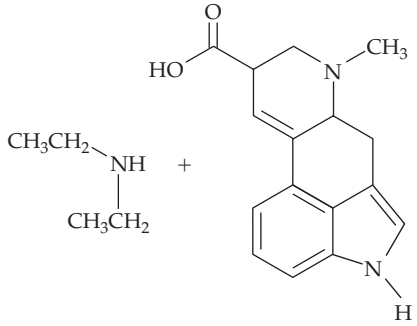
17.62



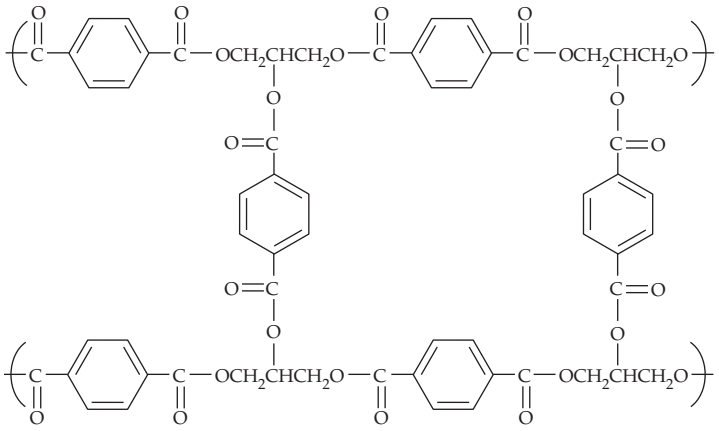
17.64 $HOCH_2CH_2CH_2COOH$

17.66



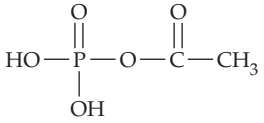


17.68



17.70 Dihydroxyacetone and hydrogen phosphate anion.

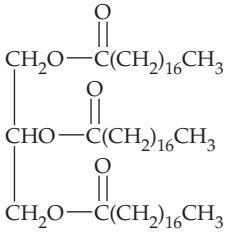
17.72



17.74 A cyclic phosphate diester is formed when a phosphate group forms an ester with two hydroxyl groups in the same molecule.

17.76 *N*, *N*-dimethylformamide is lowest boiling because it doesn't form hydrogen bonds. Propanamide is highest boiling because it forms the most hydrogen bonds. **17.78** Both propanamide and methyl acetate are water-soluble because they can form hydrogen bonds with water. Propanamide is higher boiling because molecules of propanamide can form hydrogen bonds with each other.

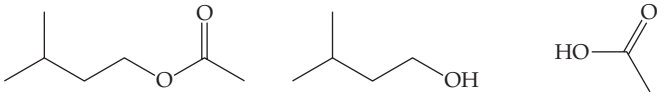
17.80



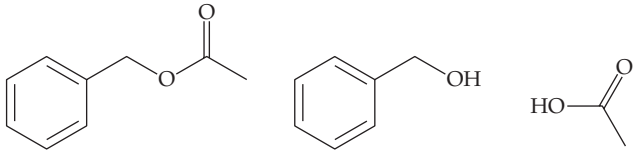
Glyceryl tristearate

17.82

(a) Ester Alcohol Carboxylic acid

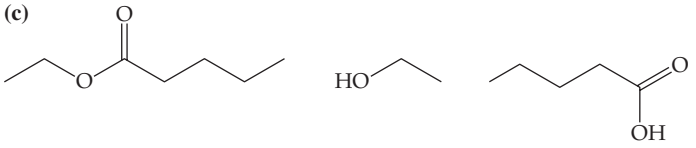


(b)



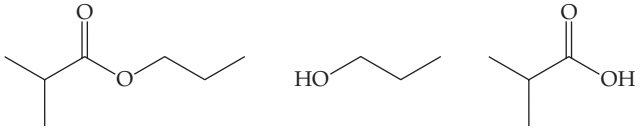
(Other possible structures for peach flavoring as well)

(c)



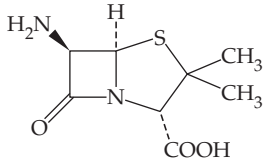
(Other possible structures for apple flavoring as well)

(d)

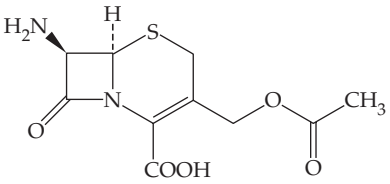


(Other possible structures for rum flavoring as well)

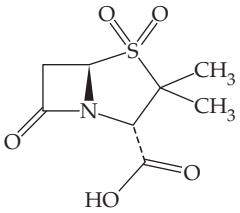
17.84 Four possible Beta-lactams; however, there are lots of other examples.



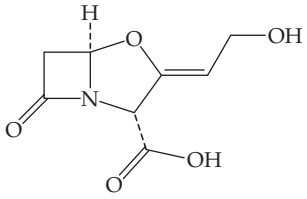
Penicillin: amides, sulfide, carboxylic acid



Cephalosporin: amide, amine, sulfide, carboxylic acid, alkene, ester



Sulbactam: amide, carboxylic acid

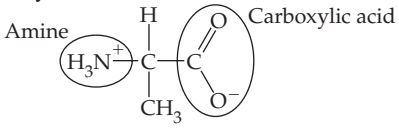


Clavulanate: amide, ether, alkene, alcohol, carboxylic acid
Common: All contain a cyclobutane and a second ring; amide within the cyclobutane, carboxylic acid

Chapter 18

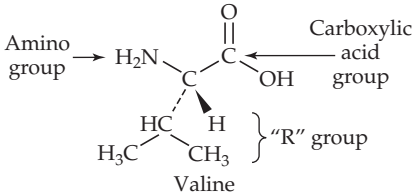
18.1 enzyme **18.2** hormones

18.3



Ala, A, Nonpolar

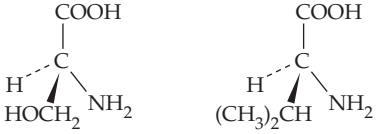
18.4



Valine

18.5 α- amino acids: **(a), (d)** **18.6** aromatic ring: phenylalanine, tyrosine, tryptophan; contain sulfur: cysteine, methionine alcohols: serine, threonine, tyrosine (phenol); alkyl side chain: alanine, valine, leucine, isoleucine

18.7

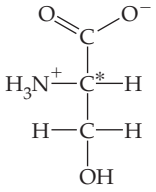


Serine Valine

(a) The serine side chain has a polar hydroxyl group; the valine side chain has a nonpolar isopropyl group. **(b)** serine—hydrophilic; valine—hydrophobic **18.8** aspartic acid; Side chain contains a polar carboxyl group.

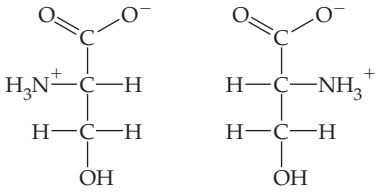
18.9 tryptophan; Side chain contains nonpolar aromatic rings.

18.10



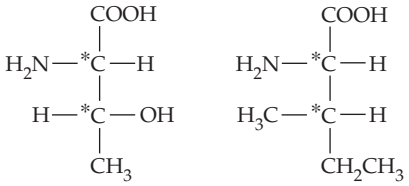
Chiral as the starred carbon is bonded to four different groups.

18.11



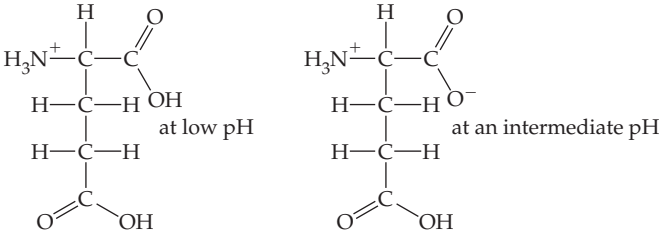
L-serine D-serine

18.12

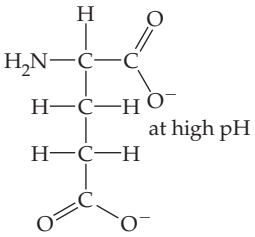


Threonine Isoleucine

18.13

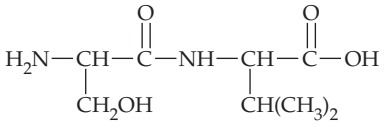


Zwitterion

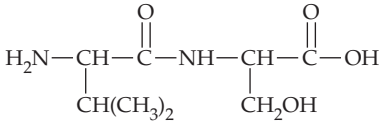


18.14 In the zwitterionic form of an amino acid, the $-NH_3^+$ group is an acid, and the $-COO^-$ group is a base.

18.15



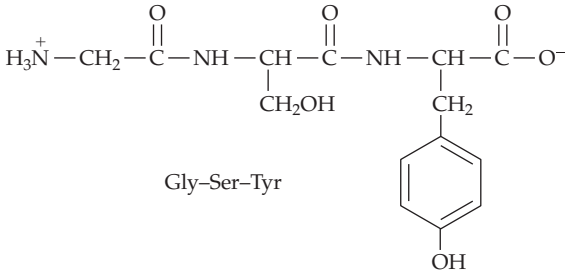
Serine Valine



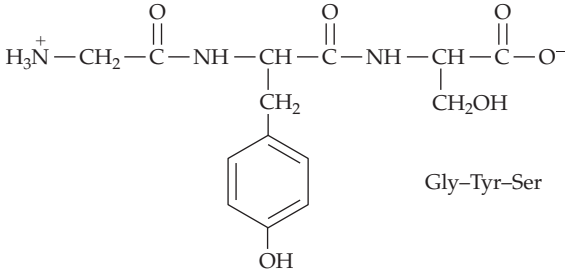
Valine Serine

18.16 **(a)** Gly—Ser—Tyr Tyr—Ser—Gly Ser—Tyr—Gly
Gly—Tyr—Ser Tyr—Gly—Ser Ser—Gly—Tyr

(b)



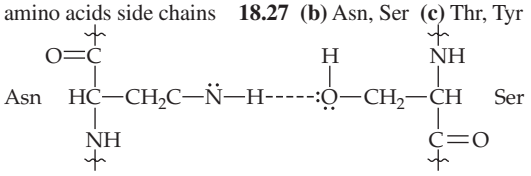
Gly–Ser–Tyr

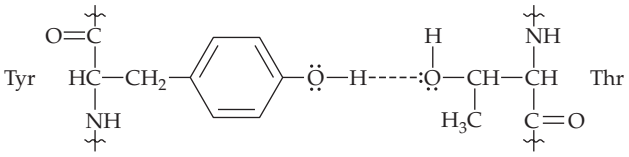


Gly–Tyr–Ser

18.17 lle—Arg—Val Arg—lle—Val Val—Arg—lle
lle—Val—Arg Arg—Val—lle Val—lle—Arg

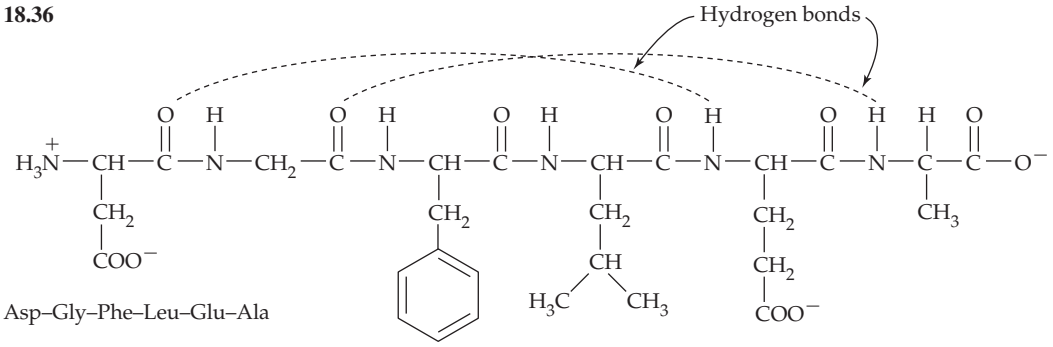
18.18 **(a)** Leu-Asp (nonpolar, polar) **(b)** Tyr-Ser-Lys (all polar) **18.19** seven peptide bonds **18.20** **(a)** six atoms **(b)** two amino acid units; the electrons of the carbonyl are shared with the C-N bond, making it rigid like a double bond **18.21** 24 **18.22** Protein function depends on the order of the amino acids **18.23** 11 backbone atoms **18.24** **(a)** hydrogen bonding **(b)** Hydrogen bonding takes place between an amide hydrogen and an amide carbonyl oxygen on an adjacent chain. **18.25** **(a)** globular or fibrous **(b)** fibrous **18.26** Outer surface consists of largely hydrophobic amino acids side chains **18.27** **(b)** Asn, Ser **(c)** Thr, Tyr





18.28 **(a)** hydrogen bond **(b)** hydrophobic interaction **(c)** salt bridge **(d)** hydrophobic interaction **18.29** **(a)** Tyr, Asp, Ser **(b)** Ala, lle, Val, Leu **18.30** **(a)** lipoproteins **(b)** metalloproteins **(c)** phosphoproteins **(d)** glycoproteins **(e)** hemoproteins **(f)** nucleoprotiens **18.31** In α-keratin, pairs of α-helixes twist together into small fibrils that are twisted into larger bundles. In tropocollagen, three coiled chains wrap around each other to form a triple helix. **18.32** Three fragments; Ala-Phe-Lys, Cys-Gly-Asp-Arg, Leu-Leu-Phe-Gly-Ala **18.33** No fragments, only 12 individual amino acids; acid hydrolysis cleaves all peptide bonds and is not selective **18.34** At low pH, the groups at the end of the polypeptide chain exist as $-NH_3^+$ and $-COOH$. At high pH, they exist as $-NH_2$ and $-COO^-$. In addition, side chain functional groups may be ionized as follows: **(a)** no change **(b)** Arg positively charged at low pH; neutral at high pH **(c)** Tyr neutral at low pH, negatively charged at high pH **(d)** Glu, Asp neutral at low pH, negatively charged at high pH **(e)** no change **(f)** Cys neutral at low pH, negatively charged at high pH. **18.35** **(a)** 1, 4 **(b)** 2, 4 **(c)** 2

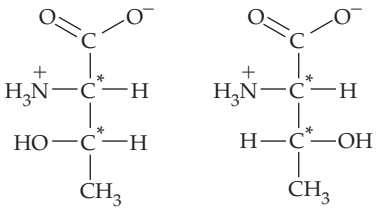
18.36



Asp–Gly–Phe–Leu–Glu–Ala

18.37 *Fibrous Proteins*: structural proteins, water-insoluble, contain many Gly and Pro residues, contain large regions of α-helix or β-sheet, few side-chain interactions. Examples: Collagen, α-Keratin, Fibroin. *Globular Proteins*: enzymes and hormones, usually water-soluble, contain most amino acids, contain smaller regions of α-helix and β-sheet, complex tertiary structure. Examples: Ribonuclease, hemoglobin, insulin. **18.38** **(a)** Leu, Phe, Ala, or any other amino acid with a nonpolar side chain. **(b), (c)** Asp, Lys, Thr, or any other amino acid with a polar side chain.

18.39

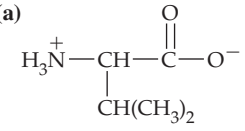


The upper chiral carbon is responsible for the *d*, *l* configuration.

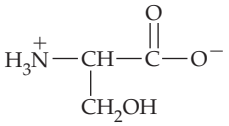
18.40

Type of Protein	Function	Example
Enzymes:	Catalyze biochemical reactions	Ribonuclease
Hormones:	Regulate body functions	Insulin
Storage proteins:	Store essential substances	Myoglobin
Transport proteins:	Transport substances through body fluids	Serum albumin
Structural proteins:	Provide shape and support	Collagen
Protective proteins:	Defend the body against foreign matter	Immunoglobulins
Contractile proteins:	Do mechanical work	Myosin and actin

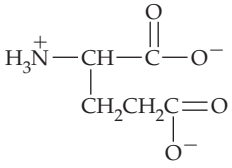
18.42 **(a)**



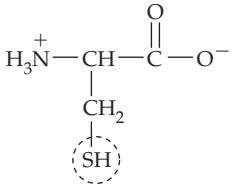
(b)



(c)

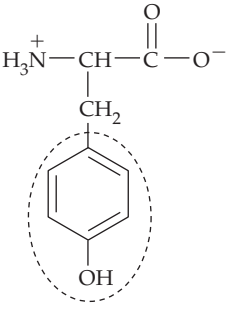


18.44 **(a)**



Cysteine (Cys)

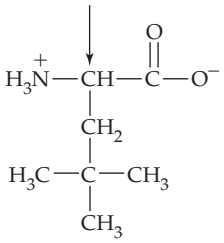
(b)



Tyrosine (Tyr)

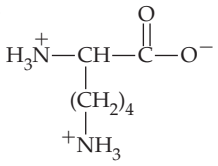
18.46 A chiral object is handed. Examples: glove, scissors.

18.48



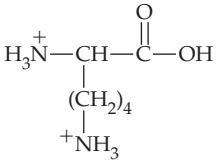
18.50 hydrophobic; side chain is nonpolar **18.52** neutral: **(a), (c)**; positive charge: **(b)** **18.54** **(a), (c)** low pH; **(b)** high pH

18.56 **(a)**



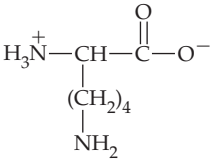
at pH = 7
(neutral pH)

(b)



at pH = 3
(low pH)

(c)

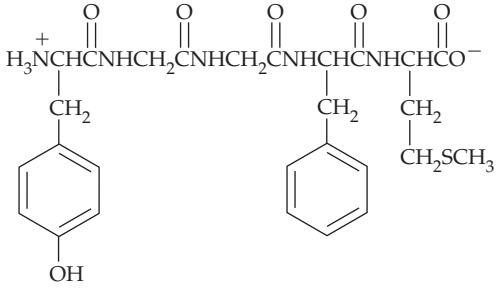


at pH = 9.7 (pI)
(high pH)

18.58 At its isoelectric point, a protein is electrically neutral which makes it insoluble in water. When a protein is charged, it is more soluble.

18.60 Val—Met—Leu, Met—Val—Leu, Leu—Met—Val, Val—Leu—Met, Met—Leu—Val, Leu—Val—Met.

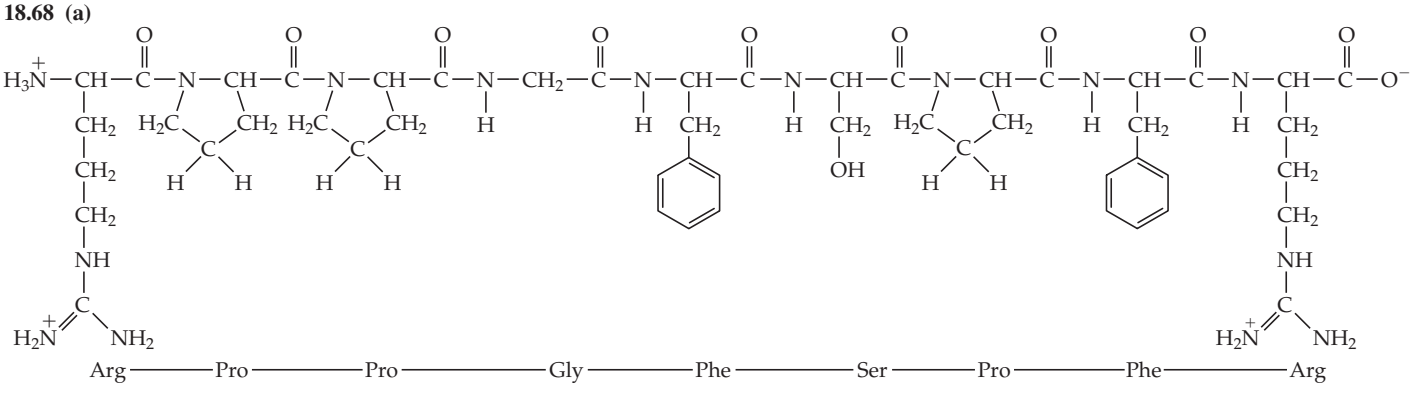
18.62 N-terminal C-terminal



18.64 *N*-terminal: Val—Gly—Ser—Ala—Asp C-terminal

18.66 *primary structure:* The sequence of connection of amino acids in a protein.

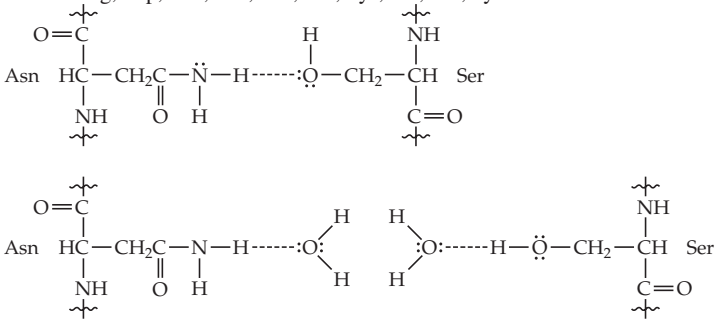
18.68 **(a)**



(b) Proline rings introduce kinks and bends and prevent hydrogen bonds from forming.

18.70 *secondary structure:* The orientation of segments of the protein chain into a regular pattern, such as an α-helix or a β-sheet, by hydrogen bonding between backbone atoms. **18.72** Stabilized by hydrogen bonds between the carbonyl oxygen of the polypeptide backbone and the amide hydrogen four amino acids later **18.74** α-keratins: wool, hair and fingernails; fibrous **18.76** **(a)** disulfide bonds **(b)** hydrophobic **(c)** salt bridge **(d)** hydrogen bonding **18.78** Hydrophilic residues interact with aqueous environment and hydrophobic residues fold into the interior away from the aqueous environment **18.80** A simple protein is composed only of amino acids. A conjugated protein consists of a protein associated with one or more nonprotein molecules. **18.82** Disulfide bonds stabilize tertiary structure. **18.84** **(a)** *primary structure:* The sequence of connection of amino acids in a protein. **(b)** *secondary structure:* The orientation of segments of the protein chain into a regular pattern, such as an α-helix or a β-sheet, by hydrogen bonding between backbone atoms. **(c)** *tertiary structure:* The coiling and folding of the entire protein chain into a three-dimensional shape as a result of interactions between amino acid side chains. **(d)** *quaternary structure:* The aggregation of several protein chains to form a larger structure. **18.86** In *hydrophobic interactions,* hydrocarbon side chains cluster in the center of proteins and make proteins spherical. Examples: Phe, Ile. *Salt bridges* bring together distant parts of a polypeptide chain. Examples: Lys, Asp. **18.88** 2 **18.90** A protein with a non-amino acid unit; myoglobin **18.92** When a protein is denatured, its nonprimary structure is disrupted, and loss of function occurs. **18.94** Protein digestion = hydrolysis of peptide bonds to form amino acids. Protein denaturation = disruption of secondary, tertiary, or quaternary structure without disrupting peptide bonds. **18.96** Canned pineapple has been heated to inactivate enzymes. **18.98** hydrophobic interactions: **(e), (f), (g), (h);** hydrogen bonding: **(a), (c), (d);** salt bridges: **(d);** covalent bonding: **(b)** **18.100** Methionine is a sulfide and not a thiol; only thiols can form disulfide bridges. **18.102** on the outside of a globular protein: Glu, Ser. on the outside of a fibrous protein: Ala, Val. On the outside of neither: Leu, Phe. **18.104** Asp is similar in size and function to Glu. **18.106** Enzymes would hydrolyze insulin. **18.108** A combination of grains, legumes, and nuts in each meal provides all of the essential amino acids. **18.110** Nonpolar amino acids, leucine and phenylalanine, are on the inside away from water. Polar amino acids, glutamate and glutamine, are on the outside as they can interact with water.

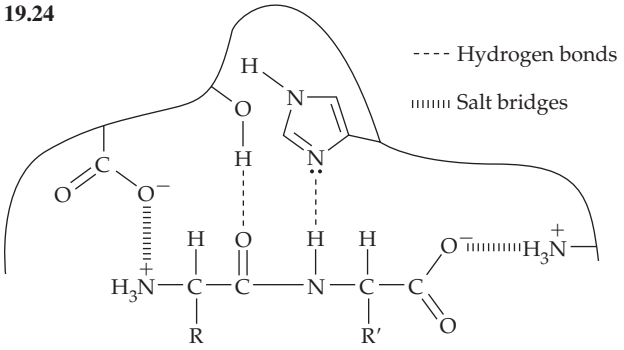
18.112 Arg, Asp, Asn, Glu, Gln, His, Lys, Ser, Thr, Tyr



Chapter 19

19.1 kinase **19.2** Enzymes are specific for one of two enantiomers; since lactate is found as both D and L, there must be two forms of LDH. **19.3** **(a)** NAD^+, coenzyme A, FAD; **(b)** The remaining cofactors are minerals. **19.4** **(a)** catalyzes the removal of two —H from an alcohol, **(b)** catalyzes the transfer of an amino group from aspartate to a second substrate, **(c)** catalyzes the synthesis of tyrosine–tRNA from tyrosine and its tRNA, coupled with ATP hydrolysis, **(d)** catalyzes the isomerization of a phosphohexose. **19.5** **(a)** urease **(b)** cellulase **19.6** transferase. It catalyzes the transfer of a phosphoryl group to a hexose. **19.7** Water adds to fumarate (substrate) to give L-malate (product). **19.8** reaction **(a)** **19.9** Acidic, basic, and polar side chains take part in catalytic activity. All types of side chains hold the enzyme in the active site. **19.10** Substrate molecules are bound to all of the active sites. **(a)** no effect **(b)** increases the rate **19.11** higher at 308 K in both cases **19.12** The rate is much greater at pH = 2. **19.13** molecule **(b)**, because it resembles the substrate **19.14** a product that resembles the substrate **19.15** **(a)** E1 **(b)** no **19.16** **(a)** competitive inhibition **(b)** covalent modification or feedback control **(c)** zymogen form present **(d)** genetic control **19.17** **(a)** needs a cofactor **(b)** needs a cofactor **(c)** does not require a cofactor **19.18** **(a)** niacin (B_3) **(b)** pantothenic acid (B_5) **19.19** vitamin A—fat-soluble as a long hydrocarbon chain; vitamin C—water-soluble as polar hydroxyl groups **19.20** retinal—aldehyde; retinoic acid—carboxylic acid. **19.21** enzyme cofactors; antioxidants; aid in absorption of calcium and phosphate ions; aid in synthesis of visual pigments and blood clotting factors. **19.22** vitamins C and E, β-carotene; These vitamins scavenge damaging free radicals. **19.23** copper, selenium; Both have a biological function and are toxic only in excess.

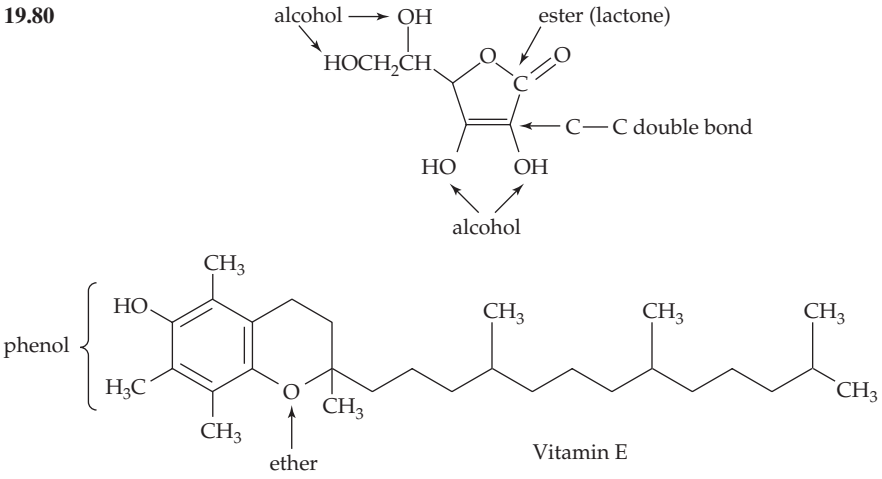
19.24



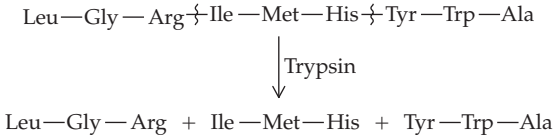
19.25 **(a)** oxidoreductase **(b)** dehydrogenase **(c)** L-lactate **(d)** pyruvate (e) L-lactate dehydrogenase **19.26** No. An enzyme usually catalyzes the reaction of only one isomer. D-Lactate might be a competitive inhibitor. **19.27** NAD^+ is an oxidizing agent and includes the vitamin niacin. **19.28** **(a)** Rate increases when [substrate] is low, but maximum rate is soon reached; maximum rate is always lower than maximum rate of uninhibited reaction. **(b)** Rate increases. **19.29** **(a)** Addition or removal of a covalently bonded group changes the activity of an enzyme **(b)** Hormones control the synthesis of enzymes. **(c)** Binding of the regulator at a site away from the catalytic site changes the shape of the enzyme. **(d)** Feedback inhibition occurs when the product of a series of reactions serves as an inhibitor for an earlier reaction. **19.30** **(a)** feedback inhibition **(b)** irreversible inhibition **(c)** genetic control **(d)** noncompetitive inhibition **19.31** from left to right: aspartate (acidic), serine, glutamine, arginine (basic), histidine (basic). **19.32** **(a)** riboflavin (B_2) **(b)** pantothenic acid (B_5) **(c)** niacin (B_3) **19.34** **(b)** **19.36** **(a)** removal of two H atoms from a substrate to form a double bond **(b)** replacement of a carboxyl group by H **(c)** hydrolysis of ester groups in lipids **19.38** **(a)** amylase **(b)** peroxidase **(c)** DNAse **19.40** An enzyme is a large three-dimensional molecule with a catalytic site into which a substrate can fit. Enzymes are specific in their action because only one or a few molecules have the appropriate shape and functional groups to fit into the catalytic site. **19.42** **(a)** hydrolase **(b)** lyase **(c)** oxidoreductase **19.44** **(a)** bonding together of two substrate molecules **(b)** transfer of a methyl group between substrates **(c)** reduction of a substrate **19.46** hydrolase **19.48** Lock-and-key: An enzyme is rigid (lock) and only one specific substrate (key) can fit in the active site. Induced fit: An enzyme can change its shape to accommodate the substrate and to catalyze the reaction. **19.50** No. Protein folding can bring the residues close to each other. **19.52** In the stomach, an enzyme must be active at an acidic pH. In the intestine, an enzyme needs to be active at a higher pH and need not be active at pH = 1.5. **19.54** At a high substrate concentration relative to enzyme concentration, the rate of reaction triples if the concentration of enzyme is tripled. **19.56** **(a)** **(b)** lowers rate and may denature the enzyme **(c)** denatures the enzyme and stops reaction **19.58** *Uncompetitive inhibition*: Inhibitor binds reversibly and noncovalently away from the active site and changes the shape of the site to make it difficult for the enzyme to catalyze reactions. *Competitive inhibition*: Inhibitor binds reversibly and noncovalently at the active site and keeps the substrate from entering. *Irreversible inhibition*: Inhibitor irreversibly forms a covalent bond at the active site and destroys the catalytic ability of the enzyme. **19.60** diagram B

19.62 (1) displacing an essential metal from an active site; (2) bonding to a cysteine residue (irreversible) **19.64** Papain catalyzes the hydrolysis of peptide bonds and partially digests the proteins in meat. **19.66** One site is for catalysis, and one site is for regulation. **19.68** The end product of a reaction series is an inhibitor for an earlier step. **19.70** A zymogen is an enzyme synthesized in a form different from its active form because it might otherwise harm the organism. **19.72** Trypsin and chymotrypsin must be inactive so they do not digest the pancreas. **19.74** Vitamins are small, essential organic molecules that must be obtained from food. **19.76** Vitamin C is excreted, but Vitamin A is stored in fatty tissue. **19.78** Bone is composed of both calcium and phosphorus.

19.80



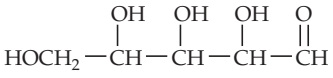
19.82 Blanching denatures enzymes to slow deterioration of food quality in frozen foods. **19.84** Amount of energy needed for a reaction to occur or for effective collisions; determines the rate of reaction **19.86** This problem requires an explaination. A brief explanation was included here. **(a)** rate decreases; not enough energy for a reaction to occur **(b)** rate decreases; enzyme denatures **(c)** rate decreases; enzyme denatures **(d)** rate decreases; enzyme denatures **(e)** rate increases/doubles; more substrate to react with the enzymes (assuming not at saturation) **(f)** rate decreases by half; less substrate to react with **19.88** 9.3 L apple juice **19.90** Look for Arg, His, and Lys (basic amino acids) in the polypeptide, and break the bond between the basic amino acid and the amino acid to its right. (There are three fragments.)



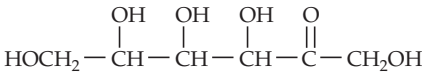
Chapter 20

20.1 **(a)** aldopentose **(b)** ketotriose **(c)** aldotetrose

20.2



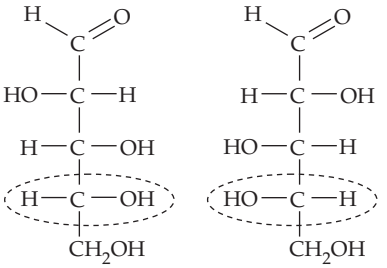
An aldopentose



A ketohexose

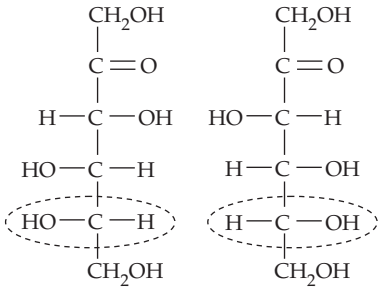
20.3 The bottom carbon is not chiral. The orientations of the hydroxyl groups bonded to the chiral carbons must be shown in order to indicate which stereoisomer is pictured. **20.4** **(d)** **20.5** 32 stereoisomers

20.6 **(a)**



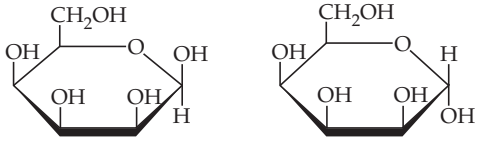
A D-aldopentose An L-aldopentose

(b)



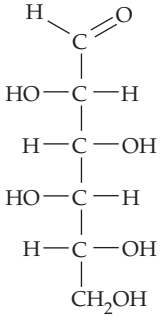
An L-ketohexose A D-ketohexose

20.7



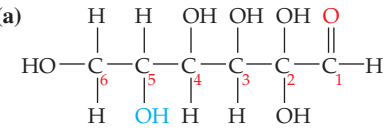
β-anomer α-anomer

20.8

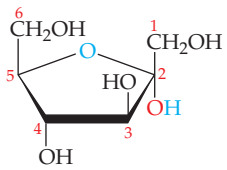


D-Idose

20.9 (a)

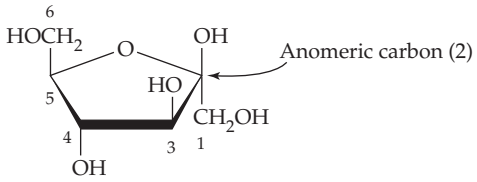


(b)



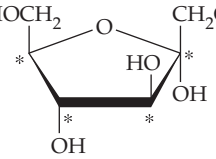
20.10 **(a)** Rings **1** and **4** (5 carbons) are amino sugars **(b)** Ring **3** (4 carbons) is an unmodified sugar **(c)** Ring **2** (6 carbons) is a nonsugar.

20.11

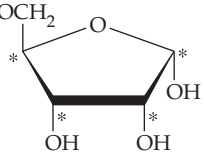


β-anomer

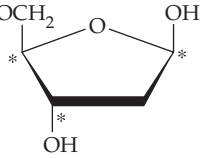
20.12 **(a)**



(b)

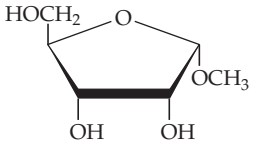


(c)

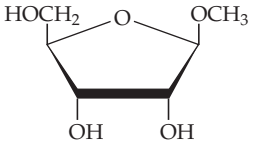


20.13 **(a)** an α anomer **(b)** carbon 6 **(c)** Groups that are below the plane of the ring in D-galactose are above the plane of the ring in L-fucose. Groups that are above the plane of the ring in D-galactose are below the plane of the ring in L-fucose. **(d)** yes

20.14 Both are acetals.



Methyl α-D-riboside



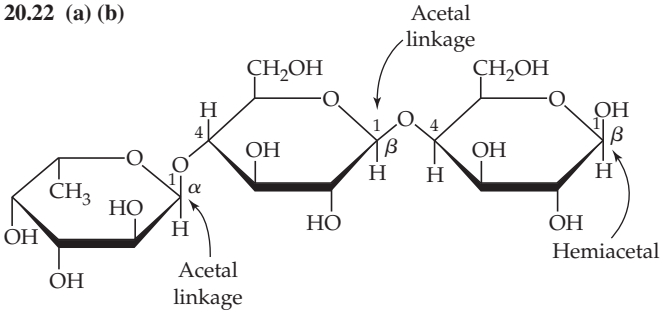
Methyl β-D-riboside

20.15 a β-1,4 glycosidic link **20.16** β-D-Glucose + β-D-Glucose

20.17 **(a)** maltose; fermenting grain **(b)** sucrose; sugar beets **(c)** lactose; milk **20.18** **(a)** On C5, there is a —CH_2OH group in glucose and a —COO^- in β-D-glucuronate. **(b)** On C2, there is a —OH group in glucose and a —NH_2 in β-D-glucosamine. **(c)** On C2, there is a —OH group in glucose and a —NH_2COCH_3 in *N*-acetyl-β-D-glucosamine. **20.19** glutamine, asparagine **20.20** Starch (polysaccharide) $\xrightarrow{\text{Amylase}}$ Maltose (disaccharide) $\xrightarrow{\text{Maltase}}$ Glucose (monosaccharide)

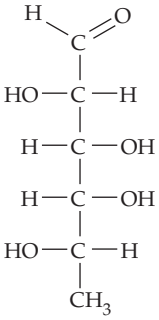
20.21 **(a)** diastereomers, anomers **(b)** enantiomers **(c)** diastereomers

20.22 **(a) (b)**

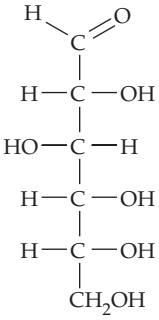


A α-anomer B β-anomer C β-anomer

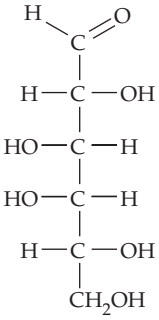
(c) α-1,4 linkage between C4 of B and C1 of A **(d)** β-1,4 linkage between C4 of C and C1 of B **20.23** **(a) (b)** No monosaccharides are identical, and none are enantiomers. **(c) (d)**



L-Fucose

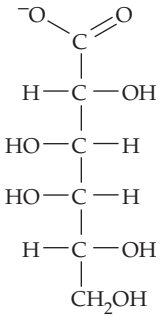


D-Glucose



D-Galactose

20.24 Monosaccharide C is oxidized. Identification of the carboxylic acid also identifies the terminal monosaccharide.



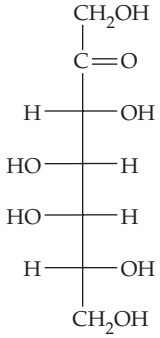
20.25 No

20.26

Polysaccharide	Linkage	Branching?
Cellulose	β-1,4	no
Amylose	α-1,4	no
Amylopectin	α-1,4	yes: α- 1,6 branches occur ~ every 25 units
Glycogen	α-1,4	yes: even more α- 1,6 branches than in amylopectin

20.27 Glucose is in equilibrium \with its open-chain aldehyde form, which reacts with an oxidizing agent. **20.28** A carbohydrate is a polyhydroxylated aldehyde or ketone that belongs to one of the biologically most important classes of compounds. **20.30** An aldose contains an aldehyde and a ketose contains a ketone. **20.32** **(a)** two **(b)** two **(c)** three **(d)** three

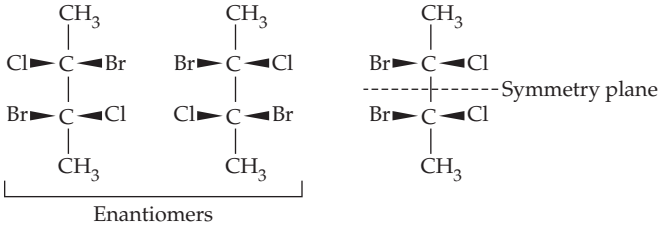
20.34



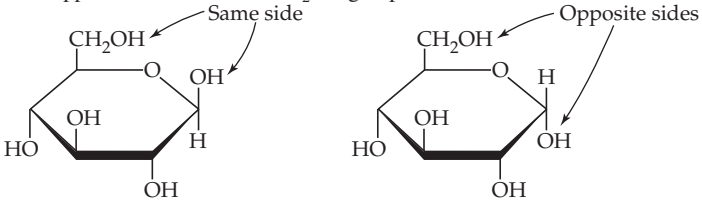
A ketoheptose

20.36 glucose—foods like fruits and vegetables; galactose—brain tissue and a component of lactose; fructose—honey and fruits; ribose—nucleic acids **20.38** Enantiomers are stereoisomers that are nonsuperimposable mirror images.

20.40

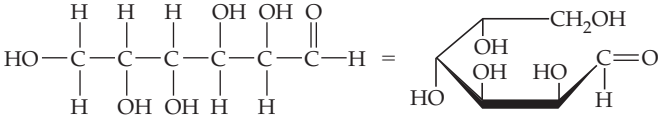


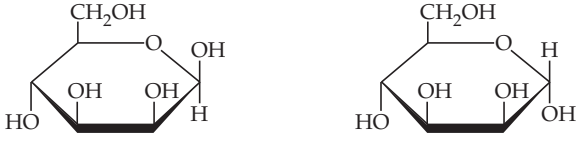
The third stereoisomer has a symmetry plan and is not chiral so there is no enantiomer. **20.42** **(a)** Fructose rotates light to the left to a greater degree than glucose. **(b)** The sign of rotation of the fructose–glucose mixtures is inverted or opposite the sign of rotation of sucrose. **20.44** A sugar that gives a positive reaction when treated with an oxidizing agent (Tollens' reagent or Benedict's reagent). **20.46** Mutarotation occurs when either a pure anomer or a mixture of anomers is dissolved in water. If the rotation of plane-polarized light is measured, the degree of rotation, as well as the ratio of anomers, changes until it reaches a constant value. At this point, an equilibrium mixture of both anomers is present in the solution. Mutarotation is not a general characteristic of all chiral compounds. **20.48** In the β form of the carbohydrate, the —OH group attached to C1 is on the same side as the $-CH_2OH$ group on C5. In the α form, the —OH group attached to C1 is on opposite sides of the $-CH_2OH$ group on C5.



A β-anomer An α-anomer

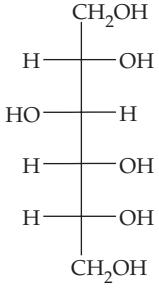
20.50





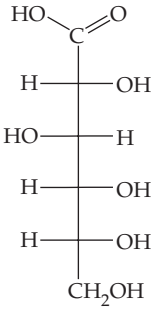
β-D-Mannose α-D-Mannose

20.52



Sorbitol

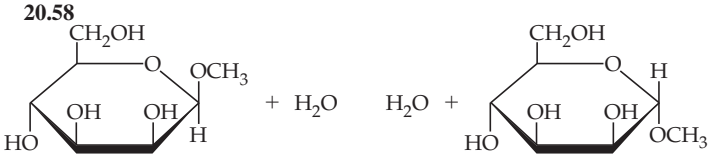
20.54



Gluconic acid

20.56 In a hemiacetal, an —OH group and an —OR group are bonded to a carbon atom that was previously a carbonyl carbon. In an acetal, the carbon is bonded to two —OR groups.

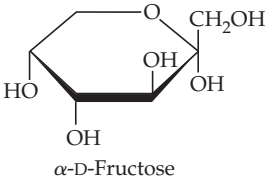
20.58



Methyl β-D-mannoside Methyl α-D-mannoside

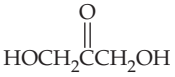
20.60 maltose: fermenting grains, two glucose units; lactose: milk, galactose, and glucose; sucrose: plants, glucose, and fructose **20.62** Amylose, a major component of the human diet, consists of α-D-glucose units linked by α-1,4 glycosidic bonds. Cellulose, a structural material in plants, consists of β-D-glucose units linked by β-1,4 glycosidic bonds. **20.64** **(c)** **20.66** Two β-D-glucose units **20.68** Two α-D-glucose units **20.70** Glycogen has many more branches and is significantly larger than amylopectin. **20.72** heparin: α-D-glucuronate and β-D-glucosamine; hyaluronate: α-D-glucuronate and *N*-acetyl-β-D-glucosamine; chondroitin 6-sulfate: α-D-glucuronate and *N*-acetyl-β-D-glucosamine **20.74** Diastereomers because they are not mirror images.

20.76



α-D-Fructose

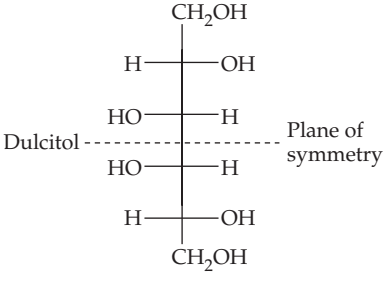
20.78



1,3-dihydroxyacetone has no optical isomers, as it is not chiral

20.80 Lactose intolerance is an inability to digest lactose; symptoms include bloating, cramps, and diarrhea.

20.82



Dulcitol is optically inactive because it has a plane of symmetry and thus doesn't have an enantiomer. **20.84** fructose: fruit; lactose: milk; amylose: wheat starch **20.86** Enzymes produced by the bacteria in yogurt predigest most of the lactose, making it possible for lactose-intolerant people to eat yogurt without symptoms. **20.88** 701 kJ

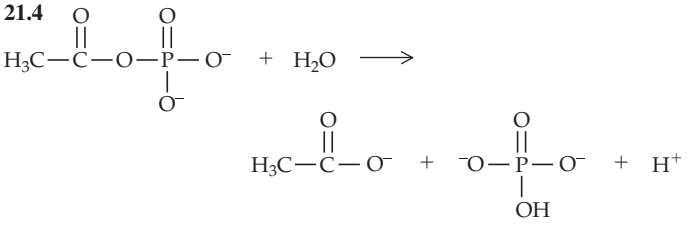
Chapter 21

21.1 Both pathways produce the same amount of energy.
21.2 **(a)** exergonic: oxidation of glucose; endergonic: photosynthesis **(b)** sunlight **21.3** **(a)**

$$\text{Carbohydrates} \xrightarrow{\text{digestion}} \text{Glucose, Sugars} \xrightarrow{\text{glycolysis}} \text{Pyruvate} \rightarrow \text{Acetyl-CoA} \xrightarrow[\text{cycle}]{\text{citric acid}} \text{Reduced coenzymes} \xrightarrow[\text{transport}]{\text{electron}} \text{ATP}$$

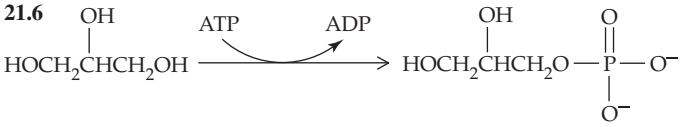
(b) pyruvate, acetyl-CoA, citric acid cycle intermediates.

21.4

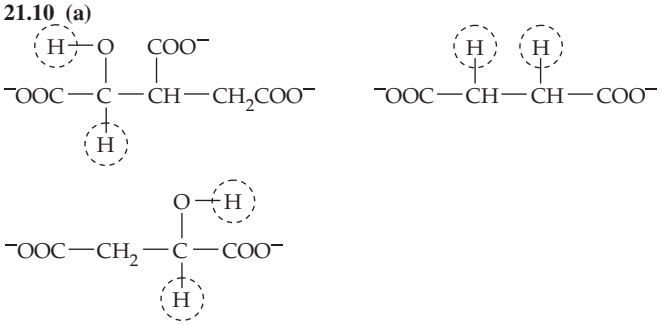


21.5 Energy is produced only when it is needed.

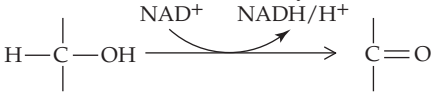
21.6



21.7 If a process is exergonic, its exact reverse is endergonic and can't occur unless it is coupled with an exergonic reaction in a different pathway.
21.8 favorable ($\Delta G = -12.3$ kJ/mol).
21.9 **(b), (c), (d)** FAD has five heterocyclic rings (three in the ADP part, and two in the site of reaction on the left).
21.10 **(a)**



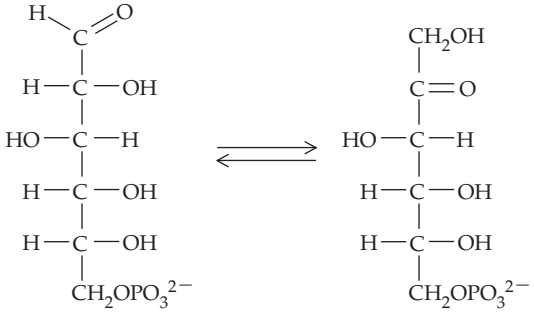
(b) oxidoreductases **21.11** citric acid, isocitric acid **21.12** steps 3, 4, 6, 8 **21.13** Succinic dehydrogenase catalyzes the removal of two hydrogens from succinate to yield fumarate, and FAD is the coenzyme associated with dehydrogenations. **21.14** citrate (tertiary); isocitrate (secondary); malate (secondary) **21.15** isocitrate **21.16** Steps 1–4 correspond to the first stage, and steps 5–8 correspond to the second stage. **21.17** mitochondrial matrix **21.18** *Similarities:* Both involve the reaction of glucose, oxygen, carbon dioxide, and water; both take place in organelles (chloroplasts, mitochondria); both involve large, metal ion–containing molecules (chlorophyll, heme); both involve electron transfer; both involve similar coenzymes. *Differences*: photosynthesis captures energy, whereas electron transport releases energy; photosynthesis requires light, whereas oxidative phosphorylation doesn't. **21.19** O_2. Movement of H^+ from a region of high $[H^+]$ to a region of low $[H^+]$ releases energy that is used in ATP synthesis.
21.20 **(a)** succinyl phosphate $+H_2O \longrightarrow$ Succinate $+ HOPO_3^{2-} + H^+$ **(b)** ADP $+ HOPO_3^{2-} + H^+ \longrightarrow$ ATP $+ H_2O$ $\Delta G = +30.5$ kJ/mol
21.21 **(a)** Stage 1 (digestion) **(b)** Stage 4 (ATP synthesis) **(c)** Stage 2 (glycolysis) **(d)** Stage 3 (citric acid cycle). **21.22** Endergonic; coupled reactions **21.23** NAD^+ accepts hydride ions; hydrogen ions are released to the mitochondrial matrix and ultimately combine with reduced O_2 to form H_2O.
21.24 **(a)** step A (NAD^+) **(b)** step B **(c)** product of A **(d)** oxidoreductase **21.25** step 1: lyase; step 2: isomerase; step 3: oxidoreductase; step 4: oxidoreductase, lyase; step 5: ligase; step 6: oxidoreductase; step 7: lyase; step 8: oxidoreductase **21.26** Metals are better oxidizing and reducing agents. Also, they can accept and donate electrons in one-electron increments. **21.28** An endergonic reaction requires energy, and an exergonic reaction releases energy. **21.30** Enzymes affect only the rate of a reaction not the size or sign of ΔG. **21.32** exergonic: **(a), (b);** endergonic: **(c).** Reaction **(b)** proceeds farthest toward products. **21.34** prokaryote: **(b), (e);** eukaryote: **(a), (b), (c), (d)** **21.36** Organelles are subcellular structures that perform specialized tasks within the cell. **21.38** Cristae, the folds of the inner mitochondrial membrane, provide extra surface area for electron transport and ATP production to take place. **21.40** Metabolism refers to all reactions that take place inside cells. Digestion is the process of breaking food into small organic molecules prior to cellular absorption.
21.42 acetyl-CoA **21.44** An ATP molecule transfers a phosphoryl group to another molecule in exergonic reactions.
21.46 $\Delta G = -18.8$ kJ/mol. **21.48** not favorable (positive ΔG)
21.50 **(a)** NAD^+ is reduced, **(b)** NAD^+ is an oxidizing agent, **(c)** NAD^+ participates in the oxidation of a secondary alcohol to a ketone, **(d)** $NADH/H^+$ **(e)**



21.52 mitochondria **21.54** Both carbons are oxidized to CO_2. **21.56** three NADH, one $FADH_2$. **21.58** step 3 (isocitrate → α-ketoglutarate), step 4 (α-ketoglutarate → succinyl-SCoA) and step 8 (malate → oxaloacetate) transfer energy as NADH. **21.60** One complete citric acid cycle produces four reduced coenzymes, which enter the electron transfer chain and ultimately generate ATP. **21.62** H_2O, ATP, oxidized coenzymes
21.64 **(a)** FAD = flavin adenine dinucleotide; **(b)** CoQ = coenzyme Q; **(c)** $NADH/H^+$ = reduced nicotinamide adenine dinucleotide, plus hydrogen ion; **(d)** Cyt *c* = Cytochrome *c* **21.66** NADH, coenzyme Q, cytochrome c **21.68** The citric acid cycle would stop. **21.70** In oxidative phosphorylation, reduced coenzymes are oxidized, and ADP is phosphorylated. **21.72** H^+ ions pass through a channel that is part of the ATP synthase enzyme, where they release energy that drives oxidative phosphorylation. **21.74** Oxygen consumption increases because the proton gradient from ATP production dissipates. **21.76** Avoids the production of large amounts of heat, allows for storage of energy, controls the rate of metabolism, and allows energetically favorable steps to be coupled with energetically unfavorable reactions. **21.78** The isomer with a *cis* double bond cannot act as a substrate for the enzyme. **21.80** Electrons from the oxidation of reduced coenzymes are used to reduce O_2, which eventually forms H_2O. **21.82** Energy from combustion is released to the surroundings as heat and is wasted. Energy from metabolic oxidation is released in several steps and is stored in each step so that is available for use in other metabolic processes. **21.84** No. Step 5 produced GTP, which is converted to ATP. **21.86** Cells store energy as polymers, which can be hydrolyzed as needed for energy. **21.88** Oxygen debt occurs because the increased metabolic rate due to running consumes oxygen in the electron-transport chain. Panting is the body's attempt to resupply tissues with oxygen.

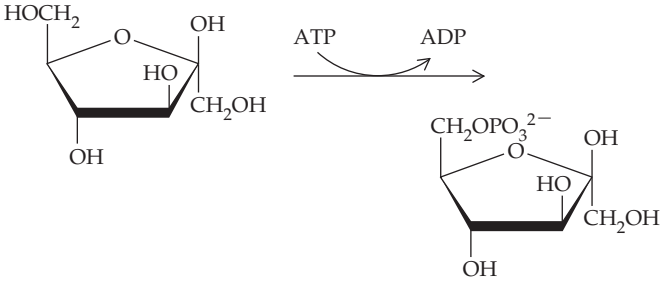
Chapter 22

22.1 **(a)** glycogenesis **(b)** glycogenolysis **(c)** gluconeogenesis
22.2 glycogenesis, pentose phosphate pathway, glycolysis **22.3** **(a)** steps 6 and 7 **(b)** steps 9 and 10 **22.4** Isomerizations: steps 2, 5, 8
22.5



22.6 **(a)** pyruvate **(b)** step 6: glyceraldehyde 3-phosphate is oxidized; NAD^+ is the oxidizing agent.

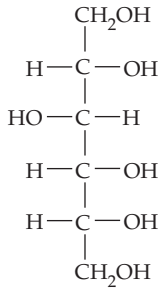
22.7



Fructose 6-phosphate enters glycolysis at step 3.

Fructose 6-phosphate enters glycolysis at step 3. **22.8** Glucose and galactose differ in configuration at C4. **22.9** **(a)** The energy is lost as heat. **(b)** The reverse of fermentation is very endothermic; loss of CO_2 drives the reaction to completion in the forward direction. **22.10** in preparation of bread, yogurt, cheese, beer, and wine **22.11** **(a)** acetyl-CoA under aerobic conditions **(b)** lactate under anaerobic conditions **(c)** glucose by gluconeogenesis, which occurs only in liver cells **22.12** 80 ATP molecules **22.13** 38 moles of ATP **22.14** Insulin decreases; blood glucose decreases, the level of glucagon increases. Glucagon causes the breakdown of liver glycogen and the release of glucose. As glycogen is used up, the level of free fatty acids and ketone bodies increases.

22.15



Sorbitol

Sorbitol can not form a cyclic acetal because it does not have a carbonyl group.

22.16 **(a)** The increase in $[H^+]$ drives the equilibrium shown in Section 22.9 to the right, causing the production of CO_2. **(b)** Le Châtelier's principle **22.17** Glycogenesis is the pathway to synthesize glycogen from glucose molecules while glycogenolysis is the pathway that breaks down glycogen, resulting in free glucose. **22.18** Glycogenesis occurs when glucose levels are high in order to store glucose molecules for later use. Glycogenolysis occurs when there is an immediate need for energy in muscle cells or when blood glucose levels are low. **22.19** phosphorylation, oxidation **22.20** the pathway for making glucose from lactate, amino acids, or glycerol **22.21** critical during fasting and early stages of starvation to provide glucose for energy production; without gluconeogenesis, death occurs **22.22** hydrolases **22.23** **(a)** when the supply of glucose is adequate and the body needs energy **(b)** when the body needs free glucose **(c)** when ribose 5-phosphate or NADPH are needed **(d)** when glucose supply is adequate, and the body doesn't need to use glucose for energy production **22.24** Phosphorylations of glucose and fructose 6-phosphate produce important intermediates that repay the initial energy investment. Fructose 1,6-bisphosphate is cleaved into two three-carbon compounds, which are converted to pyruvate. **22.25** **(a)** when the body needs energy, in mitochondria **(b)** under anaerobic conditions, in yeast **(c)** under anaerobic conditions, in muscle, red blood cells **(d)** when the body needs free glucose, in the liver **22.26** step 1: transferase; step 2: isomerase; step 3: transferase; step 4: lyase; step 5: isomerase; step 6: oxidoreductase, transferase; step 7: transferase; step 8: isomerase; step 9: lyase; step 10: transferase; transferases (because many reactions involve phosphate transfers); Ligases are associated with reactions that synthesize molecules, not with reactions that break down molecules. **22.27** **(g), (c), (b), (e), (f), (a), (d)** **22.28** Sources of compounds for gluconeogenesis: pyruvate, lactate, citric acid cycle intermediates, many amino acids. Gluconeogenesis takes place when glucose levels are low. **22.29** Germinating seeds need to synthesize carbohydrates from fats; humans obtain carbohydrates from food.

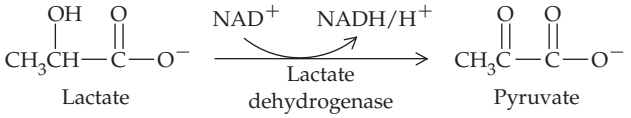
22.30 **(a)** No **(b)** Molecular oxygen appears in the last step of the electron transport chain, where it combines with water, H^+ and electrons (from electron transport) to form H_2O. **22.32** glucose + galactose; in the lining of the small intestine

22.34

Type of Food Molecules	Products of Digestion
Proteins	Amino acids
Triacylglycerols	Glycerol and fatty acids
Sucrose	Glucose and fructose
Lactose	Glucose and galactose
Starch, maltose	Glucose

22.36 acetyl-CoA; lactate; ethanol + CO_2 **22.38** glycogenesis: synthesis of glycogen from glucose; glycogenolysis: breakdown of glycogen to form glucose **22.40** ribose 5-phosphate, glycolysis intermediates **22.42** **(a)** all organs **(b)** liver **(c), (d)** muscle, liver **22.44** None of the steps of glycolysis require oxygen. **22.46** **(a)** steps 1, 3, 6, 7, 10 **(b)** step 6 **(c)** step 9 **22.48** **(a)** substrate-level phosphorylation: 2 mol ATP; oxidative phosphorylation (ideal): 6 ATP **(b)** oxidative phosphorylation: 3 mol ATP **(c)** substrate-level phosphorylation: 1 mol ATP; oxidative phosphorylation: 11 mol ATP. Substrate-level phosphorylation is formation of ATP as a by-product of a reaction; oxidative phosphorylation is formation of ATP as a by-product of electron transport.

22.50



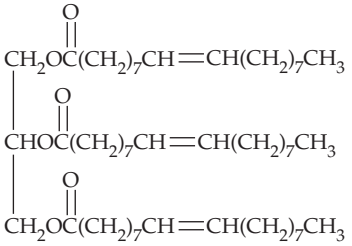
22.52 4 mol acetyl-CoA **22.54** *hypoglycemia:* low blood sugar; weakness, sweating, rapid heartbeat, confusion, coma, death; *hyperglycemia:* high blood sugar; increased urine flow, low blood pressure, coma, death **22.56** ketone bodies **22.58** muscle cells **22.60** Glycogenolysis uses less energy because it is a hydrolysis reaction. **22.62** pyruvate, lactate **22.64** Several steps in the reverse of glycolysis are energetically unfavorable. **22.66** steps 1, 3, 10 of glycolysis; all involve phosphate transfers **22.68** When muscle glucose is depleted and oxygen is in short supply **22.70** phosphoryl group transfers **22.72** Glucose obtained from the hydrolysis of glycogen is phosphorylated by reaction with inorganic phosphate ion and enters the glycolysis pathway as glucose 6-phosphate. Thus, one less ATP is needed (at step 1), and one more ATP is produced. **22.74** **(a)** consumes energy **(b)** yields energy **22.76** **(a)** when glucose is abundant and the body needs energy **(b)** when glucose is in short supply, as in starvation or fasting **22.78** Symptoms include excessive thirst, frequent urination, high concentrations of glucose in the urine and blood, and weight loss. **22.80** Metabolic syndrome resembles a prediabetic state and is a predictor for diabetes as blood sugar levels are slightly elevated, blood pressure is slightly high, and glucose tolerance is slightly impaired. **22.82** Muscle tissue needs a steady supply of glucose, and the compounds needed for glucose synthesis by gluconeogenesis are present in the liver. **22.84** In the absence of oxygen, pyruvate from catabolism of glucose in wine was fermented by yeast enzymes to ethanol and CO_2, which increased the pressure in the bottle and popped the cork.

Chapter 23

23.1 **(a)** eicosanoid **(b)** glycerophospholipid **(c)** wax

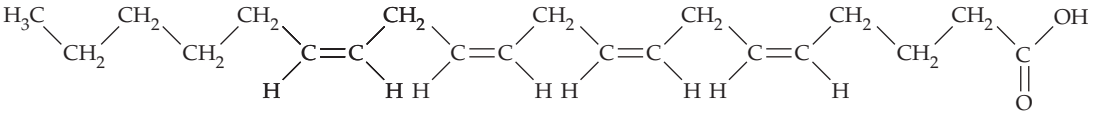
23.2

23.3

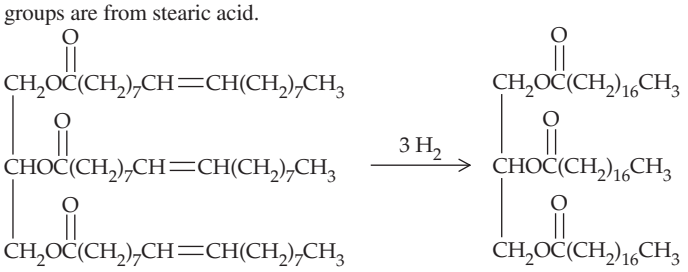


23.4 **(a)** butter **(b)** soybean oil **(c)** soybean oil

23.5

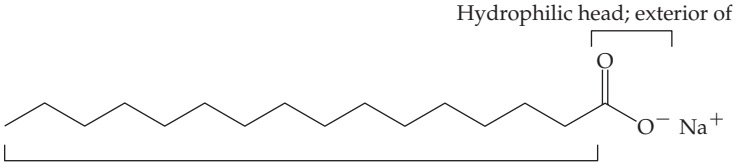


23.6 When two different fatty acids are bonded to C1 and C3 of glycerol, C2 is chiral. **23.7** London forces; weak; Hydrogen bonds between water molecules are stronger than London forces. **23.8** The resulting acyl groups are from stearic acid.

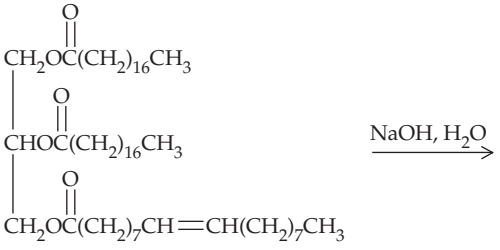


23.9 in butter: cholesterol; in margarine: *trans* fatty acids

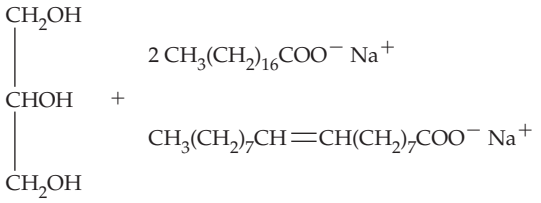
23.10



23.11

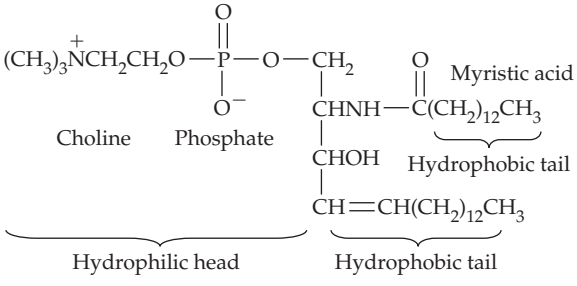


or the isomer

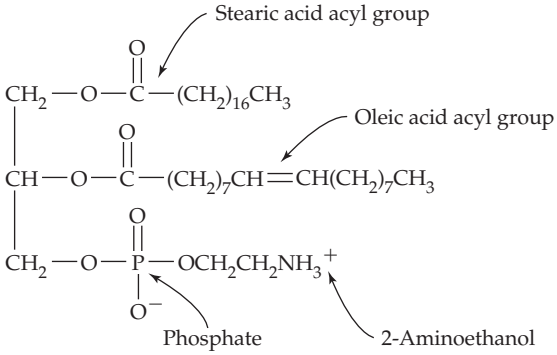


23.12 Lecithins emulsify fats in the same way as soaps dissolve grease: The fats are coated by the nonpolar part of a lecithin, and the polar part of lecithins allows fats to be suspended in aqueous solution. **23.13 (a)** glycerol, phosphate ion, choline, $RCOO^-Na^+$, $R'COO^-Na^+$ **(b)** sphingosine, phosphate ion, choline, sodium palmitate

23.14



23.15

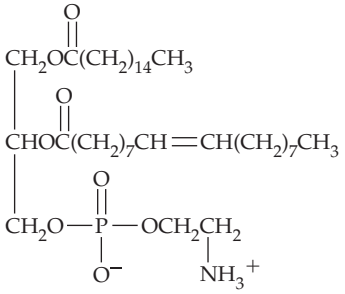


23.16 (a), (c), (e), (f)

23.17 They must be hydrophobic, contain many amino acids with nonpolar side chains, and must be folded so that the hydrophilic regions face outward. **23.18** yes **23.19** Glucose 6-phosphate has a charged phosphate group and can't pass through the hydrophobic lipid bilayer. **23.20** The surfaces are in different environments and serve different functions. **23.21** A has the highest melting point. B and C are probably liquids at room temperature.

23.22 12.2% palmitic acid, 87.5% stearic acid; more like C

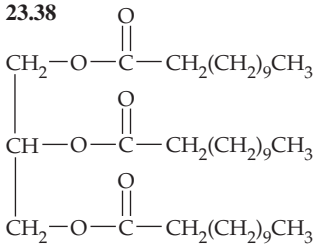
23.23



A glycerophospholipid

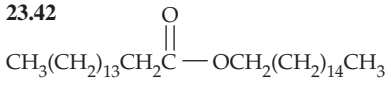
23.24 Because the membrane is fluid, it can flow together after an injury. **23.25** C_{16} saturated fatty acids. The polar head lies in lung tissue, and the hydrocarbon tails protrude into the alveoli. **23.26** A lipid is a naturally occurring molecule that dissolves in nonpolar solvents. **23.28** $CH_3(CH_2)_{16}COOH$: straight chain **23.30** *Saturated fatty acids* are long-chain carboxylic acids that contain no carbon–carbon double bonds. *Monounsaturated fatty acids* contain one carbon–carbon double bond. *Polyunsaturated fatty acids* contain two or more carbon–carbon double bonds. **23.32** An essential fatty acid can't be synthesized by the human body and must be part of the diet. **23.34 (a)** The double bonds in an unsaturated fatty acid (linolenic acid) make it harder for them to be arranged in a crystal. **23.36** fats: saturated and unsaturated fatty acids, solids; oils: mostly unsaturated fatty acids, liquids.

23.38



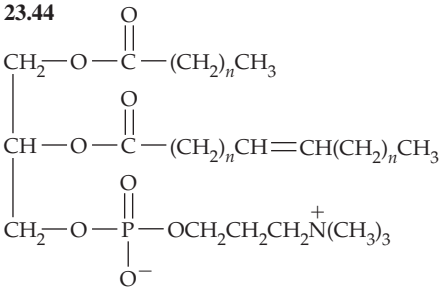
23.40 a protective coating

23.42



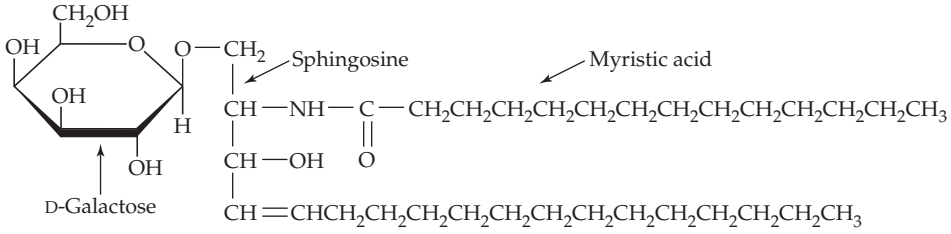
Cetyl palmitate

23.44



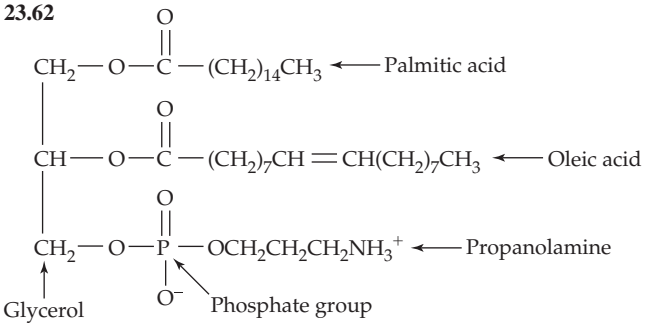
23.46 hydrogenation **23.48** saponification **23.50** The product is shown in Problem 23.8. It has a higher melting point. **23.52** Margarine contains more mono- and polyunsaturated fats but is also more likely to contain *trans* fats. **23.54** Glycerophospholipids have polar heads (point outward) and nonpolar tails that cluster to form the membrane. Triacylglycerols don't have polar heads. **23.56** A sphingomyelin and a cerebroside are similar in that both have a sphingosine backbone. The difference between the two occurs at C1 of sphingosine. A sphingomyelin has a phosphate group bonded to an amino alcohol at C1; a cerebroside has a glycosidic link to a monosaccharide at C1. **23.58** Glycerophospholipids have an ionic phosphate group that is solvated by water.

23.60



A cerebroside

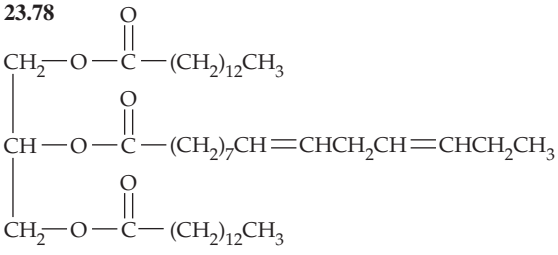
23.62



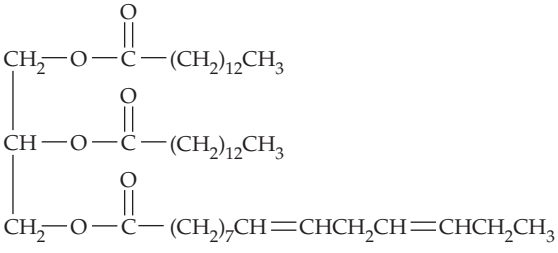
A glycerophospholipid

23.64 Cholesterol is a component of cell membranes and is the starting material for the synthesis of all other steroids. **23.66** *male sex hormones*: androsterone, testosterone *female sex hormones*: estrone, estradiol, progesterone **23.68** In a soap micelle, the polar hydrophilic heads are on the exterior, and the hydrophobic tails cluster in the center. In a membrane bilayer, hydrophilic heads are on both the exterior and interior surfaces of the membrane, and the region between the two surfaces is occupied by hydrophobic tails. **23.70** glycolipids, cholesterol, proteins **23.72** Active transport requires energy because it is a process in which substances are transported across a membrane in a direction opposite to their tendency to diffuse. **23.74** **(a)** simple diffusion **(b)** facilitated diffusion **(c)** active transport **23.76** **(b), (c), (e), (f)**

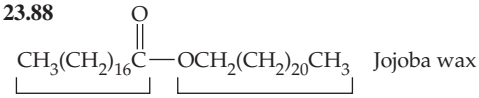
23.78



or



23.80 **(a)** beef fat **(b)** plant oil **(c)** pork fat **23.82** It is saponifiable.
23.84 coatings for nerve fibers and are present in brain tissue
23.86 0.40 g NaOH
23.88



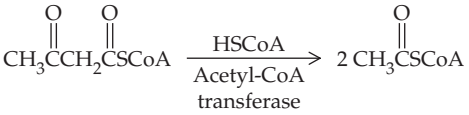
Jojoba wax is the ester formed by a C_{22} alcohol and a C_{18} carboxylic acid. Spermaceti is the ester formed by a C_{18} alcohol and a C_{16} carboxylic acid. It might be possible to substitute jojoba wax as long as the greater mass and higher melting point do not alter the cosmetic product.

Chapter 24

24.1 Cholate has four polar groups on its hydrophilic side that allow it to interact with an aqueous environment; its hydrophobic side interacts with triacylglycerides. Cholate and cholesterol can't change roles.
24.2 Dihydroxyacetone phosphate is isomerized to glyceraldehyde 3-phosphate, which enters glycolysis. **24.3** Free fatty acids travel with albumins (blood-plasma proteins). **24.4** **(a), (b)** step 1; a C═C double bond is introduced; FAD is the oxidizing agent. step 3; an alcohol is oxidized to a ketone; NAD^+ is the oxidizing agent. **(c)** step 2; water is added to a carbon–carbon double bond. **(d)** step 4; HSCoA displaces acetyl-CoA, producing a chain-shortened acyl-SCoA fatty acid. **24.5** **(a)** 8 acetyl-CoA, 7 β oxidations **(b)** 12 acetyl-CoA, 11 β oxidations **24.6** step 6, step 7, step 8
24.7 146 ATP molecules **24.8** **(d)** **24.9** **(a)** Acetyl-CoA provides the acetyl groups used in synthesis of ketone bodies **(b)** three **(c)** The body uses ketone bodies as an energy source during starvation. **24.10** seven additional acetyl-CoA; eight additional CO_2 **24.11** Oxygen is needed to reoxidize reduced coenzymes, formed in β oxidation, that enter the electron transport chain. **24.12** **(a)** chylomicrons; because they have the greatest ratio of lipid to protein **(b)** chylomicrons **(c)** HDL **(d)** LDL **(e)** HDL **(f)** VLDL; used for storage or energy production **(g)** LDL **24.13** high blood glucose → high insulin/low glucagon → fatty acid and triacylglycerol synthesis: low blood glucose → low insulin/high glucagon → triacylglycerol hydrolysis; fatty acid oxidation **24.14** Formation of a fatty acyl-CoA is coupled with conversion of ATP to AMP and pyrophosphate. This energy expenditure is recaptured in β oxidation. **24.15** Less acetyl-CoA can be catabolized in the citric acid cycle, and acetyl-CoA is diverted to ketogenesis. **24.16** Catabolism of fat provides more energy per gram than does catabolism of glycogen, and thus fats are a more efficient way to store energy. **24.17** Ketone bodies can be metabolized to form acetyl-CoA, which provides energy. **24.18** No. Although both these processes add or remove two carbon units, one is not the reverse of the other. The two processes involve different enzymes, coenzymes, and activation steps.
24.20 small intestine **24.22** liver from cholesterol **24.24** pancreatic lipase: mono- and diacylglycerols, fatty acids, and glycerol; lipoprotein lipase: fatty acids and glycerol **24.26** liver

24.28 transported by LDLs to peripheral tissue, where it is used in cell membranes and to synthesize sterols **24.30** six ATP molecules **24.32** 190 acetyl-CoA molecules **24.34** storage and mobilization of triacylglycerols; located under the skin and in the abdominal cavity **24.36** mitochondrial matrix **24.38** The activated fatty acid must be transported from the cytosol into the mitochondrial matrix. **24.40** The sequence is a spiral because the same reaction series is repeated on a two-carbon-shortened fatty acid until the original acid is consumed. In a cycle, the product of the final step is a reactant in the first step. **24.42** no; the coenzyme NADPH replaces NAD^+ and FAD. **24.44** 112 moles ATP per mole of myristic acid **24.46** fructose, mannose, palmitic acid, stearic acid

24.48

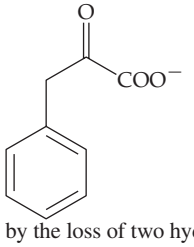


24.50 caprylic acid: three cycles; myristic acid: six cycles **24.52** Ketosis is a condition in which ketone bodies accumulate in the blood faster than they can be metabolized. Since two of the ketone bodies are carboxylic acids, they lower the pH of the blood, producing the condition known as ketoacidosis. Symptoms of ketoacidosis include dehydration, labored breathing, and depression; prolonged ketoacidosis may lead to coma and death. **24.54** Ketones have little effect on pH, but the two other ketone bodies are acidic, and they lower the pH of urine. **24.56** lipogenesis **24.58** acetyl-CoA **24.60** eight rounds **24.62** Fatty acid synthesis takes place in the cytosol; fatty acid degradation takes place in mitochondria. **24.64** The excess acetyl-CoA from catabolism of carbohydrates is stored as fat. The body can't resynthesize carbohydrate from acetyl-CoA. **24.66** The alcohol intermediate is chiral. **24.68** **(a)** endogenous **(b)** exogenous **24.70** The body synthesizes cholesterol when no cholesterol is present in the diet. The body needs cholesterol for membrane function and for synthesis of steroid hormones. **24.72** The excess carbohydrates pass through glycolysis and ends up as acetyl-CoA. Since the body doesn't need extra energy, acetyl-CoA enters lipogenesis to form fatty acids, which are stored as triacylglycerols in adipocytes, leading to weight gain.

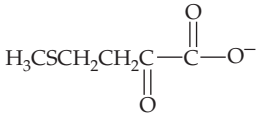
Chapter 25

25.1 **(a)** false **(b)** true **(c)** true **25.2** oxidoreductase; lyase

25.3



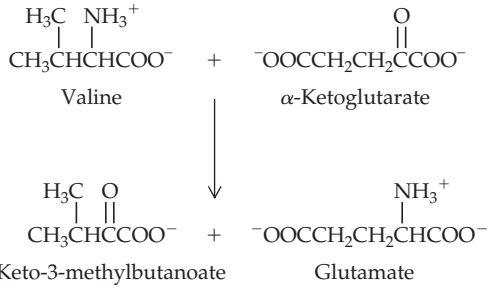
25.4



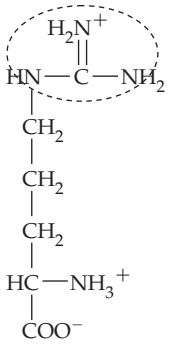
4-Hydroxy-α-ketopentanoate

25.5 by the loss of two hydrogens to either NAD^+ or $NADP^+$

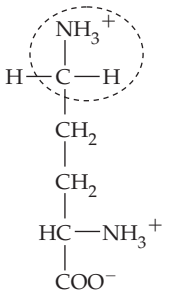
25.6 valine, leucine, isoleucine



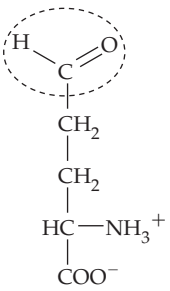
25.7 **(a)**



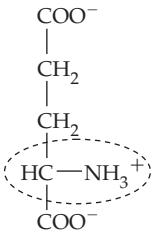
(b)



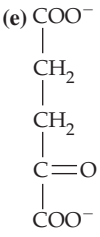
(c)



(d)

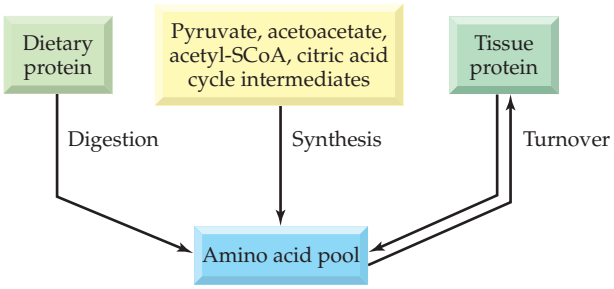


(e)



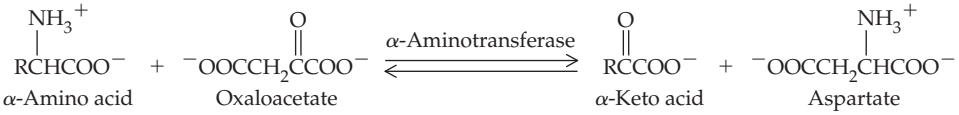
25.8 **(a)** 5 **(b)** 1 **(c)** 3 **25.9** glucogenic: Histidine, Threonine, Methionine, Valine; ketogenic: Leucine; both: Isoleucine, Lysine, Phenylalanine, Tryptophan **25.10** 3-phosphoglycerate → 3-phosphohydroxypyruvate (oxidation); 3-phosphohydroxypyruvate → 3-phosphoserine (transamination); 3-phosphoserine → serine (hydrolysis)

25.11

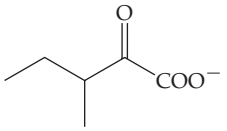


25.12 (1) Catabolism of an amino acid begins with a transamination reaction that removes the amino nitrogen. (2) The resulting α-keto acid, which contains the carbon atoms, is converted to a common metabolic intermediate. (3) The amino group of glutamate (from the amino acid) is removed by oxidative deamination. (4) The amino nitrogen is transformed to urea in the urea cycle and is excreted. **25.13** glutamate dehydrogenase; alanine aminotransferase. Alanine is the product. **25.14** The carbon atoms from ketogenic amino acids can be converted to ketone bodies or to acetyl-SCoA. The carbon atoms from glucogenic amino acids can be converted to compounds that can enter gluconeogenesis and can form glucose, which can enter glycolysis and also yield acetyl-CoA. **25.15** All amino acids are necessary for protein synthesis. The body can synthesize only some of them; the others must be provided by food and are thus essential in the diet. **25.16** to quickly remove ammonia from the body; buildup of urea and shortage of ornithine **25.18** digestion begins in the stomach **25.20** oxaloacetate and α-ketoglutarate

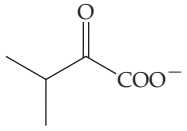
25.22



25.24 (a)



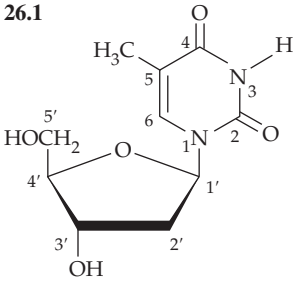
(b)



25.26 NAD^+ or $NADP^+$ **25.28** ammonium ion **25.30** Catabolized to pyruvate or citric acid cycle intermediates and is able to enter gluconeogenesis. Examples: alanine, glycine, serine. **25.32** carbamoyl phosphate **25.34** Enters the urea cycle at step 2 and leaves in step 3 as fumarate, which can enter the citric acid cycle. **25.36** glutamate **25.38** Biosynthesized by hydroxylation of phenylalanine; phenylketonuria **25.40** Aspartame is a dipeptide that contains phenylalanine, which must be severely restricted in phenylketonurics **25.42** Three molecules of ATP **25.44 (a)** succinyl-SCoA, fumarate, oxaloacetate, pyruvate **(b)** fumarate **25.46** liver; transported to the kidneys, where it is excreted in urine **25.48** storage: fats and carbohydrates are stored in the body while amino acids are not; energy: surplus amino acids must be converted to fats or carbohydrates to be an energy source; fats and carbohydrates that are not stored are catabolized. **25.50** The activated forms of the proteases would hydrolyze the proteins in the lines of the pancreas; in the inactive form, they can be safely stored. **25.52** One of the ATPs in the urea cycle is hydrolyzed to AMP, which is the equivalent of spending two ATPs. **25.54** Answer depends on what foods were consumed. Refer to Figure 25.2. Essential amino acids: histidine, lysine, threonine, isoleucine, methionine, tryptophan, leucine, phenylalanine, valine. Complete protein sources: meat and dairy product; Incomplete protein sources: grains, nuts, seeds, legumes, corn **25.56** leucine: 12 ATPs; histidine: 9 ATPs; valine: 3 ATPs; lysine: 12 ATPs; total ATPs: 36 ATPs

Chapter 26

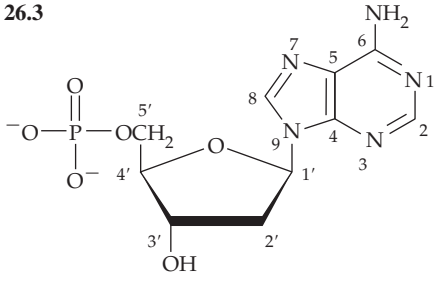
26.1



2′-Deoxythymidine

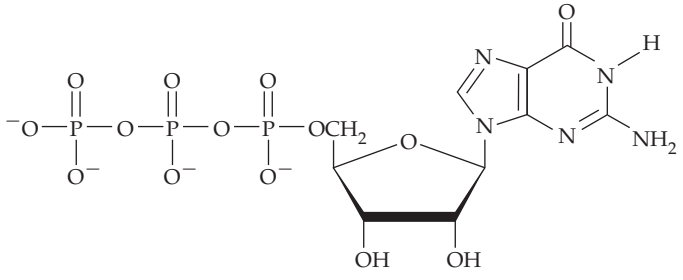
26.2 D-Ribose ($C_5H_{10}O_5$) has one more oxygen atom than 2-deoxy-D-ribose ($C_5H_{10}O_4$), and thus can form more hydrogen bonds.

26.3



2′-Deoxyadenosine 5′-monophosphate

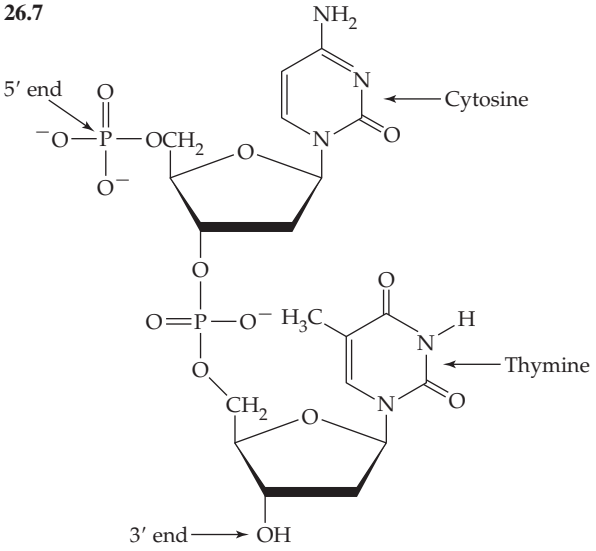
26.4



Guanosine 5′-triphosphate (GTP)

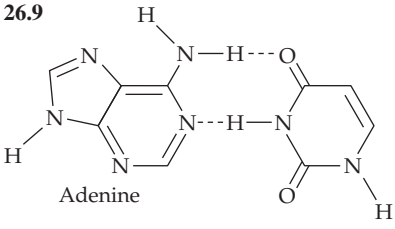
26.5 dUMP—2′-deoxyuridine 5′-monophosphate; UMP—uridine 5′-monophosphate; CDP—cytidine 5′-diphosphate; AMP—adenosine 5′-monophosphate; ATP—adenosine 5′-triphosphate **26.6** guanine–adenine–uracil–cytosine–adenine. The pentanucleotide comes from RNA because uracil is present.

26.7



26.8 (a) 3′ A-T-A-T-G-A-C 5′ **(b)** 3′ C-T-A-G-C-G-A-G-A 5′

26.9



Adenine Uracil

26.10 negatively charged (because of the phosphate groups)

26.11 (a) A longer strand has more hydrogen bonds. **(b)** A chain with a higher percent of G/C pairs has a higher melting point, because it has more hydrogen bonds. **26.12** Okazaki fragments are segments of DNA synthesized by using the lagging strand as a template. The fragments are later joined by a DNA ligase enzyme. **26.13** DNA polymerase facilitates transcription of the single-stranded DNA while DNA ligase joins short DNA strands (Okazaki fragments) together in the lagging strand. **26.14** In spliceosomes, introns are removed and the exons are spliced together to yield mRNA. **26.15 (a)** 3′ G-U-A-C-G-A-G-A-U-G-U-C 5′ **(b)** 5′ A-U-A-A-U-C-G-C-U-G-G-C 3′

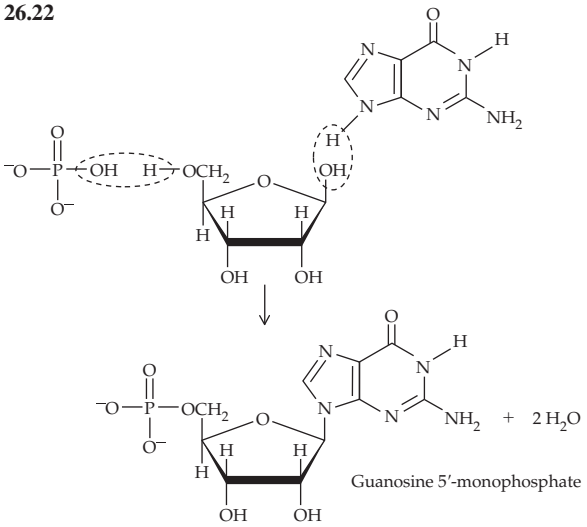
26.16 (a) GUU GUC GUA GUG **(b)** UUU UUC **(c)** AAU AAC **(d)** GGU GGC GGA GGG **(e)** AUG **26.17** The sequence GAG codes for glutamic acid as does the sequence GAA. **26.18 (a)** Ile **(b)** Ala **(c)** Arg **(d)** Lys **26.19** Six mRNA triplets can code for Leu: UUA, UUG, CUU, CUC, CUA, CUG if no codons are duplicated. Among the possible combinations:

5′ UUAUUGCUU 3′ 5′ UUAUUGCUC 3′ 5′ UUAUUGCUA 3′
5′ UUAUUGCUG 3′ 5′ UUACUUCUC 3′ 5′ UUACUUCUA 3′

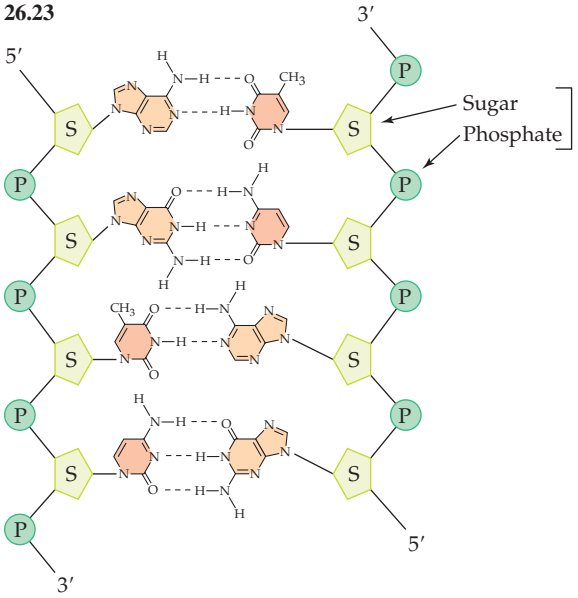
26.20–26.21

mRNA
sequence: 5′ CUC—AUU—CCA—UGC—GAC—GUA 3′
amino acid
sequence: Leu—Ile—Pro—Cys—Asp—Val
tRNA
anticodons: 3′ GAG UAA GGU ACG CUG CAU 5′

26.22

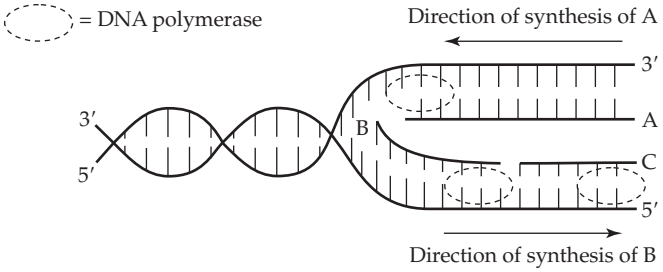


26.23



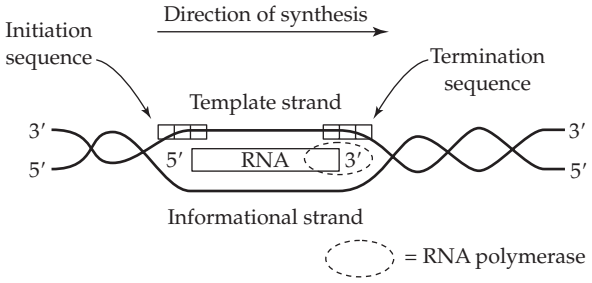
sequence of the left chain: 5′ A-G-T-C 3′
sequence of the right chain: 5′ G-A-C-T 3′

26.24



26.25 The sugar-phosphate backbone is found on the outside of the DNA double helix. Histones are positively charged; they contain groups such as Lys, Arg, and His.

26.26



26.27 More than one codon can code for each amino acid. Only one possibility is shown.

(a) 5′ | C | A | A | C | A | C | C | C | C | G | G | G | 3′ mRNA

(b) 3′ | G | T | T | G | T | G | G | G | G | C | C | C | 5′ DNA template strand

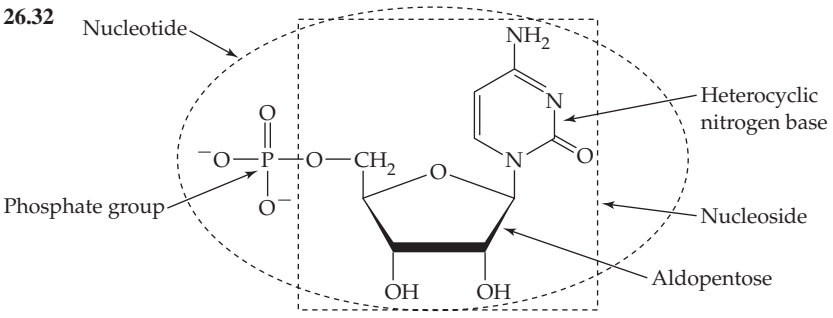
(c) 5′ | C | A | A | C | A | C | C | C | C | G | G | G | 3′ DNA informational strand

(d) 65 possible sequences

26.28 A chromosome is an enormous molecule of DNA. A gene is a part of the chromosome that codes for a single protein needed by a cell.

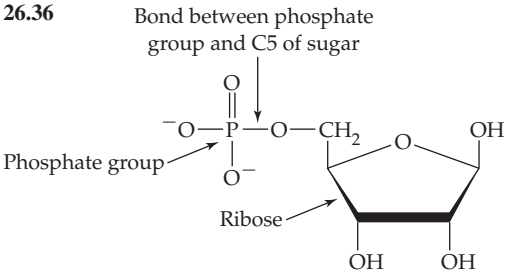
26.30 A gene carries the DNA code needed to synthesize a specific polypeptide.

26.32



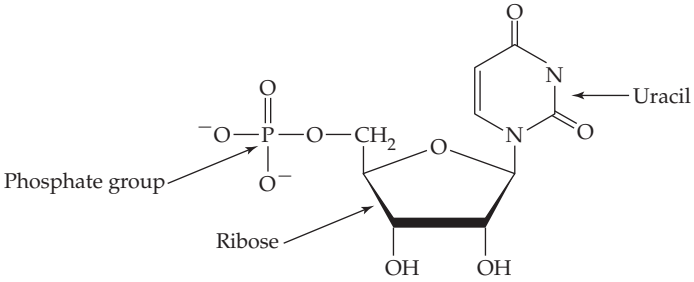
26.34 **(a)** adenine, cytosine, guanine, and thymine **(b)** adenine, cytosine, guanine, and uracil **(c)** Adenine, cytosine, and guanine are common to DNA and RNA. Thymine differs from uracil in having a methyl at position 5 of the pyrimidine ring.

26.36



A phosphate ester bond is formed between the phosphate group and the sugar.

26.38 The 5′ end of a nucleotide is a phosphate group bonded to carbon 5 of ribose. The 3′ end is an —OH group bonded to carbon 3 of ribose.
26.40 Uridine 5′-monophosphate



26.42 **(a)** Base pairing is the hydrogen-bonded pairing of two complementary heterocyclic bases in the double helix of DNA and during replication, transcription, and translation. **(b)** Adenine pairs with thymine (or uracil in RNA) and guanine pairs with cytosine. **(c)** Adenine and thymine (or uracil) form two hydrogen bonds. Cytosine and guanine form three hydrogen bonds.
26.44 They always occur in pairs: They always H bond with each other.
26.46 22% G, 22% C, 28% A, 28% T
(%G = %C; %A = %T: %T + %A + %C + %G = 100%)
26.48 to increase the speed of replication of DNA **26.50** *Messenger RNA (mRNA)* carries the genetic message from DNA to ribosomes. *Ribosomal RNA (rRNA)* complexes with protein to form ribosomes, where protein synthesis takes place. *Transfer RNA (tRNA)* transports specific amino acids to the ribosomes, where they are incorporated into proteins. **26.52** Exons are sequences of DNA that code for part of a specific protein. Introns are sequences of DNA that are found between exons and whose function is unclear; they are spliced from mRNA before protein synthesis. **26.54** template strand **26.56** An anticodon is a sequence of three nucleotides that is complementary to a sequence on a codon; tRNA
26.58

Amino Acid	Codons (5′ → 3′)					
(a) Val	GUU	GUC	GUA	GUG		
(b) Arg	CGU	CGC	CGA	CGG	AGA	AGG
(c) Ser	UCU	UCC	UCA	UCG	AGU	AGC

26.60 **(a)** 3′-GGG-5′ **(b)** 3′-CGC-5′ **(c)** 3′-AAU-5′ **26.62** template strand: 3′-ATG-GGA-5′ **26.64** Tyr-Pro
26.66
Metenkephalin: mRNA (5′ → 3′) Tyr—Gly—Gly—Phe—Met Stop
UAU–GGU–GGU–UUU–AUG–UAA
UAC GGC GGC UUC UAG
GGG GGG UGA
GGA GGA
26.68 A tRNA molecule is cloverleaf shaped. The tRNA anticodon triplet is on one "leaf," and an amino acid bonds covalently to the 3′ end.
26.70 The two mRNA codons for Glu are GAA and GAG. Of the four codons for Val (GUU, GUC, CUA, and GUG), the last two differ from the Glu codons by one base. Thus, a change in one base can result in a change from Glu to Val.
26.72
Position 9: Horse amino acid = Gly Human amino acid = Ser
mRNA codons (5′ → 3′):
GGU GGC GGA GGG UCU UCC UCA UCG AGU AGC
DNA bases (template strand 3′ → 5′):
CCA CCG CCT CCC AGA AGG AGT AGC TCA TCG
The underlined horse DNA base triplets differ from their human counterparts (also underlined) by only one base.

Position 30: Horse amino acid = Ala Human amino acid = Thr
mRNA codons (5′ → 3′):
GCU GCC GCA GCG ACU ACC ACA ACG
DNA bases (template strand 3′ → 5′):
CGA CGG CGT CGC TGA TGG TGT TGC
Each group of three DNA bases from horse insulin has a counterpart in human insulin that differs from it by only one base. It is possible that horse insulin DNA differs from human insulin DNA by only two bases out of 159!
26.74 dCTP **26.76** Avian flu viruses may be transmitted to humans from domesticated birds, which have been infected by migratory waterfowl. The virus can also be transmitted from an intermediate host, such as swine.
26.78 Influenza A viruses are described by a code that describes the hemagglutinins (H) and the neuraminidases (N) in the virus. The H1N1 virus was responsible for the 1918 influenza pandemic, and the H5N1 virus is present in avian flu. Since these viruses can undergo antigenic shift in host animals, there is concern when infected birds and animals harbor influenza viruses.

Chapter 27

27.1 "the fat red rat ate the bad rat" **27.2** As a result of the SNP, the base sequence codes for Trp, instead of Cys. This change would probably affect the functioning of the protein. **27.3** 3′-T-C-T-A-G-//-A- 5′
27.4 3′-C-T-T-A-A-//-G- 5′ **27.5** **(a)** sticky **(b)**, **(c)** not sticky
27.6 **(a)** comparative genomics **(b)** genetic engineering **(c)** pharmacogenetics **(d)** bioinformatics **27.7** (1) A genetic map, which shows the location of markers one million nucleotides apart, is created. (2) Next, comes a physical map, which refines the distance between markers to 100,000 base pairs. (3) The chromosome is cleaved into large segments of overlapping clones. (4) The clones are fragmented into 500 base pieces, which are sequenced. **27.8** The variations are only a small part of the genome; the rest is identical among humans. A diverse group of individuals contributed DNA to the project. **27.9** *telomeres* (protect the chromosome from damage, involved with aging), *centromeres* (involved with cell division), *promoter sequences* (determine which genes will be replicated), *introns* (function unknown) **27.10** Differences: A mutation is an error that is transferred during replication and affects only a few people; a polymorphism is a variation in sequence that is common within a population.
27.11 Recombinant DNA contains two or more DNA segments that do not occur together in nature. The DNA that codes for a specific human protein can be incorporated into a bacterial plasmid using recombinant DNA technology. The plasmid is then reinserted into a bacterial cell, where its protein-synthesizing machinery makes the desired protein. **27.12** Major benefits of genomics: creation of disease-resistant and nutrient-rich crops, gene therapy, and genetic screening. Major negative outcomes: misuse of an individual's genetic information and prediction of a genetic disease for which there is no cure. **27.14** Celera broke the genome into many unidentified fragments. The fragments were multiplied and cut into 500 base pieces, which were sequenced. A supercomputer was used to determine the order of the bases. This approach allowed for faster sequencing of the human genome. **27.16** 50% **27.18** **(a)** Approximately 200 genes are shared between bacteria and humans. **(b)** A single gene may produce several proteins. **27.20** The clones used in DNA mapping are identical copies of DNA segments from a single individual. In mapping, it is essential to have a sample large enough for experimental manipulation.
27.22 The youngest cells have long telomeres, and the oldest cells have short telomeres. **27.24** It is the constriction that determines the shape of a chromosome during cell division. **27.26** Error in the mRNA sequence affects only one molecule of RNA; an error in the DNA sequence can be copied into all subsequent DNA molecules during replication.
27.28 A single-nucleotide polymorphism (SNP) is the replacement of one nucleotide by another at the same location in a DNA strand. **27.30** Changes in hair and eye color, sickle-cell anemia, epilepsy, total color blindness, Alzheimer's disease, breast cancer, resistance to diseases like AIDS. **27.32** Not always as some amino acids are coded by several different base sequences.
27.34

	Normal Codon	*Codes For*	*Mutated Codon*	*Codes For*
(a)	UCA	Ser	UCG	SER
(b)	UAA	Stop	UAU	Tyr

In (a), the mutated mRNA codes for the same amino acid as the nonmutated mRNA, and thus the mutation has no effect. In (b), the mutated mRNA replaces a "stop" codon with a Tyr codon; instead of stopping protein synthesis, mRNA continues adding amino acids to the polypeptide chain. Mutation (b) is much more serious that mutation (a).

27.36 DNA of bacterial cells occurs in plasmids, which carry only a few genes. Plasmids are easy to isolate, several copies of each plasmid are within a bacterial cell, and the DNA of plasmids replicates rapidly. **27.38** electrophoresis **27.40 (a)** CCATG **(b)** TGGGT **(c)** CACAG **27.42** Pharmacogenomics is the study of the genetic basis of responses to drug treatment. Pharmacogenomics helps doctors prescribe the most effective medicine for a patient, based on the patient's genetic makeup. **27.44** corn, soybeans **27.46** Bioethics studies ethical issues such as ownership and access to genetic information, implications of genetic testing, prevention of genetic disability, and use of gene therapy. **27.48** A vector is the agent used to carry therapeutic quantities of DNA directly into cell nuclei. **27.50** The mutation would substitute Thr (hydrophilic side chain) for Ile (hydrophobic side chain), which will affect the tertiary structure of the protein. **27.52** germ cell (sperm or egg) **27.54** Some of the current developments in gene therapy; there is additional research in each of these diseases that is not provided here.

*Parkinso*n's disease: Gene therapy reprograms the brain cells to produce dopamine, which helps control motor function.

Huntington's disease: Switch the gene mutation that causes Huntington's disease off in individual brain regions in mice; gene variant that influences when Huntington's disease breaks out early or later on has also been identified.

Prostate cancer: Stimulate the body's own immune system to attack the tumor, possibly preventing surgery for prostate cancer; product of a gene known as *EZH2* could determine how aggressive the cancer is.

Pancreatic cancer: Identification of genes that can increase a person's risk of developing pancreatic cancer; developing tests for detecting gene changes that are not due to inherited genes in pancreatic cancer precancerous conditions.

Muscular dystrophy: Identification of a gene sequence that is essential for helping muscle tissues function; creation of an experimental drug in children designed to cover the gene mutation so that the mutation is skipped resulting in a functional protein

Chapter 28

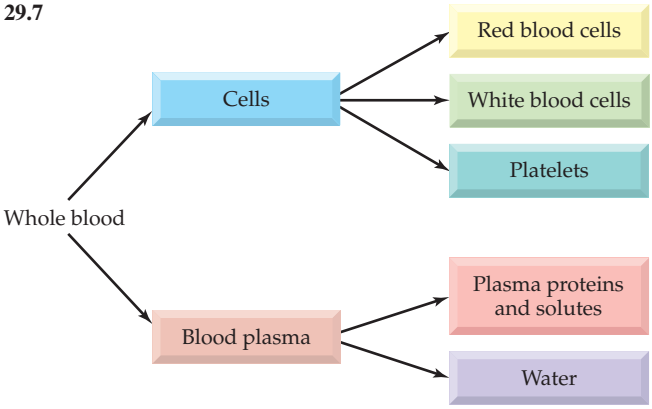
28.1 Hydrogen bonding, hydrophobic interactions, and ionic attractions or salt bridges **28.2** Amino acid derivative **28.3** Tyrosine **28.4** His **28.5 (b)** **28.6** The molecules resemble the heterocyclic part of cAMP, and they might act as inhibitors to the enzyme that inactivates cAMP. **28.7** Glu-His-Pro **28.8** Hydrophobic because the hydrophobic part of the structure is larger than the polar, hydrophilic part. **28.9** Testosterone has a $-CH_3$ group between the first two rings; nandrolone doesn't. Otherwise, their structures are identical. **28.10 (a)** 3 **(b)** 1 **(c)** 2 **28.11** Similarities: Both structures have aromatic rings, secondary amine groups, and alcohol groups. Differences: Propranolol has an ether group and a naphthalene ring system; epinephrine has two phenol hydroxyl groups; the compounds have different side-chain carbon skeletons. **28.12 (a)** Malathion: it's the least toxic. **(b)** Parathion is most toxic (smallest LD_{50}). **28.13 (a)** prolongs the effect of serotonin **(b)** blocks the response at the receptor **28.14** phenol hydroxyl group, ether, carbon–carbon double bond, aromatic ring. Tetrahydrocannabinol (THC) is hydrophobic and is likely to accumulate in fatty tissue. **28.15 (a)** antihistamine **(b)** antidepressant **28.16 (a)** polypeptide hormone (produced in the anterior pituitary gland) **(b)** steroid hormone (produced in ovaries) **(c)** Progesterone-producing cells have LH receptors. **(d)** Progesterone is lipid-soluble and can enter cells. **28.17** Adenylate cyclase can produce a great many molecules of cAMP, which phosphorylate kinase enzymes. These enzymes can cause the breakdown of gycogen to yield glucose. **28.18 (a)** insulin (polypeptide hormone) **(b)** pancreas **(c)** in the bloodstream **(d)** Insulin doesn't enter cells directly because it can't pass through cell membranes. Instead, it binds with a cell surface receptor. **28.19** binding to receptors; activating second messengers **28.20** Enzymatic inactivation; reuptake by presynaptic neuron. **28.21** These substances increase dopamine levels in the brain. The brain responds by decreasing the number and sensitivity of dopamine receptors. Thus, more of the substance is needed to elevate dopamine levels, leading to addiction. **28.22** *A chemical messenger* is a molecule that travels from one part of the body to another location, where it delivers a signal or acts to control metabolism. The *target tissue* is the cell or group of cells whose activity is regulated by the messenger. A hormone receptor is the molecule with which the chemical messenger interacts if it is a hormone. **28.24** A vitamin is usually an enzyme cofactor, whereas a hormone regulates enzyme activity. **28.26** Neither a hormone nor its receptor is changed as a result of binding to each other. The binding forces between hormone and receptor are noncovalent. **28.28** The endocrine system manufactures and secretes hormones. **28.30** polypeptide hormones, steroid hormones, amino acid derivatives **28.32** Enzymes are proteins; hormones may be polypeptides, proteins, steroids, or amino acid derivatives. **28.34** Polypeptide hormones travel through the bloodstream and bind to cell receptors, which are on the outside of a cell. The receptors cause production within cells of "second messengers" that activate enzymes. **28.36** the adrenal medulla **28.38** through the bloodstream **28.40** In order of involvement; the hormone receptor, G protein, and adenylate cyclase. **28.42** It initiates reactions that release glucose from storage. Termination occurs when phosphodiesterase converts cAMP to AMP. **28.44** anaphylaxis **28.46** Insulin contains 51 amino acids, is released from the pancreas, and acts at cells, causing them to take up glucose. **28.48** Mineralocorticoids (aldosterone), glucocorticoids (cortisone), and sex hormones (testosterone, estrone) all have the four-fused-ring skeleton. **28.50** androsterone, testosterone **28.52** Androgens increase muscle mass and strength. **28.54** epinephrine, norepinephrine, dopamine **28.56 (a)** amino acid derivative **(b)** polypeptide hormone **(c)** steroid hormone **28.58** A synapse is the gap between two nerve cells that neurotransmitters cross to transmit their message. **28.60** nerve cell, muscle cell, endocrine cell **28.62** A nerve impulse arrives at the presynaptic end of a neuron. The nerve impulse stimulates the movement of a vesicle, containing neurotransmitter molecules, to the cell membrane. The vesicle fuses with the cell membrane and releases the neurotransmitter, which crosses the synaptic cleft to a receptor site on the postsynaptic end of a second neuron. After reception, the cell transmits an electrical signal down its axon and passes on the impulse. Enzymes then deactivate the neurotransmitter so that the neuron can receive the next impulse. Alternatively, the neurotransmitter may be returned to the presynaptic neuron. **28.64** (1) Neurotransmitter molecules are released from a presynaptic neuron. (2) Neurotransmitter molecules bind to receptors on the target cell. (3) The neurotransmitter is deactivated. **28.66** They are secreted in the central nervous system and have receptors in brain tissue. **28.68** Agonists prolong the response of a receptor. Antagonists block the response of a receptor. **28.70** agonists—nicotine; antagonists—atropine **28.72** *Tricyclic antidepressant:* Elavil *MAO inhibitor:* Nardil *SSRI:* Prozac **28.74** Cocaine increases dopamine levels by blocking reuptake. **28.76** THC increases dopamine levels in the same brain areas where dopamine levels increase after administration of heroin and cocaine. **28.78** antagonist **28.80** Endorphins are polypeptides with morphine-like activity. They are produced by the pituitary gland and have receptors in the brain. **28.82** If an animal produced its own pain-suppressing molecule, it would have an advantage in escaping from prey while injured. **28.84** Curare acts as an antagonist to acetylcholine at receptors. **28.86** The *hormone receptor* recognizes the hormone and sets into motion the series of reactions that result in the response of the cell to hormonal stimulation. The hormone–receptor complex interacts with the *G protein* and causes it to bind GTP. The G protein mediates the reaction between the receptor and adenylate cyclase. The G protein–GTP complex activates adenylate cyclase, which catalyzes the formation of the second messenger, cyclic AMP. Cyclic AMP initiates the reactions that the hormone is designed to stimulate. **28.88** Signal amplification is the process in which a small signal induces a response much larger in magnitude than the original signal. For hormones, this amplification begins with the activation of the G-protein; one hormone–receptor complex can activate many G-protein–GTP complexes. Each G-protein–GTP complex, in turn, can activate many molecules of adenylate cyclase, which can stimulate production of many molecules of cyclic AMP. The importance of signal amplification is that a small amount of hormone can cause a very large response. **28.90** Ethynyl estradiol and norethindrone differ only in the ring on the far left: The ring is a phenol in ethynyl estradiol and is an enone in norethindrone. Ethynyl estradiol and estradiol differ only in the five-membered ring: A $-C\equiv CH$ group is present in ethynyl estradiol and

absent in estradiol. Norethindrone is similar to progesterone in all but two respects: Progesterone has a methyl group between the first two rings and has an acetyl group in the five-membered ring, instead of the two groups of norethindrone. **28.92** Testosterone can be converted to androsterone by reduction of the ketone group and the double bond in the first ring and by oxidation of the hydroxyl group in the five-membered ring. These reactions are reductions and oxidations. **28.94** The craving for chocolate might be explained by the stimulation of dopamine receptors by anandamides, producing feelings of satisfaction similar to those produced by THC. The effect of chocolate consumption may be a milder version of marijuana's effects.

Chapter 29

29.1 in the cell: the charged form; outside the cell: the uncharged form The uncharged form enters the cell more readily. **29.2** **(a)** iii **(b)** ii **(c)** iv **(d)** v **(e)** i **29.3** **(a)** pH goes down; more acidic **(b)** $[O_2]$, $[CO_2]$, $[pH]$ **29.4** **(a)** respiratory acidosis **(b)** metabolic acidosis **(c)** metabolic alkalosis **29.5** **(a)** respiratory alkalosis **(b)** respiratory acidosis **(c)** metabolic acidosis **29.6** **(a)** intracellular fluid **(b)** extracellular fluid **(c)** blood plasma, interstitial fluid **(d)** K^+, Mg^{2+}, HPO_4^{2-} (e) Na^+, Cl^-

29.7



29.8 **(a)** O_2 **(b)** CO_2 **(c)** nutrients **(d)** waste products **(e)** hormones **(f)** white blood cells, platelets **29.9** swelling, redness, warmth, pain **29.10** Histamine is synthesized by the enzymatic decarboxylation of histidine. Histamine dilates capillaries, increasing blood flow that reddens and warms the skin. Blood-clotting factors and defensive proteins cause pain and swelling. **29.11** *cell-mediated immune response*: T cells; *antibody-mediated immune response*: under control of B cells, assisted by T cells **29.12** Excess hydrogen ions are excreted by reaction with NH_3 or HPO_4^{2-}. H^+ ions also combine with hydrogen carbonate, producing CO_2 that returns to the bloodstream. **29.14** characteristics: ion, a gas, a small molecule, or a molecule with many polar or ionic groups on its surface **29.16** The difference in blood pressure between arterial capillaries and interstitial fluid pushes solutes and water into interstitial fluid. The difference in blood pressure between interstitial fluid and venous capillaries draws solutes and water into venous capillaries. **29.18** Collects excess interstitial fluid, cellular debris, proteins, and lipid droplets and ultimately returns them to the bloodstream. **29.20** antidiuretic hormone **29.22** Blood plasma is the fluid portion of blood that contains water-soluble solutes. Blood serum is the fluid that remains after blood has completely clotted. **29.24** erythrocytes (red blood cells), platelets, and white blood cells. **29.26** Electrolytes produce ions in water and conducts electricity. They maintain water balance, blood pH, muscle function, and more. **29.28** K^+, Mg^{2+} **29.30** inflammation, cell-mediated immune response, antibody-mediated immune response **29.32** immunoglobulins **29.34** Killer T cells destroy the invader; helper T cells enhance defenses; memory T cells can produce new killer T cells if needed. **29.36** Memory cells "remember" an antigen and are capable of producing antibodies to it for a long time. **29.38** Vitamin K, Ca^{2+} **29.40** They are released as zymogens in order to avoid undesirable clotting in noninjured tissues. **29.42** +2 **29.44** If pO_2 is below 1.5×10^3 Pa, hemoglobin is unsaturated. If pO_2 is greater than 1.5×10^4 Pa, hemoglobin is completely saturated. Between these pressures, hemoglobin is partially saturated. **29.46** a dissolved gas, bound to hemoglobin, hydrogen carbonate ion

29.48

$$CO_2 + H_2O \underset{}{\overset{\text{Carbonic anhydrase}}{\rightleftharpoons}} HCO_3^- + H^+$$

29.50 *Respiratory acidosis* occurs when there is buildup of CO_2 in the blood. *Metabolic acidosis* is due to increased production of metabolic acids. **29.52** *Respiratory alkalosis* occurs when there is a loss of CO_2. *Metabolic alkalosis* occurs when there is elevated plasma hydrogen carbonate concentration.

29.54

$$H^+ + HCO_3^- \rightleftharpoons CO_2 + H_2O$$
$$H^+ + HPO_4^{2-} \rightleftharpoons H_2PO_4^-$$

29.56 A nursing mother's antibodies can be passed to her baby in breast milk. **29.58** Active transport is the movement of solutes from regions of low concentration to regions of high concentration, a process that requires energy. Osmosis is the movement of water through a semipermeable membrane from a dilute solution to a more concentrated solution, a process that requires no energy. **29.60** In the blood, CO_2 from metabolism reacts to form $HCO_3^- + H^+$. The H^+ is bound to hemoglobin, which releases O_2, and is carried to the lungs. There, the H^+ is released and O_2 is bound to hemoglobin. In the urine, CO_2 reacts to form $HCO_3^-$and H^+. The HCO_3^- returns to the bloodstream, and the H^+ is neutralized by reaction with HPO_4^{2-} or NH_3. Whenever excess HCO_3^- accumulates in blood or urine, it can react with H^+ to form $H_2O + CO_2$. **29.62** When blood CO_2 level drops, the following reaction occurs to restore CO_2 supply:

$$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O.$$

This reaction uses up H^+ ions and leads to alkalosis. Breathing into a paper bag recaptures the expired CO_2 and restores the blood CO_2 level. **29.64** easiest to cross blood–brain barrier: Coniine, Atropine, Codeine, Heroin; hardest to cross blood–brain barrier: Solanine, Reserpine, Morphine; chemical rationale: *Coniine* has a structure similar to nicotine, as it is almost completely nonpolar and relatively small. *Atrophine* has very few polar groups on its surface, making it relatively nonpolar and able to cross the blood–brain barrier. In comparison to some of the other molecules, it is relatively small. *Solanine* has a large nonpolar surface; however, it is larger than some of the other molecules. This could slow down its rate of movement. *Reserpine* also has a large nonpolar surface with a small number of polar groups. However, it is the largest of the molecules listed in Table 16.1, which should slow down its rate of movement. *Morphine*, *codeine*, and *heroin* have similar structures and size. Except *morphine* has two alcohol groups, making the surface more polar, while *codeine* has one alcohol and an ether, and *heroin* has two esters, making it the least polar on the surface. Therefore, of this group of drugs, *heroin* can most easily pass the blood–brain barrier.

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Glossary

1,4 Link A glycosidic link between the hemiacetal hydroxyl group at C1 of one sugar and the hydroxyl group at C4 of another sugar.

Acetal A compound that has two ether-like —OR groups bonded to the same carbon atom of what was once an aldehyde.

Acetyl coenzyme A (acetyl-CoA) Acetyl-substituted coenzyme A—the common intermediate that carries acetyl groups into the citric acid cycle.

Acetyl group A $CH_3C{=}O$ group.

Acetylcholine A vertebrate neurotransmitter that is most commonly found in muscle neurons.

Achiral The opposite of chiral, having superimposable mirror images and thus no right- or left-handedness.

Acid A substance that provides H^+ ions in water.

Acid dissociation constant (K_a) The equilibrium constant for the dissociation of an acid (HA), equal to $[H^+][A^-]/[HA]$.

Acidosis The abnormal condition associated with a blood plasma pH below 7.35; may be respiratory or metabolic.

Acid-base indicator A dye that changes color depending on the pH of a solution.

Activation (of an enzyme) Any process that initiates or increases the action of an enzyme.

Activation energy (E_{act}) The amount of energy necessary for a reaction to occur; it determines the reaction rate.

Active site A pocket in an enzyme with the specific shape and chemical makeup necessary to bind a substrate.

Active transport Movement of substances across a cell membrane with the assistance of energy (for example, from ATP).

Actual Yield The amount of product actually formed in a reaction.

Acyl group An $RC{=}O$ group.

Addition reaction A general reaction type in which a substance X—Y adds to the multiple bond of an unsaturated reactant to yield a saturated product that has only single bonds.

Addition reaction, aldehydes and ketones Addition of an alcohol or other compound to the carbon-oxygen double bond to give a carbon-oxygen single bond.

Adenosine triphosphate (ATP) The principal energy-carrying molecule; removal of a phosphoryl group to give ADP releases free energy.

Aerobic In the presence of oxygen.

Agonist A substance that interacts with a receptor to cause or prolong the receptor's normal biochemical response.

Alcohol A compound that has an —OH group bonded to a saturated, alkane-like carbon atom, R—OH.

Alcoholic fermentation The anaerobic breakdown of glucose to ethanol plus carbon dioxide by the action of yeast enzymes.

Aldehyde A compound that has a carbonyl group bonded to at least one hydrogen, RCHO.

Aldose A monosaccharide that contains an aldehyde carbonyl group.

Alkali metal An element in group 1A of the periodic table.

Alkaline earth metal An element in group 2A of the periodic table.

Alkaloid A naturally occurring nitrogen-containing compound isolated from a plant; usually basic, bitter, and often poisonous.

Alkalosis The abnormal condition associated with a blood plasma pH above 7.45; may be respiratory or metabolic.

Alkane A hydrocarbon that has only single bonds.

Alkene A hydrocarbon that contains a carbon-carbon double bond.

Alkoxide ion The anion resulting from the removal of the H from an alcohol, RO^-.

Alkoxy group An —OR group.

Alkyl group The part of an alkane that remains when a hydrogen atom is removed.

Alkyl halide A compound that has an alkyl group bonded to a halogen atom, R—X.

Alkyne A hydrocarbon that contains a carbon-carbon triple bond.

Allosteric control An interaction in which the binding of a regulator at one site on a protein affects the protein's ability to bind another molecule at a different site.

Allosteric enzyme An enzyme whose activity is controlled by the binding of an activator or inhibitor at a location other than the active site.

Alpha (α) particle A helium nucleus (He^{2+}), emitted as α-radiation.

Alpha- (α-)amino acid An amino acid in which the amino group is bonded to the carbon atom next to the —COOH group.

Alpha- (α-)helix Secondary protein structure in which a protein chain forms a right-handed coil stabilized by hydrogen bonds between peptide groups along its backbone.

Amide A compound that has a carbonyl group bonded to a nitrogen atom group, $RCONR_2'$, where the R′ groups may be alkyl groups or hydrogen atoms.

Amine A compound that has one or more organic groups bonded to nitrogen; primary, RNH_2; secondary, R_2NH; or tertiary, R_3N.

Amino acid A molecule that contains both an amino functional group and a carboxyl functional group.

Amino acid pool The entire collection of free amino acids in the body.

Amino group The $—NH_2$ functional group.

Amino-terminal (N-terminal) amino acid The amino acid with the free $—NH_3^+$ group at the end of a protein.

Ammonium ion A positive ion formed by addition of hydrogen to ammonia or an amine (may be primary, secondary, or tertiary).

Ammonium salt An ionic compound composed of an ammonium cation and an anion; an amine salt.

Amorphous solid A solid whose particles do not have an orderly arrangement.

Amphoteric Describing a substance that can react as either an acid or a base.

Anabolism Metabolic reactions that build larger biological molecules from smaller pieces.

Anaerobic In the absence of oxygen.

Anion A negatively charged ion.

Anomeric carbon atom The hemiacetal C atom in a cyclic sugar; the C atom bonded to an —OH group and an O in the ring.

Anomers Cyclic sugars that differ only in positions of substituents at the hemiacetal carbon (the anomeric carbon); the α form has the —OH on the opposite side from the $—CH_2OH$; the β form has the —OH on the same side as the $—CH_2OH$.

Antagonist A substance that blocks or inhibits the normal biochemical response of a receptor.

Antibody (immunoglobulin) Glycoprotein molecule that identifies antigens.

Anticodon A sequence of three ribonucleotides on tRNA that recognizes the complementary sequence (the codon) on mRNA.

Antigen A substance foreign to the body that triggers the immune response.

Antioxidant A substance that prevents oxidation by reacting with an oxidizing agent.

Aromatic The class of compounds containing benzene-like rings.

Artificial radioisotope A radioactive isotope not found in nature.

Artificial transmutation The change of one atom into another brought about by a nuclear bombardment reaction.

Aryl halide A compound that has an aromatic group bonded to a halogen atom, Ar-X.

Atom The smallest and simplest particle of an element.

Atomic mass unit (amu) A unit for describing the mass of an atom; 1 amu = 1/12 the mass of a carbon-12 atom.

Atomic number (Z) The number of protons in the nucleus of an atom of a given element.

Atomic theory A set of assumptions proposed by English scientist John Dalton to explain the chemical behavior of matter.

Atomic mass The weighted average mass of an element's atoms.

ATP synthase The enzyme complex in the inner mitochondrial membrane where hydrogen ions cross the membrane and ATP is synthesized from ADP.

Autoimmune disease Disorder in which the immune system identifies normal body components as antigens and produces antibodies to them.

Avogadro's law The volume of a gas is directly proportional to its molar amount at a constant temperature and pressure (V/n = constant, or $V_1/n_1 = V_2/n_2$).

Avogadro's number (N_A) The number of units in 1 mole of anything; 6.02×10^{23}.

Balanced equation A chemical equation in which the numbers and kinds of atoms are the same on both sides of the reaction arrow.

Base A substance that provides OH^- ions in water.

Base pairing The pairing of bases connected by hydrogen bonding (G-C and A-T), as in the DNA double helix.

Beta- (β-)Oxidation pathway A repetitive series of biochemical reactions that degrades fatty acids to acetyl-SCoA by removing carbon atoms two at a time.

Beta (β) particle An electron (e^-), emitted as β radiation.
Beta- (β-) Sheet Secondary protein structure in which adjacent protein chains either in the same molecule or in different molecules are held in place by hydrogen bonds along the backbones forming a flat, sheet-like structure.
Bile Fluid secreted by the liver and released into the small intestine from the gallbladder during digestion; contains bile acids, cholesterol, phospholipids, hydrogen carbonate ions, and other electrolytes.
Bile acids Steroid acids derived from cholesterol that are secreted in bile.
Binary compound A compound formed by combination of two different elements.
Blood clot A network of fibrin fibers and trapped blood cells that forms at the site of blood loss.
Blood plasma Liquid portion of the blood: an extracellular fluid.
Blood serum Fluid portion of blood remaining after clotting has occurred.
Boiling point (bp) The temperature at which liquid and gas are in equilibrium.
Bond angle The angle formed by three adjacent atoms in a molecule.
Bond dissociation energy The amount of energy that must be supplied to break a bond and separate the atoms in an isolated gaseous molecule.
Bond length The optimum distance between nuclei in a covalent bond.
Boyle's law The pressure of a gas at constant temperature is inversely proportional to its volume (PV = constant, or $P_1V_1 = P_2V_2$).
Branched-chain alkane An alkane that has a branching connection of carbons.
Brønsted-Lowry acid A substance that can donate a hydrogen ion, H^+, to another molecule or ion.
Brønsted-Lowry base A substance that can accept H^+ from an acid.
Buffer A combination of substances that act together to prevent a drastic change in pH; usually a weak acid and its conjugate base.
Carbohydrate A member of a large class of naturally occurring polyhydroxy ketones and aldehydes.
Carbonyl compound Any compound that contains a carbonyl group C═O.
Carbonyl group A functional group that has a carbon atom joined to an oxygen atom by a double bond, C═O.
Carbonyl-group substitution reaction A reaction in which a new group replaces (substitutes for) a group attached to a carbonyl-group carbon in an acyl group.
Carboxyl group The —COOH functional group.
Carboxyl-terminal (C-terminal) amino acid The amino acid with the free $—COO^-$ group at the end of a protein.
Carboxylate anion The anion that results from ionization of a carboxylic acid, $RCOO^-$.
Carboxylic acid A compound that has a carbonyl group bonded to a carbon atom and an —OH group, RCOOH.
Carboxylic acid salt An ionic compound containing a cation and a carboxylate acid anion.
Catabolism Metabolic reaction pathways that break down food molecules and release biochemical energy.
Catalyst A substance that speeds up the rate of a chemical reaction but is itself unchanged.
Cation A positively charged ion.
Cellular protein A protein found inside cells.
Centromeres The central regions of chromosomes.
Chain reaction A reaction that, once started, is self-sustaining.
Change of state The conversion of a substance from one state to another—for example, from a liquid (*l*) to a gas (*g*).
Charles's law The volume of a gas at constant pressure is directly proportional to its Kelvin temperature (V/T = constant, or $V_1/T_1 = V_2/T_2$).
Chemical change A change in the chemical makeup of a substance.
Chemical compound A pure substance that can be broken down into simpler substances by chemical reactions.
Chemical equation An expression in which symbols and formulas are used to represent a chemical reaction.
Chemical equilibrium A state in which the rates of forward and reverse reactions are the same.
Chemical formula A notation for a chemical compound using element symbols and subscripts to show how many atoms of each element are present.
Chemical reaction A process in which the identity and composition of one or more substances are changed.
Chemistry The study of the nature, properties, and transformations of matter.
Chiral Having right- or left-handedness with two *different* mirror-image forms.
Chiral carbon atom (chirality center) A carbon atom bonded to four different groups; also referred to as a chiral center or stereocenter.
Chromosome A complex of proteins and DNA; visible during cell division.
Cis-trans isomers Alkenes that have the same connections between atoms but differ in their three-dimensional structures because of the way that groups are attached to different sides of the double bond.
Citric acid cycle The series of biochemical reactions that breaks down acetyl groups to produce energy carried by reduced coenzymes and carbon dioxide.
Clones Identical copies of organisms, cells, or DNA segments from a single ancestor.
Codon A sequence of three ribonucleotides in the messenger RNA chain that codes for a specific amino acid; also the three nucleotide sequence (a stop codon) that stops translation.
Coefficient A number placed in front of a formula to balance a chemical equation.
Coenzyme An organic molecule that acts as an enzyme cofactor.
Cofactor A nonprotein part of an enzyme that is essential to the enzyme's catalytic activity; a metal ion or a coenzyme.
Colligative property A property of a solution that depends only on the number of dissolved particles, not on their chemical identity.
Colloid A homogeneous mixture that contains particles that range in diameter from 2 to 500 nm.
Combined gas law The product of the pressure and volume of a gas is proportional to its temperature (PV/T = constant, or $P_1V_1/T_1 = P_2V_2/T_2$).
Combustion A chemical reaction that produces a flame, usually because of burning with oxygen.
Competititve (enzyme) inhibition Enzyme regulation in which an inhibitor competes with a substrate for binding to the enzyme active site.
Concentration A measure of the amount of a given substance in a mixture.
Concentration gradient A difference in concentration within the same system.
Condensed structure A shorthand way of drawing structures in which C—C and C—H bonds are understood rather than shown.
Configurations Stereoisomers that *cannot* be converted into one another by rotation around a single bond.
Conformation The specific three-dimensional arrangement of atoms in a molecule achieved specifically through rotations around carbon–carbon single bonds.
Conformers Molecular structures having identical connections between atoms where the interconversion of C—C bond rotations results only in a different spatial arrangement of atoms.
Conjugate acid The substance formed by addition of H^+ to a base.
Conjugate acid-base pair Two substances whose formulas differ by only a hydrogen ion, H^+.
Conjugate base The substance formed by loss of H^+ from an acid.
Conjugated protein A protein that incorporates one or more non-amino acid units in its structure.
Constitutional isomers Compounds with the same molecular formula but different connections among their atoms; also known as structural isomers.
Conversion factor An expression of the numerical relationship between two units.
Coordinate covalent bond The covalent bond that forms when both electrons are donated by the same atom.
Cosmic rays A mixture of high-energy particles—primarily of protons and various atomic nuclei—that shower the earth from outer space.
Covalent bond A bond formed by sharing electrons between atoms.
Critical mass The minimum amount of radioactive material needed to sustain a nuclear chain reaction.
Crystalline solid A solid whose atoms, molecules, or ions are rigidly held in an ordered arrangement.
Cycloalkane An alkane that contains a ring of carbon atoms.
Cycloalkene A cyclic hydrocarbon that contains a double bond.
Cytoplasm The region between the cell membrane and the nuclear membrane in a eukaryotic cell.
Cytosol The fluid part of the cytoplasm surrounding the organelles within a cell. It contains dissolved proteins and nutrients.
***d*-Block element** A transition metal element that results from the filling of *d* orbitals.
D-Sugar Monosaccharide with the —OH group on the chiral carbon atom farthest from the carbonyl group pointing to the right in a Fischer projection.

Dalton's law The total pressure exerted by a mixture of gases is equal to the sum of the partial pressures exerted by each individual gas.

Decay series A sequential series of nuclear disintegrations leading from a heavy radioisotope to a nonradioactive product.

Degree of unsaturation The number of carbon-carbon double bonds in a molecule.

Dehydration The loss of water from an alcohol to yield an alkene.

Denaturation The loss of secondary, tertiary or quaternary protein structure due to disruption of noncovalent interactions and/or disulfide bonds that leaves peptide bonds and primary structure intact.

Density The physical property that relates the mass of an object to its volume; mass per unit volume.

Deoxyribonucleotide A nucleotide containing 2-deoxy-D-ribose.

Diabetes mellitus A chronic condition due to either insufficient insulin or failure of insulin to activate crossing of cell membranes by glucose.

Diastereomers Stereoisomers that are not mirror images of each other.

Digestion A general term for the breakdown of food into small molecules.

Dilution factor The ratio of the initial and final solution volumes (V_1/V_2).

Dipole A difference in charge (+ or −) associated with one end of a covalent bond compared with the other, or one end of a molecule compared with another.

Dipole-dipole force The attractive force between positive and negative ends of polar molecules.

Disaccharide A carbohydrate composed of two monosaccharides.

Dissociation The splitting apart of an acid in water to give H^+ and an anion.

Disulfide A compound that contains a sulfur-sulfur bond, RS-SR.

Disulfide bond (in protein) An S-S bond formed between two cysteine side chains; can join two peptide chains together or cause a loop in a peptide chain.

DNA (deoxyribonucleic acid) The nucleic acid that stores genetic information; a polymer of deoxyribonucleotides.

Double bond A covalent bond formed by sharing two electron pairs.

Double helix Two strands coiled around each other in a screwlike fashion; in most organisms the two polynucleotides of DNA form a double helix.

Drug Any substance that alters body function when it is introduced from an external source.

Eicosanoid A lipid derived from a 20-carbon unsaturated carboxylic acid.

Electrolyte A substance that produces ions and therefore conducts electricity when dissolved in water.

Electron A negatively charged subatomic particle.

Electron affinity The energy released on adding an electron to a single atom in the gaseous state.

Electron capture A process in which the nucleus captures an inner-shell electron from the surrounding electron cloud, thereby converting a proton into a neutron.

Electron configuration The specific arrangement of electrons in an atom's shells and subshells.

Electron shell A grouping of electrons in an atom according to energy.

Electron subshell A grouping of electrons in a shell according to the shape of the region of space they occupy.

Electron-dot (Lewis) symbol An atomic symbol with dots placed around it to indicate the number of valence electrons.

Electron-transport chain The series of biochemical reactions that passes electrons from reduced coenzymes to oxygen and is coupled to ATP formation.

Electronegativity The ability of an atom to attract electrons in a covalent bond.

Element A fundamental substance that cannot be broken down chemically into any simpler substance.

Elimination reaction A general reaction type in which a saturated reactant yields an unsaturated product by losing groups from two adjacent atoms.

Enantiomers (optical isomers) The two mirror-image forms of a chiral molecule.

Endergonic A nonspontaneous reaction or process that absorbs free energy and has a positive ΔG.

Endocrine system A system of specialized cells, tissues, and ductless glands that secretes hormones and shares with the nervous system the responsibility for maintaining constant internal body conditions and responding to changes in the environment.

Endothermic A process or reaction that absorbs heat and has a positive ΔH.

Energy The capacity to do work or supply heat.

Enthalpy A measure of the amount of energy associated with substances involved in a reaction.

Enthalpy change (ΔH) An alternative name for heat of reaction.

Entropy (S) A measure of the amount of molecular disorder in a system.

Entropy change (ΔS) A measure of the increase in disorder $(\Delta S = +)$ or decrease in disorder $(\Delta S = -)$ as a chemical reaction or physical change occurs.

Enzyme A protein or other molecule that acts as a catalyst for a biological reaction.

Equilibrium constant (K) Value obtained at a given temperature from the ratio of the concentrations of products and reactants, each raised to a power equal to its coefficient in the balanced chemical equation.

Equivalent For ions, the amount equal to 1 mol of charge.

Equivalent of acid Amount of an acid that contains 1 mole of H^+ ions.

Equivalent of base Amount of base that contains 1 mole of OH^- ions.

Erythrocytes Red blood cells (RBCs); transporters of blood gases.

Essential amino acid An amino acid that cannot be synthesized by the body and thus must be obtained in the diet.

Ester A compound that has a carbonyl group bonded to an —OR′ group, RCOOR′.

Esterification The reaction between an alcohol and a carboxylic acid to yield an ester plus water.

Ether A compound that has an oxygen atom bonded to two organic groups, R—O—R.

Ethyl group The $-CH_2CH_3$ alkyl group.

Exergonic A spontaneous reaction or process that releases free energy and has a negative ΔG.

Exon A nucleotide sequence that is part of a gene and codes for part of a protein.

Exothermic A process or reaction that releases heat.

Extracellular fluid Fluid outside cells.

***f*-Block element** An inner transition metal element that results from the filling of *f* orbitals.

Facilitated diffusion Passive transport across a cell membrane with the assistance of a protein that changes shape.

Factor-label method A problem-solving procedure in which equations are set up so that unwanted units cancel and only the desired units remain.

Fat A mixture of triacylglycerols that is solid because it contains a high proportion of saturated fatty acids.

Fatty acid A long-chain carboxylic acid; those in animal fats and vegetable oils often have 12–22 carbon atoms.

Feedback control Regulation of an enzyme's activity by the product of a reaction later in a pathway.

Fermentation The production of energy under anaerobic conditions.

Fibrin Insoluble protein that forms the fiber framework of a blood clot.

Fibrous protein A tough, insoluble protein whose protein chains form fibers or sheets.

Filtration (kidney) Filtration of blood plasma through a glomerulus and into a kidney nephron.

Fischer projection Structure that represents chiral carbon atoms as the intersections of two lines, with the horizontal lines representing bonds pointing out of the page and the vertical lines representing bonds pointing behind the page. For sugars, the aldehyde or ketone is at the top.

Formula unit The formula that identifies the smallest neutral unit of an ionic compound.

Formula mass The sum of the atomic masses of the atoms in one formula unit of any compound, whether molecular or ionic.

Free-energy change (ΔG) A measure of the change in free energy as a chemical reaction or physical change occurs.

Free radical An atom or molecule with an unpaired electron.

Functional group An atom or group of atoms within a molecule that has a characteristic structure and chemical behavior.

Functional group isomer Isomers having the same chemical formula but belonging to different chemical families due to differences in bonding.

Gamma radiation (γ) Radioactivity consisting of high-energy light waves.

Gas A substance that has neither a definite volume nor a definite shape.

Gas constant (R) The constant R in the ideal gas law, $PV = nRT$.

Gas laws A series of laws that predict the influence of pressure (P), volume (V), and temperature (T) on any gas or mixture of gases.

Gay-Lussac's law For a fixed amount of gas at a constant voume, pressure is directly proportional to the Kelvin temperature $(P/T = \text{constant}, \text{or } P_1/T_1 = P_2/T_2)$.

Gene Segment of DNA that directs the synthesis of a single polypeptide.

Genetic (enzyme) control Regulation of enzyme activity by control of the synthesis of enzymes.

Genetic code The sequence of nucleotides, coded in triplets (codons) in mRNA, that determines the sequence of amino acids in protein synthesis.

Genome All of the genetic material in the chromosomes of an organism; its size is given as the number of base pairs.

Genomics The study of whole sets of genes and their functions.

Globular protein A water-soluble protein whose chain is folded in a compact shape with hydrophilic groups on the outside.

Glomerular filtrate Fluid that enters the nephron from the glomerulus; filtered blood plasma.

Gluconeogenesis The biochemical pathway for the synthesis of glucose from non-carbohydrates, such as lactate, amino acids, or glycerol.

Glycerophospholipid (phosphoglyceride) A lipid in which glycerol is linked by ester bonds to two fatty acids and one phosphate, which is in turn linked by another ester bond to an amino alcohol (or other alcohol).

Glycogenesis The biochemical pathway for synthesis of glycogen, a branched polymer of glucose.

Glycogenolysis The biochemical pathway for breakdown of glycogen to free glucose.

Glycol A dialcohol, or diol having the two —OH groups on adjacent carbons.

Glycolipid A lipid with a fatty acid bonded to the C2—NH_2 and a sugar bonded to the C1—OH group of sphingosine.

Glycolysis The biochemical pathway that breaks down a molecule of glucose into two molecules of pyruvate plus energy.

Glycoprotein A protein that contains a short carbohydrate chain.

Glycoside A cyclic acetal formed by reaction of a monosaccharide with an alcohol, accompanied by loss of H_2O.

Glycosidic bond Bond between the anomeric carbon atom of a monosaccharide and an —OR group.

Group One of the 18 vertical columns of elements in the periodic table.

Guanosine diphosphate (GDP) An energy-carrying molecule that can gain or lose a phosphoryl group to transfer energy.

Guanosine triphosphate (GTP) An energy-carrying molecule similar to ATP; removal of a phosphoryl group to give GDP releases free energy.

Half-life ($t_{1/2}$) The amount of time required for one-half of a radioactive sample to decay.

Halogen An element in group 7A of the periodic table.

Halogenation (alkene) The addition of Cl_2 or Br_2 to a multiple bond to give a 1,2-dihalide product.

Halogenation (aromatic) The substitution of a halogen group (—X) for a hydrogen on an aromatic ring.

Heat A measure of the transfer of thermal energy.

Heat of fusion The quantity of heat required to completely melt 1 gram of a substance once it has reached its melting point.

Heat of reaction (ΔH) The difference between the energy of bonds broken in the reactants and the energy of bonds formed in the products.

Heat of vaporization The quantity of heat needed to completely vaporize 1 gram of a liquid once it has reached its boiling point.

Hemiacetal A compound with both an alcohol-like —OH group and an ether-like —OR group bonded to the carbon atom that was at one time the aldehyde carbonyl carbon.

Hemiketal A compound with both an alcohol-like —OH group and an ether-like —OR group bonded to the carbon atom that was at one time the ketone carbonyl carbon.

Hemostasis The stopping of bleeding.

Henderson-Hasselbalch equation The logarithmic form of the K_a equation for a weak acid, used in applications involving buffer solutions.

Henry's law The solubility of a gas in a liquid is directly proportional to its partial pressure over the liquid at constant temperature.

Heterocycle A ring that contains nitrogen or some other atom in addition to carbon.

Heterogeneous mixture A nonuniform mixture that has regions of different composition.

Heterogeneous nuclear RNA (hnRNA) The initially synthesized mRNA strand containing both introns and exons.

Homogeneous mixture A uniform mixture that has the same composition throughout.

Hormone A chemical messenger secreted by cells of the endocrine system and transported through the bloodstream to target cells with appropriate receptors where it elicits a response.

Hydration The addition of water to a multiple bond to give an alcohol product.

Hydrocarbon An organic compound that contains only carbon and hydrogen.

Hydrogen bond The attraction between a hydrogen atom bonded to an electronegative atom (O, N, or F) and another nearby electronegative N or O atom.

Hydrogenation The addition of H_2 to a multiple bond to give a saturated product.

Hydrohalogenation The addition of HCl or HBr to a multiple bond to give an alkyl halide product.

Hydrolysis A reaction in which a bond or bonds are broken and the H— and —OH of water add to the atoms of the broken bond or bonds.

Hydronium ion The H_3O^+ ion, formed when an acid reacts with water.

Hydrophilic Water-loving; a hydrophilic substance dissolves in water.

Hydrophobic Water-fearing; a hydrophobic substance does not dissolve in water.

Hyperglycemia Higher-than-normal blood glucose concentration.

Hypertonic Having an osmolarity greater than the surrounding blood plasma or cells.

Hypoglycemia Lower-than-normal blood glucose concentration.

Hypotonic Having an osmolarity less than the surrounding blood plasma or cells.

Ideal gas A gas that obeys all the assumptions of the kinetic-molecular theory.

Ideal gas law A general expression relating pressure, volume, temperature, and amount for an ideal gas: $PV = nRT$.

Immune response Defense mechanism of the immune system dependent on the recognition of specific antigens, including viruses, bacteria, toxic substances, and infected cells; either cell-mediated or antibody-mediated.

Induced-fit model A model of enzyme action in which the enzyme has a flexible active site that changes shape to best fit the substrate and catalyze the reaction.

Inflammation Result of the inflammatory response: includes swelling, redness, warmth, and pain.

Inflammatory response A nonspecific defense mechanism triggered by antigens or tissue damage.

Inhibition (of an enzyme) Any process that slows or stops the action of an enzyme.

Inner transition metal element An element in one of the 14 groups shown separately at the bottom of the periodic table.

Intermolecular force A force that acts between molecules or discrete atoms and holds them close to one another. Also called van der Waals forces.

Interstitial fluid Fluid surrounding cells: an extracellular fluid.

Intracellular fluid Fluid inside cells.

Intron A nucleotide sequence in mRNA that does not code for part of a protein; removed before mRNA proceeds to protein synthesis.

Ion An electrically charged atom or group of connected atoms.

Ion-product constant for water (K_w) The product of the H_3O^+ and OH^- molar concentrations in water or any aqueous solution ($K_w = [H_3O^+][OH^-] = 1.00 \times 10^{-14}$).

Ionic bond The electrical attractions between ions of opposite charge in an ionic compound.

Ionic compound A compound that contains ionic bonds.

Ionic equation An equation in which ions are explicitly shown.

Ionic solid A crystalline solid held together by ionic bonds.

Ionization energy The energy required to remove one valence electron from a single atom in the gaseous state.

Ionizing radiation A general name for high-energy radiation of all kinds.

Irreversible (enzyme) inhibition Enzyme deactivation in which an inhibitor forms covalent bonds to the active site, permanently blocking it.

Isoelectric point (pI) The pH at which a sample of an amino acid has equal number of + and − charges.

Isomers Compounds with the same molecular formula but different structures.

Isopropyl group The branched-chain alkyl group $—CH(CH_3)_2$.

Isotonic Having the same osmolarity.

Isotopes Atoms with identical atomic numbers but different mass numbers.

Ketal A compound that has two ether-like —OR groups bonded to the same carbon atom of what was once a ketone.

Ketoacidosis Lowered blood pH due to accumulation of ketone bodies.

Ketogenesis The synthesis of ketone bodies from acetyl-CoA.

Ketone A compound that has a carbonyl group bonded to two carbons in organic

groups that can be the same or different, $R_2C{=}O$, RCOR′.

Ketone bodies Compounds produced in the liver that can be used as fuel by muscle and brain tissue; 3-hydroxybutyrate, acetoacetate, and acetone.

Ketose A monosaccharide that contains a ketone carbonyl group.

Kinetic energy The energy of motion of an object in motion.

Kinetic-molecular theory (KMT) of gases A group of assumptions that explain the behavior of gases.

L-Sugar Monosaccharide with the —OH group on the chiral carbon atom farthest from the carbonyl group pointing to the left in a Fischer projection.

Law of conservation of energy Energy can be neither created nor destroyed in any physical or chemical change.

Law of conservation of mass Matter is neither created nor destroyed in any physical or chemical change.

Le Châtelier's principle When a stress is applied to a system in equilibrium, the equilibrium shifts to relieve the stress.

Leukocytes White blood cells (WBCs).

Lewis base A compound containing an unshared pair of electrons.

Lewis structure A molecular representation that shows both the connections among atoms and the locations of lone-pair valence electrons.

Limiting reagent The reactant that runs out first in a chemical reaction.

Line structure Also known as line-angle structure; a shorthand way of drawing structures in which carbon and hydrogen atoms are not explicitly shown. Instead, a carbon atom is understood to be wherever a line begins or ends and at every intersection of two lines, and hydrogens are understood to be wherever they are needed to have each carbon form four bonds.

Lipid A naturally occurring molecule from a plant or animal that is soluble in nonpolar organic solvents.

Lipid bilayer The basic structural unit of cell membranes; composed of two parallel sheets of membrane lipid molecules arranged tail to tail.

Lipogenesis The biochemical pathway for synthesis of fatty acids from acetyl-CoA.

Lipoprotein A lipid-protein complex that transports lipids.

Liposome A spherical structure in which a lipid bilayer surrounds a water droplet.

Liquid A substance that has a definite volume but that assumes the shape of its container.

Lock-and-key model A model of enzyme action in which the enzyme is a rigid lock that exactly fits the substrate, the key for the reaction.

London dispersion force The short-lived attractive force due to the constant motion of electrons within molecules.

Lone pair A pair of electrons that is not used for bonding.

Main group element An element in one of the two groups on the left or the six groups on the right of the periodic table.

Markovnikov's rule In the addition of HX to an alkene, the major product arises from the H attaching to the double-bond carbon that has the larger number of H atoms *directly* attached to it and the X attaching to the carbon that has the smaller number of H atoms attached.

Mass A measure of the amount of matter in an object.

Mass/mass percent concentration [(m/m)%] Concentration expressed as the number of grams of solute per 100 grams of solution.

Mass number (*A*) The total number of protons and neutrons in an atom.

Mass/volume percent concentration [(m/v)%] Concentration expressed as the number of grams of solute per 100 mL of solution.

Matter The physical material that makes up the universe; anything that has mass and occupies space.

Melting point (mp) The temperature at which solid and liquid are in equilibrium.

Metabolism The sum of all of the chemical reactions that take place in an organism.

Messenger RNA (mRNA) The RNA that carries the code transcribed from DNA and directs protein synthesis.

Metal A malleable element with a lustrous appearance that is a good conductor of heat and electricity.

Metalloid An element whose properties are intermediate between those of a metal and a nonmetal.

Methyl group The $-CH_3$ alkyl group.

Methylene Another name for a $-CH_2$ unit.

Micelle A spherical cluster formed by the aggregation of soap or detergent molecules so that their hydrophobic ends are in the center and their hydrophilic ends are on the surface.

Miscible Mutually soluble in all proportions.

Mitochondrial matrix The space surrounded by the inner membrane of a mitochondrion.

Mitochondrion (plural, mitochondria) An egg-shaped organelle where small molecules are broken down to provide the energy for an organism.

Mixture A blend of two or more substances, each of which retains its chemical identity.

Mobile protein A protein found in body fluids such as blood.

Mobilization (of triacylglycerols) Hydrolysis of triacylglycerols in adipose tissue and release of fatty acids into the bloodstream.

Molar mass The mass in grams of one mole of a substance, numerically equal to the molecular mass.

Molarity (*M*) Concentration expressed as the number of moles of solute per liter of solution.

Mole The amount of a substance whose mass in grams is numerically equal to its molecular or formula mass.

Molecular compound A compound that consists of atoms joined by covalent bonds to form molecules rather than ions.

Molecular formula A formula that shows the numbers and kinds of atoms in one molecule of a compound.

Molecular mass The sum of the atomic masses of the atoms in a molecule.

Molecule A group of atoms held together by covalent bonds.

Monomer A small molecule that is used to prepare a polymer.

Monosaccharide (simple sugar) A carbohydrate with 3–7 carbon atoms.

Mutagen A substance that causes mutations.

Mutarotation Change in rotation of plane-polarized light resulting from the equilibrium between cyclic anomers and the open-chain form of a sugar.

Mutation An error in base sequence that is carried along in DNA replication and passed on to the offspring.

Native protein A protein with the shape (secondary, tertiary, and quaternary structure) in which it exists naturally in living organisms.

Natural radioisotope Radioactive isotopes that occur naturally and are found in the Earth's crust.

Net ionic equation An equation that does not include spectator ions.

Neurotransmitter A chemical messenger that travels between a neuron and a neighboring neuron or other target cell to transmit a nerve impulse.

Neutralization reaction The reaction of an acid with a base.

Neutron An electrically neutral subatomic particle.

Nitration The substitution of a nitro group ($-NO_2$) for a hydrogen on an aromatic ring.

Noble gas An element in group 8A of the periodic table.

Noncovalent forces Forces of attraction other than covalent bonds that can act between molecules or within molecules.

Nonelectrolyte A substance that does not produce ions when dissolved in water.

Nonessential amino acid One of 11 amino acids that are synthesized in the body and are therefore not necessary in the diet.

Nonmetal An element that is a poor conductor of heat and electricity.

Normal boiling point The boiling point at a pressure of exactly 1 atmosphere.

Normality (N) A measure of acid (or base) concentration expressed as the number of acid (or base) equivalents per liter of solution.

Nuclear decay The spontaneous emission of a particle from an unstable nucleus.

Nuclear fission When heavy nuclei fragment into lighter nuclei.

Nuclear fusion When lighter nuclei combine to form a heavier nuclide.

Nuclear reaction A reaction that changes an atomic nucleus, usually causing the change of one element into another.

Nucleic acid A polymer of nucleotides.

Nucleon A general term for both protons and neutrons.

Nucleoside A 5-carbon sugar bonded to a heterocyclic nitrogenous base; like a nucleotide but with no phosphate group.

Nucleotide A 5-carbon sugar bonded to a heterocyclic nitrogen base and a phosphate group; monomer for nucleic acids.

Nucleus The dense, central core of an atom that contains protons and neutrons.

Nuclide The nucleus of a specific isotope of an element.

Octet rule The tendency of atoms to gain or lose electrons to achieve a stable, noble gas configuration, that is, a completely filled subshell containing eight electrons.

Oil A mixture of triacylglycerols that is liquid because it contains a high proportion of unsaturated fatty acids.

Orbital A region of space within an atom where an electron in a given subshell can be found.

Orbital diagram A representation of the electron distribution into orbitals, in which orbitals are indicated by a line or a box, and electrons in each orbital are represented as arrows.

Organic chemistry The study of carbon compounds.

Osmolarity (osmol/L) The sum of the molarities of all dissolved particles (osmol) in 1 liter of solution.

Osmosis The passage of solvent through a semipermeable membrane separating two solutions of different concentration.

Osmotic pressure The amount of external pressure that must be applied to the more concentrated solution to halt the passage of solvent molecules across a semipermeable membrane.

Oxidation The loss of one or more electrons by an atom.

Oxidation number A number that indicates whether an atom is neutral, electron-rich, or electron-poor.

Oxidation-reduction (redox), reaction A reaction in which electrons are transferred from one atom to another.

Oxidative deamination Conversion of an amino acid $-NH_2$ group to an α-keto group, with removal of NH_4^+.

Oxidative phosphorylation The synthesis of ATP from ADP using energy released in the electron-transport chain.

Oxidizing agent A reactant that causes an oxidation by taking electrons from another reactant.

***p*-Block element** A main group element that results from the filling of *p* orbitals.

***p* Function** The negative common logarithm of some variable, $pX = -(\log X)$.

Partial pressure The contribution of a given gas in a mixture to the total pressure.

Parts per billion (ppb) Number of parts of solute (in mass or volume) per one billion parts of solution.

Parts per million (ppm) Number of parts of solute (in mass or volume) per one million parts of solution.

Passive transport Movement of a substance across a cell membrane without the use of energy, from a region of higher concentration to a region of lower concentration.

Pathway A series of enzyme-catalyzed chemical reactions that are connected by their intermediates, that is, the product of the first reaction is the reactant for the second reaction, and so on.

Pentose phosphate pathway The biochemical pathway that produces ribose (a pentose), NADPH, and other sugar phosphates from glucose; an alternative to glycolysis.

Peptide bond An amide bond that links two amino acids together.

Percent yield The percentage of the theoretical yield actually obtained from a chemical reaction.

Period One of the seven horizontal rows of elements in the periodic table.

Periodic table A tabular format listing all known elements where the atomic number (top), symbol for the element (middle), and atomic mass (bottom) are given in each box that represents the element.

pH A measure of the acid strength of a solution; the negative common logarithm of the H_3O^+ concentration.

Phenol A compound that has an $-OH$ group bonded directly to an aromatic, benzene-like ring, $Ar-OH$.

Phenyl The C_6H_5- group.

Phosphate ester A compound formed by reaction of an alcohol with phosphoric acid; may be a monoester, $ROPO_3H_2$; a diester, $(RO)_2PO_3H$; or a triester, $(RO)_3PO$; also may be a di- or triphosphate.

Phospholipid A lipid that has an ester link between phosphoric acid and an alcohol (glycerol or sphingosine).

Phosphoryl group The $-PO_3^{2-}$ group in organic phosphates.

Phosphorylation Transfer of a phosphoryl group, $-PO_3^{2-}$, between organic molecules.

Physical change A change that does not affect the chemical makeup of a substance or object.

Physical quantity A physical property that can be measured.

Polar covalent bond A bond in which the electrons are attracted more strongly by one atom than by the other.

Polyatomic ion An ion that is composed of more than one atom.

Polymer A large molecule formed by the repetitive bonding together of many smaller molecules.

Polymorphism A variation in DNA sequence within a population.

Polysaccharide (complex carbohydrate) A carbohydrate that is a polymer of monosaccharides.

Polyunsaturated fatty acid A long-chain fatty acid that has two or more carbon-carbon double bonds.

Positron A "positive electron," which has the same mass as an electron but a positive charge.

Potential energy Energy that is stored because of position, composition, or shape.

Precipitate An insoluble solid that forms in solution during a chemical reaction.

Pressure The force per unit area pushing against a surface.

Primary (1°) carbon atom A carbon atom with one other carbon attached to it.

Primary protein structure The sequence in which amino acids are linked by peptide bonds in a protein.

Product A substance that is formed as the result of a chemical reaction and is written on the right side of the reaction arrow in a chemical equation.

Property A characteristic useful for identifying a substance or object.

Propyl group The straight-chain alkyl group $-CH_2CH_2CH_3$.

Protein A large biological molecule made of many amino acids linked together through amide (peptide) bonds.

Proton A positively charged subatomic particle.

Pure substance A substance that has uniform chemical composition throughout.

Quaternary ammonium ion A positive ion with four organic groups bonded to the nitrogen atom.

Quaternary ammonium salt An ionic compound composed of a quaternary ammonium ion and an anion.

Quaternary (4°) carbon atom A carbon atom with four other carbons attached to it.

Quaternary protein structure The way in which two or more protein chains aggregate to form large, ordered structures.

Radioactivity The spontaneous emission of radiation from a nucleus.

Radioisotope A radioactive isotope.

Radionuclide The nucleus of a radioactive isotope.

Reabsorption (kidney) Movement of solutes out of filtrate in a kidney tubule.

Reactant A substance that undergoes change in a chemical reaction and is written on the left side of the reaction arrow in a chemical equation.

Reaction mechanism A description of the individual steps by which old bonds are broken and new bonds are formed in a reaction.

Reaction rate A measure of how rapidly a reaction occurs; determined by E_{act}.

Rearrangement reaction A general reaction type in which a molecule undergoes bond reorganization to yield an isomer.

Receptor A molecule or portion of a molecule with which a hormone, neurotransmitter, or other biochemically active molecule interacts to initiate a response in a target cell.

Recombinant DNA DNA that contains segments from two different species.

Reducing agent A reactant that causes a reduction of another reactant by giving up electrons to it.

Reducing sugar A carbohydrate that reacts in basic solution with a mild oxidizing agent.

Reduction The gain of one or more electrons by an atom.

Reductive deamination Conversion of an α-keto acid to an amino acid by reaction with NH_4^+.

Regular tetrahedron A geometric figure with four identical triangular faces.

Replication The process by which copies of DNA are made when a cell divides.

Residue (amino acid) An amino acid unit in a polypeptide.

Resonance The phenomenon where the true structure of a molecule is an average among two or more conventional Lewis structures that differ only in the placement of double bonds.

Restricted rotation The limited ability of a molecule to rotate around a given bond.

Reversible reaction A reaction that can go in either the forward direction or the reverse direction, from products to reactants or reactants to products.

Ribonucleotide A nucleotide containing D-ribose.

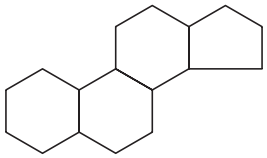
Ribosomal RNA (rRNA) The RNA that is complexed with proteins in ribosomes.

Ribosome The structure in the cell where protein synthesis occurs; composed of protein and rRNA.

Ribozyme RNA that acts as an enzyme.

RNA (ribonucleic acids) The nucleic acids responsible for putting the genetic information to use in protein synthesis; polymers of ribonucleotides. Includes messenger (mRNA), transfer (tRNA), and ribosomal RNA (rRNA).

Rounding off A procedure used for deleting non-significant figures.
s-Block element A main group element that results from the filling of an *s* orbital.
Salt An ionic compound formed from reaction of an acid with a base.
Saponification The reaction of an ester with aqueous hydroxide ion to yield an alcohol and the metal salt of a carboxylic acid.
Saturated A molecule in which each carbon atom has the maximum number of single bonds possible (four).
Saturated fatty acid A long-chain carboxylic acid containing only carbon-carbon single bonds.
Saturated solution A solution that contains the maximum amount of dissolved solute at equilibrium.
Scientific Method Systematic process of observation, hypothesis, and experimentation to expand and refine a body of knowledge.
Scientific notation A number expressed as the product of a number between 1 and 10, times the number 10 raised to a power.
Second messenger Chemical messenger released inside a cell when a hydrophilic hormone or neurotransmitter interacts with a receptor on the cell surface.
Secondary (2°)carbon atom A carbon atom with two other carbons attached to it.
Secondary protein structure Regular and repeating structural patterns (e.g., α-helix, β-sheet) created by hydrogen bonding between backbone atoms in neighboring segments of protein chains.
Secretion (kidney) Movement of solutes into filtrate in a kidney tubule.
Shell (electron) A grouping of electrons in an atom according to energy.
SI units Units of measurement defined by the International System of Units. Examples include kilograms, meters, and kelvins.
Side chain (amino acid) The group bonded to the carbon next to the carboxyl group in an amino acid; different in different amino acids.
Significant figures The number of meaningful digits used to express a value.
Simple diffusion Passive transport by the random motion of diffusion through the cell membrane.
Simple protein A protein composed of only amino acid residues.
Single bond A covalent bond formed by sharing one electron pair.
Single-nucleotide polymorphism (SNP) Common single-base-pair variation in DNA.
Soap The mixture of salts of fatty acids formed on saponification of animal fat.
Solid A substance that has a definite shape and volume.
Solubility The maximum amount of a substance that will dissolve in a given amount of solvent at a specified temperature.
Solute A substance dissolved in a solvent.
Solution A homogeneous mixture that contains particles the size of a typical ion or small molecule.
Solvation The clustering of solvent molecules around a dissolved solute molecule or ion.
Solvent The substance in which another substance (the solute) is dissolved.
Specific gravity The density of a substance divided by the density of water at the same temperature.
Specific heat The amount of heat that will raise the temperature of 1 g of a substance by 1 °C.
Specificity (enzyme) The limitation of the activity of an enzyme to a specific substrate, specific reaction, or specific type of reaction.
Spectator ion An ion that appears unchanged on both sides of a reaction arrow.
Sphingolipid A lipid derived from the amino alcohol sphingosine.
Spontaneous process A process or reaction that, once started, proceeds on its own without any external influence.
Standard molar volume The volume of one mole of an ideal gas at standard temperature and pressure (22.4 L).
Standard temperature and pressure (STP) Standard conditions for a gas, defined as 0 °C (273 K) and 101,325 Pa (1 atm) pressure.
State of matter The physical state of a substance as a solid, a liquid, or a gas.
Stereochemistry The study of the relative three-dimensional spatial arrangement of the atoms in a molecule.
Stereoisomers Isomers that have the same molecular and structural formulas, but different spatial arrangements of their atoms.
Sterol A lipid whose structure is based on a fused tetracyclic (four-ring) carbon skeleton.



Straight-chain alkane An alkane that has all its carbons connected in a row.
Strong acid An acid that gives up H^+ easily and is essentially 100% dissociated in water.
Strong base A base that has a high affinity for H^+ and holds it tightly.
Strong electrolyte A substance that ionizes completely when dissolved in water.
Structural formula A molecular representation that shows the connections among atoms by using lines to represent covalent bonds.
Subatomic particles Three kinds of fundamental particles from which atoms are made: protons, neutrons, and electrons.
Subshell (electron) A grouping of electrons in a shell according to the shape of the region of space they occupy.
Substituent An atom or group of atoms attached to a parent compound.
Substitution reaction A general reaction type in which an atom or group of atoms in a molecule is replaced by another atom or group of atoms.
Substrate A reactant in an enzyme catalyzed reaction.
Sulfonation The substitution of a sulfonic acid group ($-SO_3H$) for a hydrogen on an aromatic ring.
Supersaturated solution A solution that contains more than the maximum amount of dissolved solute; a nonequilibrium situation.
Synapse The place where the tip of a neuron and its target cell lie adjacent to each other.
Telomeres The ends of chromosomes; in humans, contain long series of repeating groups of nucleotides.
Temperature The measure of the amount of heat energy in an object.
Tertiary carbon atom (3°) A carbon atom with three other carbons attached to it.
Tertiary protein structure The way in which an entire protein chain is coiled and folded into its specific three-dimensional shape.
Theoretical yield The amount of product formed assuming complete reaction of the limiting reagent.
Thiol A compound that contains an —SH group, R—SH.
Titration A procedure for determining the total acid or base concentration of a solution.
Transamination The interchange of the amino group of an amino acid and the keto group of an α-keto acid.
Transcription The process by which the information in DNA is read and used to synthesize RNA.
Transfer RNA (tRNA) The RNA that transports amino acids into position for protein synthesis.
Transition metal element An element in one of the 10 smaller groups near the middle of the periodic table.
Translation The process by which RNA directs protein synthesis.
Transmutation The change of one element into another.
Triacylglycerol (triglyceride) A triester of glycerol with three fatty acids.
Triple bond A covalent bond formed by sharing three electron pairs.
Turnover The continual renewal or replacement of biomolecules; for protein it is defined by the balance between protein synthesis and protein degradation.
Turnover number The maximum number of substrate molecules acted upon by one molecule of enzyme per unit time.
Uncompetitive (enzyme) inhibition Enzyme regulation in which an inhibitor binds reversibly to the enzyme-substrate complex, blocking the binding of the second substrate to the active site.
Unit A defined quantity used as a standard of measurement.
Unsaturated A molecule that contains one or more carbon–carbon multiple bonds.
Unsaturated fatty acid A long-chain car-boxylic acid containing one or more carbon-carbon double bonds.
Urea cycle The cyclic biochemical pathway that produces urea for excretion.
Valence electron An electron in the outermost, or valence, shell of an atom.
Valence shell The outermost electron shell of an atom.
Valence-shell electron-pair repulsion (VSEPR) model A method for predicting molecular shape by noting how many electron charge clouds surround atoms and assuming that the clouds orient as far away from one another as possible.
Vapor The gas molecules in equilibrium with a liquid.
Vapor pressure The partial pressure of gas molecules in equilibrium with a liquid.

Vicinal Referring to groups on adjacent carbons.
Vitamin An organic molecule, essential in trace amounts that must be obtained in the diet because it is not synthesized in the body.
Volume/volume percent concentration [(v/v)%] Concentration expressed as the number of milliliters of solute dissolved in 100 mL of solution.
Wax A mixture of esters of long-chain carboxylic acids with long-chain alcohols.
Weak acid An acid that gives up H^+ with difficulty and is less than 100% dissociated in water.
Weak base A base that has only a slight affinity for H^+ and holds it weakly.
Weak electrolyte A substance that is only partly ionized in water.
Weight A measure of the gravitational force that the earth or other large body exerts on an object.
Whole blood Blood plasma plus blood cells.
X rays Electromagnetic radiation with an energy somewhat less than that of γ rays.
Zwitterion A neutral dipolar ion that has one + charge and one − charge.
Zymogen A compound that becomes an active enzyme after undergoing a chemical change.

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Functional Groups of Importance in Biochemical Molecules

Functional Group	Structure	Type of Biomolecule
Amino group	$-NH_3^+$, $-NH_2$	Alkaloids and neurotransmitters; amino acids and proteins (Sections 16.1, 16.3, 16.6, 18.3, 18.7, 28.6)
Hydroxyl group	$-OH$	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 14.1, 14.2, 20.1, 23.2)
Carbonyl group	$-\overset{\overset{O}{\|}}{C}-$	Monosaccharides (carbohydrates); in acetyl group (CH_3CO) used to transfer carbon atoms during catabolism (Sections 16.1, 17.4, 20.4, 20.8, 21.4)
Carboxyl group	$-\overset{\overset{O}{\|}}{C}-OH$, $-\overset{\overset{O}{\|}}{C}-O^-$	Amino acids, proteins, and fatty acids (lipids) (Sections 17.1, 18.3, 18.7, 23.2)
Amide group	$-\overset{\overset{O}{\|}}{C}-N-$	Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Sections 17.1, 17.4, 18.7)
Carboxylic acid ester	$-\overset{\overset{O}{\|}}{C}-O-R$	Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Sections 17.1, 17.4, 23.2)
Phosphates: mono-, di-, tri-	$-C-O-\overset{\overset{O}{\|}}{P}-O^-$ $-C-O-\overset{\overset{O}{\|}}{P}-O-\overset{\overset{O}{\|}}{P}-O^-$ $-C-O-\overset{\overset{O}{\|}}{P}-O-\overset{\overset{O}{\|}}{P}-O-\overset{\overset{O}{\|}}{P}-O^-$	ATP and many metabolism intermediates (Sections 17.6, 21.4, and throughout metabolism sections)
Hemiacetal group, Hemiketal group	$-\overset{\overset{OR}{\|}}{C}-OH$	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 15.7, 20.3)
Acetal group, Ketal group	$-\overset{\overset{OR}{\|}}{C}-OR$	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 15.7, 20.3, 20.5)
Thiols Sulfides Disulfides	$-SH$ $-S-$ $-S-S-$	Found in amino acids cysteine, methionine; structural components of proteins (Sections 14.8, 18.3, 18.8, 18.10)

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Amino group	$-NH_3^+$, $-NH_2$	Alkaloids and neurotransmitters; amino acids and proteins (Sections 16.1, 16.3, 16.6, 18.3, 18.7, 28.6)
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Phosphates: mono-, di-, tri-	$-C-O-\overset{\overset{O}{\|}}{P}-O^-$ (mono-) $-C-O-\overset{\overset{O}{\|}}{P}-O-\overset{\overset{O}{\|}}{P}-O^-$ (di-) $-C-O-\overset{\overset{O}{\|}}{P}-O-\overset{\overset{O}{\|}}{P}-O-\overset{\overset{O}{\|}}{P}-O^-$ (tri-)	ATP and many metabolism intermediates (Sections 17.6, 21.4, and throughout metabolism sections)
Hemiacetal group, Hemiketal group	$-\overset{\overset{OH}{\|}}{\underset{\underset{OR}{\|}}{C}}-$	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 15.7, 20.3)
Acetal group, Ketal group	$-\overset{\overset{OR}{\|}}{\underset{\underset{OR}{\|}}{C}}-$	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 15.7, 20.3, 20.5)
Thiols Sulfides Disulfides	$-SH$ $-S-$ $-S-S-$	Found in amino acids cysteine, methionine; structural components of proteins (Sections 14.8, 18.3, 18.8, 18.10)

Elements Essential for Human Life†

Element	Symbol	Function
Carbon	C	These four elements are present throughout all living organisms
Hydrogen	H	
Oxygen	O	
Nitrogen	N	
Arsenic	As	May affect cell growth and heart function
Boron	B	Aids in the use of Ca, P, and Mg
Calcium†	Ca	Necessary for growth of teeth and bones
Chlorine†	Cl	Necessary for maintaining salt balance in body fluids
Chromium	Cr	Aids in carbohydrate metabolism
Cobalt	Co	Component of vitamin B_{12}
Copper	Cu	Necessary to maintain blood chemistry
Fluorine	F	Aids in the development of teeth and bones
Iodine	I	Necessary for thyroid function
Iron	Fe	Necessary for oxygen-carrying ability of blood
Magnesium†	Mg	Necessary for bones, teeth, and muscle and nerve action
Manganese	Mn	Necessary for carbohydrate metabolism and bone formation
Molybdenum	Mo	Component of enzymes necessary for metabolism
Nickel	Ni	Aids in the use of Fe and Cu
Phosphorus†	P	Necessary for growth of bones and teeth; present in DNA/RNA
Potassium†	K	Component of body fluids; necessary for nerve action
Selenium	Se	Aids vitamin E action and fat metabolism
Silicon	Si	Helps form connective tissue and bone
Sodium†	Na	Component of body fluids; necessary for nerve and muscle action
Sulfur†	S	Component of proteins; necessary for blood clotting
Zinc	Zn	Necessary for growth, healing, and overall health

†C, H, O, and N are present in all foods. Other elements listed vary in their distribution in different foods. Those marked with a dagger are *macronutrients,* essential in the diet at more than 100 mg/day; the rest, other than C, H, O, and N, are *micronutrients,* essential at 15 mg or less per day.

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