Angelo Albini

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Past, Present and Future

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Preface

The chemical changes induced by light on substances have been long known. The advancement of this discipline has been somewhat irregular, however, with an outburst at the beginning of the twentieth century corresponding to the first in-depth preparative studies on one hand and to the development of quantum physics on the other hand, and a much more consistent development after 1950 when the general framework of this science was recognized.

As we now understand this phenomenon, absorption of a photon leads to an electronically excited state, characterized by high energy and a strongly perturbed electronic structure. The result often is an in-depth—but selective—chemical transformation. As everyone can easily appreciate, photochemistry has a key role in nature (e.g., chlorophyll photosynthesis, vision) and in a variety of applications. Photography and other methods of reproducing an image, the fast hardening of varnishes and of dental cement, and many other applications are based on photochemical reactions.

Furthermore, photochemistry has a particular role in learning and teaching chemistry, as was recognized already in 1926 (see Sect. 2.5), in that it concerns *all* of the electronic states of a given species, in particular the lowest singlet excited and triplet states, not only the lowest-lying (ground) one as does normal (thermal) chemistry. Thus, not only one but at least two new dimensions are added to chemistry by light absorption, and learning how to exploit and direct the system toward a specific goal is one of the main issues of future time's chemistry. Retracing the path that has led to the present state of photochemistry may give some hints of those that still lay open to exploration.

What has been attempted here is to understand the actual experiments and the intellectual effort that have led to the development of this wonderful discipline, and perhaps to extend the enthusiasm of scientists already engaged in the field toward new facets of it.

I would have not expected writing this book to be such a hard task. I am grateful to the many scientists from whom I had the opportunity to learn over the years and I hope that the many inefficiencies of the manuscript will be indicated to me. The colleagues who helped me in this adventure are thanked for their enthusiasm and competence (prof. Maurizio Fagnoni, drs Stefano Protti, Davide Ravelli, Stefano Crespi, and prof Elisa Fasani). My sons and my friends, in particular Mr Nicola Scuro, are likewise thanked for their help.

Pavia, Italy Angelo Albini

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Chapter 1
Early Times of Photochemistry

1.1 Introduction

The perception of light is one of the fundamental experiences of living beings and its power to reveal the world has always been recognized. In Genesis, creation of matter is immediately followed by creation of light that allows to detect the created world through its forms and colors:

And God said:
Let there be Light,
and there was Light.
And God saw the Light, that it was good;
and God divided the Light from the darkness.
(Genesis I: 1–4)

Similar tales are present in the oldest texts of other cultures. The deepest impressions are expressed as an overwhelming flood of light, as Dante mentions for the vision of Paradise:

I think the keenness of the living ray
Which I endured would have bewildered me,
If but mine eyes had been averted from it
(Paradise XXXIII: 76–78)

Light reveals matter through what is the most powerful sense for humans, sight, and indeed the more so in contemporary society where the other senses have in part lost their role. Not only that, light is also able to modify living beings, and this in a way that is vital for them. Thus, mankind always perceived the relation between the long days of solar irradiation in summer and the abundance of the fruits Earth produced in that time and has attempted to exploit in the best way such an inexhaustible source of energy and of materials. This has been achieved through

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agriculture, the science and technique that improves the harvest unperturbed nature produces, arriving at much better results (from men point of view). The beginning of modern human culture is generally taken as the moment when previously nomadic populations permanently settled. A more abundant harvest has been necessary for the increasing population and has always been sought by mankind, whether through ceremonies and sacrifices to the god sun in ancient times or by introducing innovative agrochemical techniques in the modern ones.

The advancement of society has seen a more and more pervasive role of light. Indeed, light was often taken as the symbol itself of progress guided by science. This was enlightenment, out of the darkness of earlier, less technologically advanced times. A celebrated example is the ballet "Excelsior" that was staged at La Scala theatre in Milan in 1881 (story by Manzotti, music by Marenco) that culminated in the triumph of light. Or at least, this was the predominating view (at least among the upper classes) in the rapidly growing western world, in particular during the industrial development from the eighteenth century up to the early years of the twentieth century. Although an optimistic overall attitude based on the confidence in a continuous improvement of mankind conditions may be no more predominating 100 years afterward, vision-based communication develops at an increasing pace and is more and more at the basis of society, with such media as the net and television pervading everyday life.

As mentioned above, light has a strict relation with the modification of matter and thus with the science that studies it, that is chemistry, through a dedicated discipline, photochemistry. This has extended to an unbelievable variety of applications, certainly primarily concerned with the reproduction of images, but involving many other cases where the characteristics of light, that is, the high-energy of UV and visible quanta and the possibility to deliver them when, where, and how desired offer a decisive advantage, from building and operating "intelligent" materials or machines to carrying out complex manipulations (including surgery) at the submicroscopic level and to innumerable further applications.[1]

As illustrated in Sect. 2.5, already in 1926 it was remarked [1] that photochemistry is concerned with all of the electronically states of chemical entities, and thus in a sense it is photochemistry that includes chemistry and not vice versa, since ground states are but a particular case of electronic states. Furthermore, comparing the reactivity of excited states with that of the corresponding ground states makes particularly apparent the direct relation between chemical properties and electronic structure of each species and thus the role of the electronic structure in the reactions of chemical species. In view of this situation, it may be thought that all chemistry, through photochemistry, is included in atomic physics, the science that studies the intimate structure of the matter and thus the electronic structure of atoms and molecules. This peculiar relation endows photochemistry both with a particularly

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[1] Sensu stricto, if the prefix photo is taken etymologically, this science should be limited to the effect of visible light, but of course the affinity of UV and visible-light photochemistry is too strict for allowing a separate treatment.

rich approach for understanding and teaching chemistry - and science in general - as well as with a rich vision toward innovation.

As a matter of fact, the applications of photochemistry are so rich and diverse that the relation with a common basic discipline tends to be lost. This is unfortunate, because the abovementioned central role of photochemistry is a continuous source of inspiration and there is much to gain from conserving a unified point of view. In this sense, some historic knowledge is helpful, as always in science. The present volume is not a proper history of photochemistry, but rather a discussion of some turning points during the formation of the basic postulates of photochemistry and an attempt to present some directions of future development.

1.2 Light and Chemistry

Of the two parts of the word photochemistry, the former one refers to the discipline that arrived first at a fully scientific description. The advancement of the understanding of what is light advanced rapidly from the experiments on the dispersion of (visible) light and the corpuscle theory of colors by Newton (1704) [2] and the discovery of ultraviolet (Ritter, 1801) [3] and infrared (Herschel, 1800) [4] components to the formulation by Maxwell of the equations for the electromagnetic field (1862–1864) and then to the theoretical contributions by Planck that concluded that a black body emits light only in discrete bundles (quanta, 1900) and by Einstein that viewed all quanta of light as actual particles (1905). These were later called photons (as proposed by G. N. Lewis, 1926) in analogy to other elementary particles that had been discovered, such as electrons and protons (and then phonons, plasmons). The study of light-related effects is the core of modern physics and set the stage for a particular role of photochemistry in that it combines photons with molecular structure and thus with the properties of electrons and protons. Lewis conceived photons as actual particles, different from the light they transported.

“Whatever view is held regarding the nature of light, it must now be admitted that the process whereby an atom loses radiant energy, and another near or distant atom receives the same Energy, is characterized by a remarkable abruptness and singleness. We are reminded of a process in which a molecule loses or gains a whole atom or a whole electron but never a fraction of one or the other… Had there not seemed to be insuperable objections, one might have been tempted to adopt the hypothesis that we are dealing here with a new type of atom, an identifiable entity, uncreatable and indestructible, which acts as the carrier of radiant energy and, after absorption, persists as an essential constituent of the absorbing atom until it is later sent out again bearing a new amount of energy. If I now advance this hypothesis of a new kind of atom, I do not claim that it can yet be proved, but only that consideration of the several objections that may be adduced shows that there is not one of them that can not be overcome. It would seem inappropriate to speak of one of these hypothetical entities as a particle of light, a corpuscle of light, a light quantum, or a light quant, if we are to assume that it spends only a minute fraction of its existence as a carrier of radiant energy, while the rest of the time it remains as an important structural element within the atom. It would be also cause confusion to call it merely a quantum, for later it will be necessary to distinguish between the number of these entities present in an atom and the so called quantum number. I therefore take the liberty of proposing for this hypothetical new atom, which is not light but plays an essential part in every process of radiation the name photon." Lewis postulates that the total number of (intrinsically identical) photons was constant in an isolated system. Serious objections against this idea of the conservation of photons could be raised on the basis of the thermodynamics of radiation and of the laws of spectroscopy. As mentioned, Lewis thought that they could be overcome, but this theory was never accepted and seems unpalatable today, although this is the last manifestation of the view of light as one of the "imponderables" that can be accumulated in matter, a representation that has a long tradition (see Sect. 2.3). The name photon, however, remained and became of general use [5, 6].

1.3 Historic Notes

As mentioned, the observation of chemical effects of light is as old as mankind itself. Accounts of the earlier history of photochemistry have been presented by several authors. Long erudite lists of reference are of little usefulness, however. Here, it has been chosen to present a brief historic profile based on a document itself of historic value, the introduction written by a great authority, professor Ivan Plotnikov. This well-known Russian-born scientist published in 1910 a book on photochemistry which was followed in 1936 by a second, much extended, edition of over 900 pages. The view he had on this science, or at least on some aspects of it, in particular the unconditioned refusal of the Stark–Einstein "equivalence law," appeared obsolete at the time of the second edition, as it is discussed in Sect. 2.3. However, Plotnikov can certainly not be accused of insufficient knowledge of the matter or of insufficient exploration of the literature and his book is a rich mine of data and thoughts [7].

The chapter devoted to the historic aspects of photochemistry in Plotnikov's book may thus offer a convenient approach. The key early events are presented and discussed with reference to three periods, by adopting a scheme that he thinks had general validity. The first one, during which much experimental material was collected and progressively acquired a scientific character, lasted, he thought, until the first third of the nineteenth century. Apart the role sunlight had in monotheistic religions and cultures, he lists a series of important events, of which some are reported below, as characterizing this period:

- 50 BC—Vitruvius mentions the light-induced fading of paintings.
- 1342 AC—Petrus de Alexandria describes the camera obscura (in principle, already known to Aristotle's).
- 1575—Niccolò Monardes in Venice reports the fluorescence of lignum nephriticum.

- 1602—Casciarolo in Bologna reports the phosphorescence of feldspar.
- 1674—Brand in Homburg reports the chemical luminescence of phosphor.
- 1725–1757—Several reports on the light sensitivity of inorganic salts appear ($FeCl_3$, $AgNO_3$, AgCl) and applications for sympathetic inks and for reproducing images are published.
- 1782—After several partial reports (by Priestley, Bergmann, Scheele, Ingenhousz), Senebier publishes a comprehensive and successful book on the effect of solar light on plants, oils, dyes, wood, etc. This not only mentions that silver chloride blackens at light but also that this darkening depends on the color of the light.
- 1785—Berthollet reports the photocleavage of HCl.
- 1790—Saussure builds the first photochemical photometer, based on the development of gas by irradiation of chlorine water.
- 1802—The first photographs on silver paper by Wedgwood and Davy.
- 1814—Nièpce and Daguerre begin their work on photography.
- 1817—Grotthuss formulates the law that only absorbed light has a chemical effect while studying the photodecomposition of iron salt solutions.

After this period, the moment would have been mature for the full blowing of photochemistry as a science, as it happened with most disciplines. Unfortunately, at least in the opinion of Plotnikov, a major stumbling block intervened, viz., the enormous success of photography that concentrated the effort on technical aspects of the chemistry of the silver salt emulsion, the sensitization, the stability of images, and so on. Therefore, this is named the “technical–photographic period” and the purely scientific advancement had been less significant that it may have otherwise be. Furthermore, when a scientific issue was confronted, then the topic was ill chosen. Thus, the first photochemical kinetic study was devoted to the formation of hydrogen chloride from the components by Bunsen and Roscoe in the1850s [8, 9].

These authors found in their initial study that the progress of the reaction was proportional to light intensity and time of irradiation. Unfortunately, this held only under the conditions they had chosen, that is, under removal of the product and by maintaining constant the concentration of the reagents. Then, they found a more complex course in the presence of moisture and air and furthermore observed an induction period. The authority of Bunsen spurred a large number of scientists to concentrate their efforts on the study of this really complex reaction, perhaps retarding the development of photochemistry in general. Apart from these considerations, Plotnikov lists several key events of this second period lasting until the last years of the nineteenth century, some of which are indicated below:

- 1838—Preparation of the first daguerreotype.
- 1839—Ponton discovers the sensitivity to light of paper tramped with a potassium bichromate solution.
- 1843—Draper rediscovers, independently from Grotthuss, that only absorbed light is chemically active.
- 1850—Regnault discovers the development of images by pyrogallol.
- 1851—Archer discovers the properties of collodium.

- 1852—Beer formulates the light absorption law.
- 1869—Fritsche discovers the dimerization of anthracene and other substances.
- 1869—Timiriaseff and Engelmann study quantitatively the assimilation of carbon dioxide by green plants.
- 1872—Baumann discovers the photopolymerization of vinyl chloride.
- 1875—Balmer discovers the line structure of the hydrogen spectrum.
- 1879—Eder describes a mercury-oxalate photometer and establishes that photochemical reactions have no temperature coefficient.
- 1894—Joly reports the first trichromatic print.

In the third part of his historic introduction, Plotnikov notices that, as it is generally the case for a mature science, the development of contemporary photochemistry was characterized by the advancement in theory coupled with the advancement in experimental methods and instruments. The possibility of obtaining quantitative data about the amount of light and matter in photochemical reactions and the availability of convenient mercury arcs in substitution of solar light opened the way for new applications. The initial phase of the development of every discipline, "in which an accumulation of experimental data takes place, and confusion of opinion prevails," had been overgrown and photochemistry had arrived where fundamental laws are established. This phase "always represents a turning-point in the history of a given branch of science… characterized by great intellectual exertion on the part of the leading investigators, as well as by the sharp clash of mutually opposing tendencies." A number of books were printed [10–12], besides Plotnikov's own, that related on the whole of photochemistry, whereas in previous periods these had been practically limited to photography [13]. Single events that Plotnikov considered important included:

- 1897—Kinetic characterization of the HI photolysis by Bodenstein.
- 1900—Ciamician and Silber begin their work on organic photochemistry.
- 1905—Trautz formulates a theory of chemiluminescence.
- 1904–1907—van't Hoff suggests and Lazareff demonstrates the proportionality between absorbed light and reaction (quantitative application of the Grotthuss law).
- 1907—Warburg publishes the first paper on energy measurements in a photochemical reaction.
- 1908—Plotnikov builds his light thermostat.
- 1908—Stark suggests that a molecule requires a quantum for reacting.
- 1908—Stobbe discovers the photochromism in the case of fulgides.
- 1910—D. Berthelot begins his studies on the photochemistry of organic compounds.
- 1912—Einstein gives a thermodynamic base to the Stark hypothesis on the light quantum.

Although a lessening of the rate of the scientific advancement in photochemistry after the war was noticeable, Plotnikov hoped that this would have not lasted long and the discipline would early find a shared, comprehensive theory as well as new applications (he thought particularly of biology and medicine).

Plotnikov had been somewhat hasty in judging that photochemistry had become a mature science in 1930. In fact, many seeds were close to germinate, the paradigms of photochemistry had been not yet formulated, the number of known photochemical reactions was too small for reaching generalizations, and apart from the fact that in many cases it was difficult to recognize which chemical change occurred upon irradiation, key instruments that were able to afford a more detailed view of excited states had yet to be devised and assembled.

In the present case, further extending his list of key dates would lead to a treatise of photochemistry that may be conveniently found elsewhere. This will not be attempted, therefore, and only a few indications are given of the main instrumental advancements that made possible to understand the complex mechanism of photochemical reactions. A list of dates can at any rate be found in the Webster's timeline history [14]:

- 1933—Jabłonski proposes a metastable electronic state for the long-lived emission of some dyes.
- 1940–1946—Lewis and Kasha recognize the role of triplet state and introduce the state diagram.
- 1950—The role of triplet states in photochemical reactions is recognized.
- 1950—Flash photolysis instrument.
- 1950—The availability of modern chromatographic and spectroscopic techniques makes possible to discover (and sometime rediscover) many photochemical reactions; quantum yields are routinely determined.
- 1955—Steady-state luminescence routinely investigated for the role of excited states, excited complexes, electron/energy transfer, and intermediates; steady-state luminescence in rigid media.
- 1965—Time-correlated single-photon counting techniques for determining the lifetime of short-lived excited states.
- 1970—Laser flash photolysis.
- 1970—Photochemical reactions in rigid matrix (rigid solvent, codeposition with inert gas) with spectroscopic detection.
- 1980—Laser flash photolysis with IR detection.

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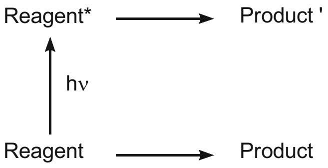
Chapter 2
The Framework of Photochemistry: The Laws

The conceptual framework of photochemistry is now firmly established. Excellent introduction to this discipline can be found in several recent books and appropriate definitions for vocabulary of photochemistry have been published [1, 2]. The key point is that this discipline is better defined as the chemistry of electronically excited states and actually treats the chemical reactions of such states. The absorption of a photon is simply the most convenient way for generating them (Scheme 2.1), although there are also thermal entries to excited states.



Scheme 2.1 Different courses of photochemical (from an electronically excited state) and thermal (from the ground state) reactions

The chemical behavior of excited states is quite different from the corresponding ground state species, because of the different electronic structures. This perfectly fits in the frame of present-day chemistry, where it is customary to rationalize reactions on the basis of the electronic structure. However, arriving at such a view involved a long and difficult path, where early investigators had to combine chemical results with the new vision of the intimate nature of the matter physicists were revealing at the time. The difficult step was in fact recognizing the peculiar object of this discipline, viz., electronically excited states, and overcoming the tendency to depict the chemistry observed as some kind of catalysis operating on a "normal" (ground state) chemical reaction. This is apparent already in the language, where often terms such as "photocatalyzed," "photoinduced," and "photo-accelerated" reactions were used, in preference to straightforward photochemical reactions, in an attempt to

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incorporate photochemical reaction into the large realm of catalytic chemistry. These terms continued to be used much after that the role of excited states had been clarified and are basically inappropriate because, unlike catalytic effects that open new paths in the *ground* state surface, here one has reactions starting from a high-lying state located on a *different* surface (see further below).

This approach was not accessible to early investigators that noticed the effect light had upon matter. In which way light caused a chemical effect? The search for a relation between light and reaction observed led to the formulation of what are now known as the "laws" of photochemistry. More detailed questions had to be answered then. Could the kinetic methods that had been found so useful for thermal reactions be applied to light-induced reactions? Were light-induced reactions basically different from their thermal counterpart? Were different intermediates involved? By answering to these questions, the framework of photochemistry was gradually built, mainly in the period 1910–1960, and may be discussed under two headings, the laws of photochemistry and the state diagram.

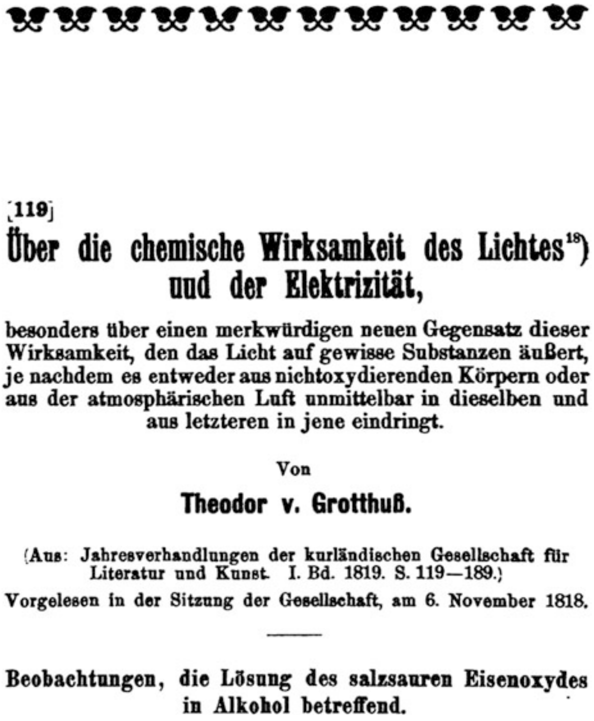
2.1 The Relation with Light Wavelength

The first topic concerns the two "laws of photochemistry" that correspond to the following (or similar) statements:

1. Only light which is absorbed by a system can cause chemical change (first law, Grotthuss or Grotthuss–Draper law).
2. For every quantum of light that is absorbed, one molecule of substrate reacts (second law, Einstein or Stark–Einstein law).

These statements are not fully satisfactory in such a form and are usually reported along with some specifications. On the other hand, they may sound as a mere obviousness if, as everybody concurs at present, in every case it is one electronically excited state, formed by absorption of one photon, that reacts in some way (see Scheme 2.1). Actually, one may think that there is no need of laws of photochemistry, and several textbooks dispense with this notion. At any rate, it seems wortwhile to retrace the intellectual path underlying. Starting from the first law, that light needs to be absorbed to have a chemical action seems obvious and, importantly, easy to check. In the everyday practice, its application is taken for granted, and actually the first move when planning a photochemical reaction is (or rather should be for the wise experimentalist) measuring the absorption spectrum of the reagent and checking that the emission spectrum of the lamp used does overlap at least to some degree with it; otherwise, there is little hope to obtain any chemical effect. However, we are the great grandchildren of the scientists that established this principle, and when this was done, there was little experimental support. Thus, checking whether light was absorbed was not an easy and precise operation as it is now.

Let us consider a photochemical experiment as it was carried out by the baron Theodor Grotthuss, then living in his native Courland, a part of modern day Latvia [3–5] (Fig. 2.1).



[119]

Über die chemische Wirksamkeit des Lichtes[18]) und der Elektrizität,

besonders über einen merkwürdigen neuen Gegensatz dieser Wirksamkeit, den das Licht auf gewisse Substanzen äußert, je nachdem es entweder aus nichtoxydierenden Körpern oder aus der atmosphärischen Luft unmittelbar in dieselben und aus letzteren in jene eindringt.

Von

Theodor v. Grotthuß.

(Aus: Jahresverhandlungen der kurländischen Gesellschaft für Literatur und Kunst. I. Bd. 1819. S. 119—189.)

Vorgelesen in der Sitzung der Gesellschaft, am 6. November 1818.

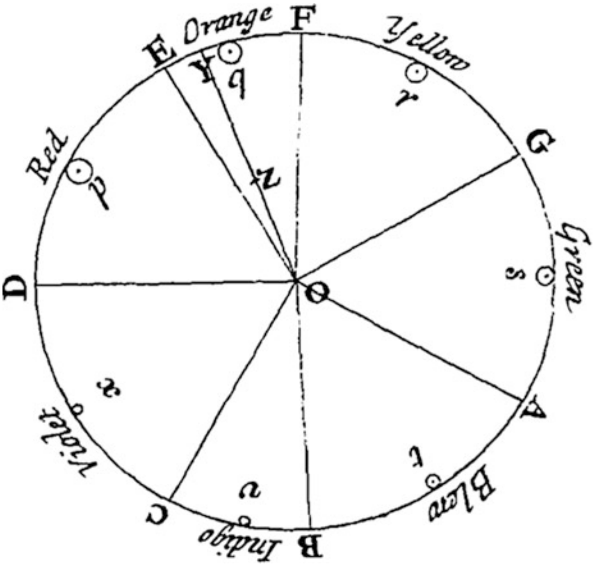
Beobachtungen, die Lösung des salzsauren Eisenoxydes in Alkohol betreffend.

Fig. 2.1 Title page of the well-known paper by Grotthuss on the chemical action by light; see [6]

High-born Grotthuss carried out his experiments in the family palace, but certainly was no simple-minded amateur, had an excellent background, and gave important contributions to photochemistry and, even more extensively, to electrochemistry. He published his research in several European journals, but the photochemical part is contained in a detailed paper presented at the Academy of Courland. There he reported several experiments about the effect of light on salts and the different results depending on whether air was present or not [6].

He remarked that no satisfactory general rationalization was available; in particular the proposal by Rumsford that light simply heated the sample was untenable. He further explored the matter and in particular proposed to determine whether light of different colors had a different chemical effect. From his observations he concluded that "independently on its chemical nature, each body reacts more strongly to the color that is complementary to that it shows in the normal state. As an example, when a red light falls onto a red body, this either goes through undisturbed, if such body is transparent, or is reflected with no loss if it is not transparent. However, if a blue-green light ray (complementary to the red in the Newton wheel [7]; see Fig. 2.2) hits the same body, then in both cases, much of the ray is absorbed, that is, it penetrates with difficulty in the defects of the substance of the body. This had to be, at least in many cases, the cause of a large chemical effect.

Fig. 2.2 Newton wheel of complementary colors; see [7]



Should not the white silver chloride thus be transformed in the darkest colors of the spectrum, since these colors are mainly complementary to its bright color and therefore find the biggest resistance to the penetration in the substance and stay there longer?. . .Should not the flea-colored lead oxide, to the color of which dark violet is the least similar hue. . .be most extensively transformed (reduced) by the less refracted rays (violet), if these were not the most contrasting ones to its own color?" Several further examples follow in the list by Grotthuss, all of them indicating that only colors absorbed are chemically active. In his pictorial view, "light strives to pursue as easily as possible its path in the substance in which it penetrates, and this tendency has to be the larger, the less similar is its color to the natural color of the substance". And the color of a substance had to do with its structure. Already Newton had found that the ray of a color could go through transparent bodies only when the appropriate oscillations or separation into elementary parts was possible ("accessus facilioris transmissionis et reflexionis luminis," access of light more easily transmitted and reflected). At the places where this did not happen, the colored light did not go through but was reflected and/or absorbed (i.e., transformed into heat) in a way that "depended on the nature of the substance hit by light." Grotthuss thus suggested both optical properties and photochemical reactions had a common origin in the structure of a substance.

After these initial observations, Grotthuss developed two chemical systems well suited for finally answering the question of the dependence on the color, because their high sensitivity allowed a fast comparison. These were the intensely red iron rhodanide (or thiocyanate) and the blue iodine complex with starch, both of which faded under irradiation. In the experiment, two thin tubes 18-cm long and 0.6-cm diameter were filled with these solutions, a stopper was inserted, and the tubes were placed on the floor in front of a prism dispersing bright solar light over a spectrum 12-cm broad. In these thin tubes mixing of the aqueous solution was very slow, actually occurring to a significant extent only when the tube was strongly shacken, as Grotthuss tested. He took care to shift the tubes in such a way that the same color fell always on the same spot, while the direction of solar rays changed during the day. After 3 hours he lifted the tubes with care and observed the discoloration. The rhodanide tube was fully discolored at the center of the spectrum (corresponding to blue green) and more and more conserved as long as one proceeded toward either extreme (orange, red on one hand; dark blue, violet, on the other one).

The iodine solution was markedly discolored where it had been hit by the yellow ray and, when carefully replaced in front of the refracted light, fully bleached in that part after a further hour exposure. Thus, the color complementary of that of the solutions was both absorbed and chemically active, or as Grotthuss put it, light of a color tended to destroy the body that has a color contrary to its own and to conserve that that has the same or a similar one. This observation was occasionally verified by other scientists [8].

Grotthuss further prepared an instrument for measuring light intensity, a "chemical photometer," built by connecting by short tubes a series of spherical flasks of increasing volume. This was filled with the rhodanide solution and a stopper was inserted in order to avoid contact with the atmosphere. When exposed to solar light, the content of each flask bleached, starting from the smallest one and progressing to the larger ones, each becoming colorless at regular time intervals, provided that solar radiation remained constant (Fig. 2.3). This, he observed, would have been a convenient instrument for measuring the intensity of solar light all over the world.

Further important points that he demonstrated, against the suggestion of previous scientists, are (1) that neither a specifically oxidizing nor a reducing effect could be attributed to light, since under irradiation oxidations take always place along with reductions; (2) that a specific color cannot be connected with a specific chemical action, but only the fact that it is absorbed or not determines whether it has some action; and (3) that photochemical reactions are not caused by heat originating from light absorption.

As a matter of fact, Grotthuss stated very clearly his findings but was not the first to arrive at these conclusions [9]. Under the title "On the power light per se has of changing not only colors, but sometimes also the surface of things, leaving the colors unchanged," a "commentary" from the Academy of Sciences and Arts in Bologna reports a discussion of the theme that took place in 1757 and the contribution by Beccari. This scientist is well known for his experiments on the phosphorescence of minerals and on bioluminescence. In this case, it was question at the academy of how to conserve the beauty of flowers, and one of the academician suggested protecting them from the contact with air. "Why not from light?," added Beccari. The proposal was judged new, but many were not convinced that colors could be changed by light. Beccari answered that not only the color but also the surface of materials could be altered and then referred to his experimental work. He was interested by a previous observation by Duhamelius, who had found that "the secretion of a shell when exposed to sun light, became crimson, and the more so, the stronger was light. … However, while a cloth bathed in that liquid became red when exposed to the sun,

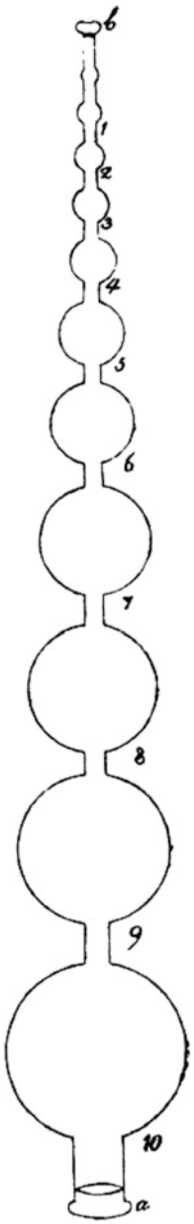


Fig. 2.3 Chemical photometer by Grotthuss. Exposing to a constant light, balls filled with the actinometer bleach one after the other; see [6]

even when covered by a rather thick glass, this did not happen when it was covered by a brass foil, thin as it may be. Glass was able to transmit light, the metal foil not at all." This hypothesis was confirmed by Beccari (compare Sect. 4.4.1). He noticed that a sample of "luna cornea" (silver chloride) was white when freshly prepared but after some time tended to take a yellow hue and later turned almost to violet (the AgCl activation by invisible UV light was noticed by Ritter; see Sect. 1.2). He attributed this change first to air and second to light. He checked this point experimentally in this way. He placed a sample of luna cornea in a glass container and put this at 8 ft from a window, so that solar light flooded it. After some time, he remarked that the part of the sample that faced the window—and received more light—had become violet, while the opposite face—that was not exposed to light—retained the original color. It could be concluded that light exerted an impulse toward color change. For confirming this, Beccari turned the container in such a way that the back face was now turned toward the window. And to make the experiment still more convincing, he covered half of the container by a dark screen, in order to see what would happen in the covered part. Indeed, all of the samples became violet, except the part covered by the screen, where the initial color was conserved, and this clearly supported the role of light in changing colors, even if air had its own. Beccari then reported further experiments carried out by the late G. Bonzius by exposing strips of paper dyed by various substances to light in air. By comparison he also explored the effect upon exposing some of these strips to light after having evacuated the containers and also by keeping them in the dark at a temperature higher than that reached under solar irradiation. He found that some of the dyes were bleached even in the absence of air and concluded from these experiments that light had per se the power of affecting colors. Thus, the notion that absorption was required for chemical action of light was present in the scientific literature around the world, but apparently only locally, and did not reach a large diffusion [10, 11].

Two decades after Grotthuss report and not being aware of it, William Draper[1] proceeded after similar lines and investigated in which way light and light-sensitive substances interacted. His purpose was highly practical, he aimed to enhance the corrosion of exposed photographic plates, in order to produce engraved (and thus stable) Daguerreotypes by deep etching, and he was actually successful in this project. In this technique, the image was formed on a silvered metal plate that had been activated by exposing it to iodine vapor. After exposing in the camera, the image was revealed through the action of mercury fumes, but the stability of the image remained moderate. Draper prepared a light-sensitive plate by iodization at the appropriate level and exposed it “to the diffuse light of the day, setting it in such a position that it behaved like a mirror and reflected the light falling upon it through the window to the objective of a camera oscura, which formed an image of it upon a second sensitive plate.”

As soon as the first plate had become brown, the scientist closed the opening of the camera, “mercurialized” the plate, and found that the rays reflected by the first plate “had lost the quality of changing silver iodide in silver.” Thus, the rays which had impinged on the surface of yellow silver iodide “had lost the quality of causing any further change on a second similar plate.” In other words, the active color had been absorbed by the first plate and was no more present in the reflected ray.

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[1] Professor at the University of the City of New York and founding president of the American Chemical Society.

Furthermore, he illuminated an iodinated plate through a solar spectrum formed by a prism and after 5 min "mercurialized" the plate. He found that the less refrangible colors (blue violet) produced the strongest blackening, and the other end of the spectrum also had some action, though a lower one. On the other hand, the center of the spectrum corresponding to the yellow light had no effect at all.

Several further experiments were carried out, in every case supporting that the silver iodide present on the plate reflected yellow light, which had no effect on it, and absorbed the other rays that on the contrary caused a chemical effect. The ray absorbed also caused heating of the sample [12].

Draper built a light concentrator based on a convex lens that had been prepared in such a way that the focal point remained the same during all of the sun progress in the sky. The sample was placed in that point and irradiated. Considerable heath was evolved, as shown by the melting of various substances, including silver chloride. In chlorine water, water was consumed much faster than it was by exposure to non-concentrated light, and iron oxide oxalate evolved carbon dioxide and led to a precipitate of the Fe(II) oxalate, likewise at a much enhanced rate.

However, a ray that had caused the reaction of a chlorine water solution caused no more reaction when directed on a second tube containing the same solution. In a particularly convincing experiment, when a tube containing a solution of iron(III) oxalate was placed within a larger tube containing the same solution, reaction in the internal tube began only after that the external part had been completely consumed. Many other experiments were carried out with oxides and sulfides, and concentrated light had results not different from those obtained under non-concentrated light; only the rate was increased. Draper arrived at the conclusion that the chemical effect could not be separated from the absorption of light and was proportional to it. In conclusion, the chemical action produced by the rays of light depended upon the absorption of those rays by sensitive bodies, just as an increase of temperature is produced by the absorption of heat (or at least this is the comparison that he drew).

2.2 Relation with Light Intensity

In order to support the hypothesis of the proportionality between chemical action and intensity of the light ray, Draper set up to prepare a convenient instrument for measuring light intensity (recall that the experiments were done with solar light or by using flames as light sources). Those previously used were admittedly not sufficiently sensitive and precise, and the result was subjective, e.g., it depended on the observer's opinion to establish whether a Daguerro-type plate was stained or not. He chose as a reference the reaction between hydrogen and chlorine as a highly sensitive system, "affected by rays of the feeblest intensity and of the briefest duration." He called the instrument "tithonometer" [13] because this was meant to measure Tithonic light, a name he introduced in order to design specifically the chemically active light. The name arose from that of Τιθωνος, semi-god and lover of Ηως, the sunrise, and thus was, he thought, a more precise alternative to actinic light (from the Greek ακτις, ray). The instrument he built "consisted in a glass tube bent into the form of a siphon, in which chlorine and hydrogen could be evolved from muriatic acid, containing chlorine in solution, by the agency of a voltaic current" (Fig. 2.4). Passing the current through Pt electrodes in x, y develops hydrogen and chlorine that fill the transparent tube a–c that is protected from light by a cap. When the two gases have filled the tube and the system is in equilibrium (with the components in exactly equal amounts), which requires a few seconds (and presumably an admirable skill), the cap is taken away from the "sentient" part, the tube a–d, and thus exposed to light. The gases begin to react and the liquid in siphon c–f to descend (Fig. 2.4). Periodical reading gave a constant result when a lamp of constant intensity was used and Draper concluded that the effect caused by light was proportional to the intensity.

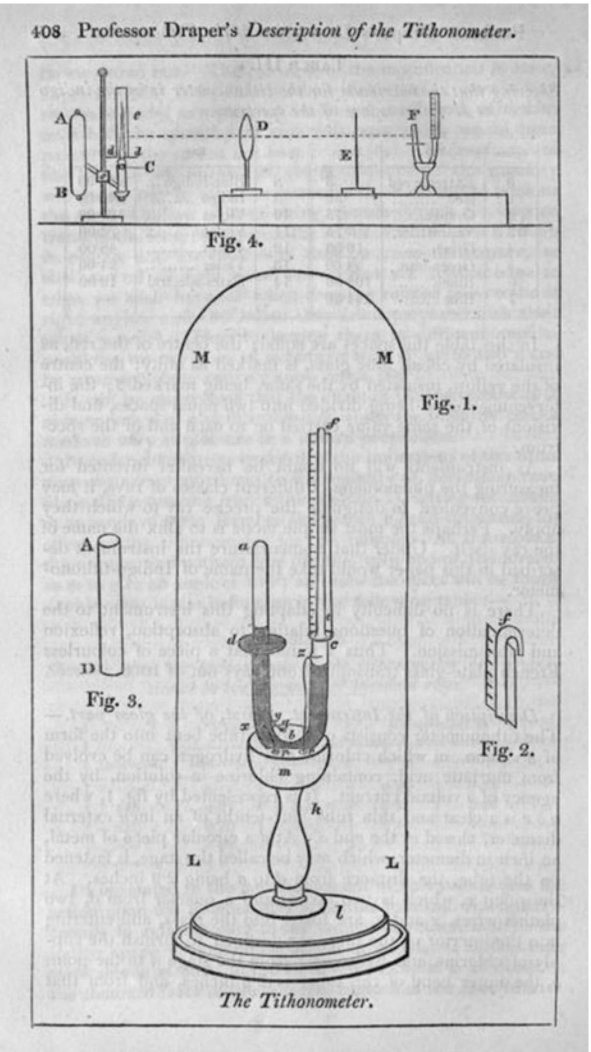

Fig. 2.4 The tithonometer by Draper. A mixture of hydrogen and chlorine is prepared by electrolysis in the tube a–d. When this is exposed to light, the change in volume of gases is monitored in the tube c–f; see [13]

This result was challenged both qualitatively and quantitatively. Thus, Herschel did think "that the rays effective in destroying a given tint, are in a great many cases, those whose union produces a color complementary to the tint destroyed, or at least one belonging to that class of colors to which such complementary tint is to be referred," but admitted that this rule was not general and that it "was to be interpreted with considerable latitude" [14]. From the quantitative point of view [15], the majority of researchers in photochemistry tended to assume that the amount of chemical change in a given system effected by light of a specified wavelength was proportional to the light absorbed and later studies appeared to support the validity of the original experiment [16], though very delicate.

The above statement was referred to as the Draper law or, when the Grotthuss paper was rediscovered, the Grotthuss–Draper law, generally stated in a qualitative, rather than quantitative, way. Notice that the quantitative aspect, indeed quite important in both of the original proposals by the two scientists, was rather referred to as the Bunsen–Roscoe law. This was stated as "in two photochemical reactions, if the product of the intensity of illumination and the time of exposure are equal, the quantities of chemical material undergoing change will be equal" [17].[2]

Plotnikov later took pain in demonstrating [19] that taking the Grotthuss–Draper law in a quantitative sense, that is, that not only light has to be adsorbed, but that the effect is proportional to the radiation absorbed, could replace the Stark–Einstein law, but he obviously missed the point. The equivalence law states much more precisely that absorption of one quantum of light causes one photochemical act. Whether this applies in every single case or, more correctly, which is the mean probability that this statement applies to one type of "acts" or to another one, and under which conditions it can be affirmed that this applies to a chemical reaction, is another question (see below). That the effect is proportional to the absorbed flux—provided that the terms are properly defined—is obvious.

2.3 Early Attempts to Rationalize Photochemical Reactions

Both Draper and Grotthuss were concerned with the mechanism underlying the effect of light unto matter. In order to appreciate their contribution, it must be recalled that although the theory of light as oscillating electric and magnetic fields had been formulated, the relation with chemical structure of the media it traversed had not yet been established (see above). Along with "ponderable" elements (the mass), the existence of "imponderable" entities, such as light, heat, and electricity, was still postulated for rationalizing chemical reactions. The fact that the darkening

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[2] This is known as the "reciprocity law" in photomedicine but rarely named in this way in photochemistry; see, e.g., [18].

of silver iodide was caused only by a part of the visible spectrum (blue-violet light) as well as by ultraviolet light led Draper to admit that rays causing a chemical effect were further "imponderables" different from those that were revealed in vision. He thought that "it depends on the chemical nature of the ponderable material what rays shall be absorbed . . . and . . . whilst the specific rays thus absorbed depend upon the chemical nature of the body, the absolute amount is regulated by its optical qualities." In his late years, Draper accepted the unifying application of oscillatory theory to both calorific and chemically active rays, since these obeyed to the same laws as luminous rays [20] and thus there was no reason to maintain a categorical separation.

The important point, however, was considering the photochemical effect an intrinsic property of the chemical substance. Draper thought that the particles of matter are in a continuous oscillation and that color and temperature of bodies and finally their chemical constitution are in part depending on the strength and in part on the frequency of the vibrations that propagated over the ether and transmitted to the material. Draper explained the relation between absorption of light and chemical activation as promoting vibrations, so that, when in a molecule not every atom could follow a certain vibration, then light of a certain wavelength was only partially transmitted and in part was absorbed and caused the cleavage of the molecule. While in thermal activation, molecular vibrations could be transmitted in any direction to other molecules, it was in the nature of the molecules that in this particular case this did not happen. Whether a chemical activation occurred depended on the wavelength and the frequency of the vibration, but the amount of the activation depended on the intensity of the radiation absorbed [21]. As for Grotthuss, when republishing his papers, Ostwald commented on the primogeniture of the law preceding the (independent) Draper formulation by 24 years, as well as the important characterization of photochemical reactions and the prophetically perceived analogy between photochemical and electrochemical processes. In fact, being electrochemistry his main topic of interest, Grotthuss was in the best position to appreciate the relation with electrochemistry and indeed concluded that "generally and in best accord with the facts, the chemical effect of light can be compared with that of polar electricity (Galvanism). Light separated the parts of many ponderable compounds and forced them to give new compounds through its own imponderable elements (+E, −E), exactly as the poles of the Volta battery, only to a higher degree," a formulation that conserves its appeal even today (apart the "imponderable" issue; see above).

As mentioned above, the analogy between photochemistry and electrochemistry was an important guide for understanding these phenomena. Ostwald thought that light in some way accumulated energy in the substances until reaction occurred but that science was very far from understanding how this happened [22], and Nernst, while lamenting that photochemical reactions could not be described by leading to equilibrium as thermal reactions, thought that "in the chemical action of light we are dealing with phenomena analogous to the formation and decomposition of chemical compounds under the influence of electric current" [23].

This point of view was strongly developed by Bancroft, who thought "probable" that two of the laws of photochemistry, both of them he attributed to Grotthuss, were:

(I) Only those rays of light which are absorbed can produce chemical action.
(II) The action of a ray of light is analogous to that of a voltaic cell.

At the beginning of the twentieth century, Bancroft reviewed essentially all of the photochemistry known at the time and found that in every case, Grotthuss theory was useful for the rationalization of the results [24–32].

The reviews by Bancroft report a variety of "laws" aiming to correlate light parameters with the effect caused. This approach was the only possible before quantum theory had developed a strong framework for this discipline and allowed to develop a structure–reaction relationship. It makes probably no sense to retrace the history of such attempts. A single case will be reported, with the mechanistic conclusions by a scientist of such an experience as Plotnikov. The observation of the high reactivity of halogen and the photostability of noble gases suggested to him a connection between electronic structure and photoreactivity of elements and their compounds. He felt that a photochemical behavior could be attributed to each atom, as another of the periodical properties, and drew the following conclusions (see Table 2.1, compare Sect. 4.4.1) [33]:

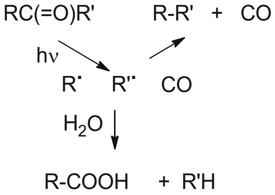
- Elements that have free-valence electrons and double or triple bonds are to be considered photochemically unsaturated and possess a certain photoactivity.
- The photoreactivity of elements is one of their periodic properties.
- Light tends to transform an unsaturated system in a saturated one, so that both work-consuming and work-generating processes are possible.
- When in a photochemical reaction the saturation degree remains unchanged, and the energy involved governs the processes occurring. Longer waves have a favorable effect on those producing work and the shorter ones on the work-consuming processes.
- Unsaturated elements and compounds can be considered as photocatalysts. These introduce new classes of processes that however follow the general rules of photochemical processes.
- The actual sphere of photochemical effects is the external ring of the atomic models, where electrons are coordinated in specific modes and access photochemical reactions.

As an example, Plotnikov thought that water was photochemically unsaturated—and actually photoreactive—because oxygen was bonded to two atoms of hydrogen only, leaving four electrons free for interactions, while the photostability of methane (in the absence of molecules that were themselves photounstable, such as chlorine or oxygen) was related to the fact that all of the electrons were involved in bonds. On the basis of this reasoning he expected that linear alkanes as well as non-tensioned cycloalkanes would not react but doubted that this would apply to tensioned compounds, such as cyclopropane.

Table 2.1 Photoactivity as periodical property of elements

0	I	II	III	IV	V	VI	VII	VIII				VII	VI	V	IV	III	II	I	0
	H																		
He o	Li	Be	B	C x	N x	O xx						F							
												Cl	S	P	Si	Al	Mg	Na	Ne o
A o	K	Ca	Sc	Ti x	V x	Cr xx	Mn xx	Fe xx	Ni x	Co x	Cu xx								
												Br xx	Se xx	As x	Ge	Ga	Zn		
Kr o	Rb	Sr	Y	Zr x	Nb x	Mo x		Ru	Rh	Pd x	Ag xx								
												J xx	Te x	Sb x	Sn x	In	Cd		
Xe o	Cs	Ba	La																
																ΣCe x			
			Yb		Ta	W x		Os	Ir x	Pt xx	Au xx								
														Bi x	Pb x	Tl x	Hg x		
		Ra		Th x		U xx													
					Temperature coefficient = 1.45 in the liquid state									Temperature coefficient = 145 absorption in the blue-violet					

With other unsaturated compounds, he considered the transient formation of radical or atoms, e.g., he rationalized the photochemical α-cleavage of ketones as indicated in Scheme 2.2. In the presence of water, the fragments were trapped (photochemical theory of valence).



Scheme 2.2 The photochemical cleavage of a C–(C=O) bond

More down to earth, Plotnikov examined the effect that different atoms had on the spectra and noticed that metal iodides absorbed at longer wavelength than bromides and even more of chlorides, again an indication of the periodicity of photochemical properties, and likewise λ increased with the atomic weight of the cation.

Summing up, attempts to correlate structure and photoreactivity, as indeed reactivity in general, were repeatedly done, and the feeling that this had something to do with electron removal/shift was diffuse, but a real step forward would have been possible only when physical theories would have been not only formulated but also assimilated by chemists.

2.4 Relation with Light Quanta

A paper published by Einstein in 1912 [34] is usually taken as the source of the "second law of photochemistry." In the opening paragraph, he states:

> In the following the Wien irradiation law and the photochemical equivalence law will be derived through an essentially thermodynamic way. As for the latter law, I mean the statement that for the destruction of one equivalent through a photochemical process the irradiation energy Nhv is required, where N is the number of molecules in a gram-molecule, h the known constant in the Planck irradiation energy formula and v the frequency of the active radiation. Such law appears to be essentially a consequence of the assumption that the number of molecules destroyed per unit of time is proportional to the density of the active radiation. It should be stressed, however, that the thermodynamic dependence and the irradiation law do not allow substituting this hypothesis by a preferred one, as it will be mentioned at the end of the paper.

This paper prompted a note by Stark [35], who remarked that in a paper of his in 1908 [36], he had stated that "the direct chemical effect of light consists in the separation of valence electrons from their bonds" and had arrived to the following statement: "the amount of substance primarily reacting upon light absorption is proportional to the intensity of the active light, since both the reacting amount of substance and the number of absorbed photons are proportional to the number of valence electrons that absorb an amount of light of a certain frequency that is equal or larger than the bond energy. Specifying this statement for the amount of gram-moles (N molecules) for the case that the work $V = hv$ is afforded upon absorption of a quantum of light hv per molecule leads to the sentence: the primary reacted gram-mol corresponds to the amount of light Nhv."

Stark thus claimed that he had correlated the number of reacted molecules and the amount of light absorbed through the Plank constant h some years in advance to Einstein and that this was one of the cases where the same conclusion had been arrived at through different paths. Einstein answered to Stark about the priority issue that "himself did not comply with it, since this would be of interest for practically nobody, and he had rather intended to show that it could be arrived at the equivalence law through a purely thermodynamic procedure, avoiding to invoke the quantum hypothesis." He added that there was no need to discuss priority, since the equivalence law "was a fully obvious consequence of the quantum hypothesis and indeed he had formulated the law already in his first paper on quantum hypothesis for the case of the dissociation of a photosensitive molecule into ions" [37].

Actually, this appears to be the case. In the first one of his 1905 papers (the "miracle" year during which he revolutionized physics), he found an expression for the volume dependence of the entropy of monochromatic radiation and, by comparing it with the Boltzmann's principle, arrived to the conclusion that a "monochromatic radiation of low density behaves—as long as Wien's radiation formula is valid—in a thermodynamic sense, as if it consisted of mutually independent energy quanta of magnitude $R\beta v/N$" (the dual matter-wave nature). He observes that it is then "plausible to investigate whether the laws on creation and transformation of light are also such as if light consisted of such energy quanta." Considering photoluminescence, where "monochromatic light is changed to light of a different frequency," he assumed on this basis that "both the original and the changed light consisted of energy quanta of magnitude $(R/N)\beta v$, where v is the corresponding frequency." He then added: "we must then interpret the transformation process as follows. Each initial energy quantum of frequency v_1 is absorbed and is—at least when the distribution density of the initial energy quanta is sufficiently low—by itself responsible for the creation of a light quantum of frequency $v_2 \ldots$ as well as energy of other kinds, e.g. heat. It is immaterial through what intermediate processes the final result is brought about. Unless we can consider the photoluminescing substance as a continuous source of energy, the energy of a final light quantum can, according to the energy conservation law, not be larger than that of an initial light quantum; we must thus have the condition:

$$(R/N)\beta v_2 \leq (R/N)\beta v_1$$

or

$$v_2 \leq v_1$$

This is the well-known Stokes' rule. We must emphasize that according to our ideas the intensity of light produced must—other things being equal—be proportional to the incident light intensity for weak illumination, as every initial quantum will cause one elementary process of the kind indicated above, independent of the action of the other incident energy quanta. Especially, there will be no lower limit for the intensity of the incident light below which the light would be unable to produce photoluminescence" [38].

It should also be noticed that, apart from the above thermodynamic demonstration, Einstein also offered a deduction of the law. In this case, he considered the Bohr states between which a molecule passed by absorption or emission of a quantum. He considered two such states, Z_m and Z_n, of energy $E_m > E_n$, with $E_m - E_n = hv$ in equilibrium at a temperature T where the radiation density ρ corresponding to the frequency v is very low. Under these conditions practically all of the molecules would be in the lower quantum state E_n. If, besides reverting to E_n by emission of a photon, a molecule in the higher state E_m could also, and far more rapidly, undergo a unimolecular reaction to give product W ($Z_m \rightarrow W$), then at a temperature higher than T, one molecule will be promoted to the E_m state per photon absorbed, and almost all of them will react to give W. This results into the deduction of the practical validity of the law.

In this case, Einstein explicitly distinguished primary and secondary photochemical processes [39], a point that was obvious for him but unfortunately not for many chemistry practitioners. This point was even more clearly stated by Stern and Volmer, who evidenced that the Einstein law could not be applied to the chemical products without consideration of the overall process. In fact, a satisfactory rationalization was offered on this basis for some reactions, e.g., assuming that the cleavage

$$\text{H-Br} \rightarrow \text{H} + \text{Br}$$

was the only primary process in the photodecomposition of HBr, and adding to it the possible secondary processes

$$\begin{aligned}
&\text{H} + \text{H} \rightarrow \text{H}_2 \\
&\text{Br} + \text{Br} \rightarrow \text{Br}_2 \\
&\text{H} + \text{HBr} \rightarrow \text{H}_2 + \text{Br} \\
&\text{Br} + \text{HBr} \rightarrow \text{H} + \text{Br}_2
\end{aligned}$$

led to the prediction that one molecule of hydrogen and one molecule of bromine were formed and two molecules of HBr were destroyed for every quantum absorbed, as indeed found experimentally.

Likewise, the occurring after the primary act:

$$Cl_2 \rightarrow 2Cl$$

of a chain process upon irradiation of a mixture of chlorine and hydrogen:

$$Cl + H_2 \rightarrow HCl + H$$

and

$$H + Cl_2 \rightarrow HCl + Cl$$

well explained that in this case many thousands of molecules were decomposed for every quantum absorbed.

Furthermore, the occurrence of a reaction could not be correlated with the energy involved in the primary process, e.g., iodine absorbed quanta higher in energy than the I–I bond but cleaved with efficiency much less than unitary and part of the radiation absorbed was given back as fluorescence.

All of these observations were best accommodated by having an electronically excited (Bohr) state as the primary photoproduct, to which the Einstein equivalence law applied, and then considering which chemical processes could occur within the lifetime of the excited state, the role of collisions, and the effect of the environment [40, 41].

2.5 Measured Quantum Yield

The postulated equivalence between molecules destroyed and quanta absorbed so clearly expressed in the 1912 paper seemed to offer an ideal field for verification. In the meantime, mercury arcs had become available and a much easier measurement of quantum yield was possible. An early version of the optical bench for the measurement of quantum yield is reported in Fig. 2.5. The emission ray from a quartz mercury concentrated on a cuvette trough a condenser behind which was placed the actinometric cuvette (Fig. 2.5) [42].

As a matter of fact, experimental attempts for the determination of molecules/quanta relation had been carried out also before or at the same time as Einstein's paper [44, 45]. Thus, Winther remarked in the same year (1912) that a limitation of "the well established Grotthuss law, generally and correctly recognized as necessary for the foundation of a theory of the photochemical phenomena" is that it establishes no quantitative connection between the absorption and the rate of the reaction. This was a very important point and actually light absorbed caused reaction to a varied extent.

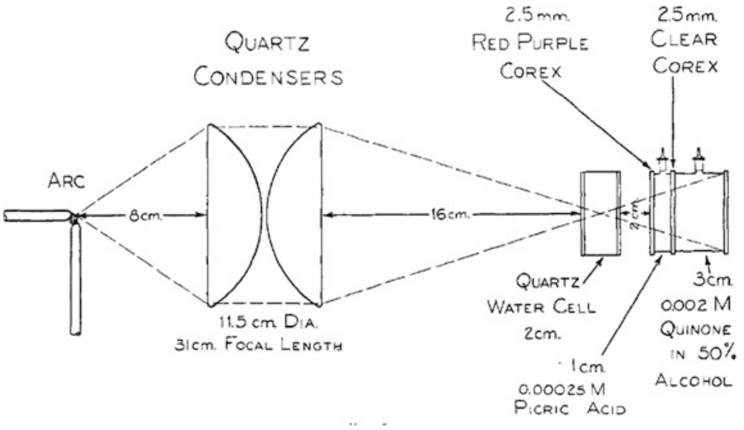


Fig. 2.5 Optical bench used by Dorcas and Forbes for quantum yield measurements. Reprinted with permission from [43]

Examples are on the one hand the strongly light-sensitive hydroiodic acid—the absorption of which is so small as to be hardly measured but reacts extensively—and on the other one any light-fast substance that may absorb strongly but did not react at all. Thus, the law appeared to have a merely qualitative significance. This limitation might be lifted, Winther thought, by appropriately taking care of the dark reactions and by making use of the recent advancement of physics. He considered photochemical processes consisting in the liberation of an electron, thus oxidoreductions in an extended meaning, a single electron being involved in the primary act. As many other scientists, he thought that absorption led to electron ejection and reaction of the positively charged residue of the molecule.

Winther selected a number of known solar light-induced reactions and calculated the energy of the light absorbed (or rather its upper limit) by using a table of the wavelength distribution of solar irradiation (in erg cm^{-2} min^{-1}, measured for each 50 nm intervals) and the absorption spectra of the reagent. Thus, the number of molecules transformed [$n_{tr}(M)$] multiplied by the energy of the photons at the wavelength concerned [$n_{tr}(M) \times h\nu$] was compared with the number of photons absorbed [$h\nu$]. In this way, he was able to calculate the quantum yield or, as he defined it, the photochemical effectiveness (photochemische Nutzeffekt),[3] viz., the ratio between the number of electrons that became differently bonded (corresponding to the molecules reacting) and the number of electrons set free (corresponding to the quanta absorbed) [46, 47]. Table 2.2 gathers the results he obtained.

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[3] The variety of definitions equivalent to quantum yield and the symbols used have been thoroughly studied and published; see: Rubin MB, Braslavski SE (2010) Quantum yield: the term and the symbol. A historical search. Photochem Photobiol Sci 9:670–674.

Table 2.2 Effectiveness of photochemical reactions

	λ_{irr}	$[n_{\mathrm{tr}}(\mathrm{M}) \times h\nu]/[h\nu]$
AgBr/gelatin reduction	350	2.5×10^6
Eder solution[a]	350	3
HI oxidation	450[b]	>6
Oxalic acid oxidation	350[b]	Large
Ferrioxalate degradation	430	0.9
Anthracene dimerization	375	0.05
Ammonia decomposition	206	0.02
Cyanine	593	0.001

See [46]

[a] Indicated by this name is the solution of mercury(II) oxalate obtained by mixing ammonium oxalate and mercury(II) chloride

[b] Very probably due to impurities

The large values obtained for the first four reactions corresponded to a large chemical change obtained by affording a small amount of energy. This could be explained, according to Winther, only with the hypothesis that light served for the generation of a catalyst, but then a thermal reaction actually operated (in this sense, a photocatalytic reaction). In the other cases, however, more energy was absorbed than it was required for the chemical reaction. Indeed in the last case, he thought, electrons were set free, and the positive ions, or parts of the molecules, could be changed in some way, under the *direct* action by light. He tagged these as direct photoreactions, via what can be considered as excited states, at least in a preliminary representation.

After 1912, accepting or not accepting the Einstein “photochemical equivalence” law became a qualifying flag in the scientific debate after the world war. Recognizing the theoretical validity and the experimental support of the law sharply divided the battlefield. Physicists, or at least theoretical physicists, regarded the quantitative application to photochemistry as one of the most significant successes of the quantum theory, concurring, as seen above, with Einstein himself [38] that there was simply nothing to dispute. On the other hand, the fact that the absorption of one photon by a molecule produces one electronically excited state is indeed obvious to present-time students, but this was surely not the case for chemistry practitioners at the beginning of the twentieth century. Experimentalists initially failed to grasp the innermost nature of the theoretical model, while they saw very well that measurements did not support in any way the required equivalence.

The importance of the issue is attested by the decision by the Faraday Society of convening an international meeting in 1925 in Oxford. This was attended by more than 30 scientists and was subdivided in two sections, the first one devoted to the validity and experimental support of the equivalence law and the latter one to mechanistic photochemistry. In introducing the first section, A J Allmand evidenced [48] that “this simple and attractive relation, put forward with the authority of Einstein, has proved a great stimulus to research in a somewhat neglected field of chemistry, and a field, moreover, in which an impasse seemed to have been reached in respect of such matters as the primary mechanism of photochemical change, the significance of the part played by the absorbed light, and the whole question of the classification of photochemical reactions. In this sense then, the relation has proved itself a working hypothesis of great value," although it had to be recognized that using it as a law required some care.

As for the experimental support, Allmand referred particularly to the highly important contribution by Emil Warburg [49], who had a long-standing interest in the energetics of photochemical reactions, and after 1905 and 1912 had investigated in detail this issue while remaining in touch with Einstein.[4] This scientist had defined a number of physical magnitudes for accounting for the varied quantum yields measured. Thus, two parameters were defined, the first one based on the literal formulation of the law, stating that the decomposition of one molecule occurs after absorption of one quantum of energy, and the other one on the actual measurement. The fundamental photochemical equivalent (p) was thereby defined as the "number of gram-molecules required for the absorption of one gram-calorie of radiant energy of frequency v, and consequently the number of gram-molecules primarily decomposing per absorbed gram-calorie (λ expressed in microns)."

$$p = 4.186 \times 10^7 / Nhv = \lambda / 28,470 \ \text{mols}$$

In the experiment, p was a limiting value and such a theoretical figure was reached only when the equivalence law was obeyed. Correspondingly, Warburg defined ϕ, the specific photochemical effect that is the actually measured number of gram molecules decomposed per absorbed gram calorie. Thus, the quantum efficiency (γ) represented the number of absorbing molecules which had reacted per absorbed (by the reagent) quantum. By using the above definitions, one obtained $\gamma = \phi/p$, viz., the ratio of the effective to the fundamental photochemical equivalent, obviously unitary when "the law held."

To the scientific community, this formulation showed a comforting kinship with the magnitudes used in connection with electrolytic decomposition. Thus, the equivalent radiant energy $1/p = 28{,}470/\lambda = 1/Nhv$ calories per absorbing gram molecules corresponded to the Faraday, which is 96,500 coulombs per gram equivalent. It was thus possible to define in a strictly analogous way the faradaic efficiency of an electrochemical reaction and the quantum yield of a photochemical reaction. Allmand proposed that the magnitude $1/p$ should be named Warburg [48].

It was Bodenstein that introduced the name Einstein (E), noticing that $1/p$ was a molar equivalent amount of light, that is, 6.06×10^{23} photons, analogously to the choice of the Faraday, $F = 6.06 \times 10^{23}$ electrons or elemental charges and more akin to the chemists' habit of calculating in moles, not molecules [50].

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[4] Emil Warburg was the president of the advanced research institute, the Physical-Technisches Anstalt in Berlin, from 1905 to 1922 and among those that were behind the call of Einstein to a professorship in Berlin. He was the father of Otto Warburg, Nobel Prize laureate in medicine, who brought a strong quantitative aspect in photobiology; see Sect. 4.6.

Thus, rather than considering molecules:

$$A + h\nu \rightarrow A^*$$

or

$$A + h\nu \rightarrow \text{products}$$

it was better referring to moles and write

$$A + E \rightarrow A^*$$

or

$$A + E \rightarrow \text{products}$$

The proposal became accepted and is now universally adopted.

In reviewing the work by Warburg, Allmand evidences his persistent attempt to build a consistent theoretical frame where the numerical results he was finding could be accommodated. Thus, when studying gas phase reactions such as the decomposition of ammonia and the ozonization/deozonization of oxygen, he had found an unexpected dependence of the reaction efficiency on the irradiation wavelength and suggested that it should be taken care of this fact through an appropriate function $f(\lambda, P)$ and adopting a corrected value $1/p \times f(\lambda, P)$ in the place of the simple $1/p$. On the other hand, in further studies of the decomposition of HBr and HI, he had found that the Einstein law was obeyed, while later measurements on KNO_3 photolysis had given γ values far lower than expected, a fact that he had explained by energy transfer to the solvent so fast as to compete with the reaction of the molecule (“damping”) [49].

At any rate, Warburg had maintained the idea that any molecule absorbing a “photochemical equivalent” p larger than the dissociation energy should actually dissociate, unless a very efficient damping by the solvent occurred.

These empirical adjustments were not universally accepted, and as a matter of fact, a generally accepted theory was surely not yet available. Plotnikov, who certainly did not fail to manifest his idea, thought that [19] Einstein’s law was in a sense simply a natural consequence of the Grotthuss–Draper law requiring that light was absorbed if it had to cause a chemical effect and in another sense wrong and generating confusion. To him it was inacceptable “that photochemical processes were likewise subject to this purely photo-physical law, which is obviously nonsense, because it means the forcible elimination of the chemical principle from photochemistry,” a statement that reveals how far many chemists of this time were from the concepts of the atomic structure introduced by quantum physics.

The numerical values of quantum yields were reviewed both by Allmand and by Dhar and Mukerji in presentations at Oxford [48, 51]. These varied greatly, with *ca* 20 % measured values close to unitary, 30 % below, and 50 % above it.

The wide range of topics presented at the meeting, both theoretical and experimental, demonstrate how keen were chemistry and physics practitioners to fully understand what photochemistry actually was. Thus, D. Berthelot developed a theoretical frame where the equivalence law and the quantum theory were considered in relation to the atomic theory and energetics [52]. Winther thought that it was important to establish whether a change in the wavelength, and thus in the energy supplied by irradiation, would affect the quantum sensitivity of the photochemical process and found that in the few cases where this issue had been examined, the sensitivity had been found either to remain constant or to vane in such a way that the relation between the two quantities had always the same form. He had carried out himself some experiments on the oxidation of hydrogen iodide and found that values resulting from the use of five wavelengths from 280 to 436 nm all lie on the same curve, thus there was no dependence, and he could not afford a physical model to account for this fact [53].

The variety of issues pursued in the debate is certainly remarkable and gives a feeling of how difficult was to "incarnate" the law in practical chemistry. Thus, attempts to calculate kinetic parameters were unsuccessful. Were only monochromatic quanta corresponding to the exact value of the excited state absorbed, as initially postulated? But calculation on this basis brought to a rate of photochemical activation far too low. Could this discrepancy be remediated by assuming that light was absorbed over a broad band and this increased the amount of energy absorbed? As Rice reported, this did not go without major problems [54]. Ornstein proposed a different approach, based on the observation by Frank that photochemical reactions and chemiluminescence are opposite phenomena. By calculating the corresponding equilibrium, acceptable values were obtained for the rate constants of the process [55].

During the general discussion, Frank pointed out that "from the physicist's standpoint the first action of absorption is excitation of the molecule, but this is followed by the complexities of subsequent chemical reactions. The Einstein law is surely fulfilled in respect to the absorption of light. It is not in every case sufficient that the quantum is equal to or greater than the energy required by the primary reaction. While we may disregard the loss of energy by fluorescence at high pressures, there still exists the possibility of loss of energy through a chemical reaction on collision and also the probability of its dissipation as thermal energy on collision. When one takes the many possibilities of secondary chemical reactions into consideration, it is not surprising that only in a very few cases it is possible to test the Einstein law of photochemical equivalence" [56].

Among the many notes, the one by R. Luther [57] is notable for the ability to put the matter in the appropriate historic perspective. He declared to be "not at all antagonistic to the Einstein law," but "considered, in accordance with Ornstein, the ideas of Einstein in the case of liquid or solid bodies to form a very good working hypothesis in the first case only." Despite this limited application, he was impressed by the dramatic change the introduction of a unifying perspective in photochemistry had brought with respect to the early days, as it had happened in other fields of chemistry when a unifying hypothesis had been presented, and "expected that the chemistry of the future would be a subsection of photochemistry, and this a branch of physics." This appears to be a recognition of the ability of modern physics to describe the chemical properties of the various electronic states of photochemistry, all of which were the field of work of photochemistry, and only one, the lowest-lying one, of "standard" (ground state) chemistry (see Sect. 2.1).

The second part was introduced by Bodenstein, who, given as generally accepted that the absorption took place in quanta, pointed out to the large amount of energy the molecule received in this way, of the order of the average energy of molecules at a temperature of some thousand degrees. Still, this did not necessarily lead to a chemical reaction and in many cases this enormous amount was degraded into increased thermal motion or reemitted by fluorescence. The last phenomenon was typically observed in a very dilute gas. Thus, he concluded "that the molecule tends to radiate its surplus energy, in as far as it has no opportunity of communicating it as "flight" energy to other molecules by collision shortly after the act of absorption has taken place, or of accommodating itself to its increased energy during the collision by dissociation or some similar chemical reaction." Experiments on the fluorescence of vapors of iodine and mercury and its quenching by collision suggested a lifetime of 10^{-8} s for the activated species and, although the corresponding competition between chemical reaction and collisional deactivation had not yet been carried out (and at a low pressure it was obviously much more difficult to monitor reactions rather than emission), this was hoped to come next [58].

Bowen cautioned against the use of the "dissociation theory," that is, the assumption that a molecule dissociates "in atoms or radicals" after the absorption of a quantum of light and likewise against a correlation between the bond dissociation energy and the excitation energy: there was no clear-cut case for a threshold over which excitation led to dissociation. He was also doubtful about the role of chain reactions [59].

The mechanism remained the main issue, really difficult to prove even in thoroughly investigated reactions such as hydrogen + chlorine. The recent finding that perfectly dried gases did not combine forced to postulate an intermediate adduct between "activated" chlorine and water, and the observed induction period was difficult to rationalize [60, 61].

Sensitization was another word requiring definition and correct application. Thus, a stable molecule could be made photosensitive by the addition of a small amount of another molecule, but this might involve different phenomena, as illustrated by Berthoud [62]. These ranged from the photochemical formation of a reactive compound to that of a catalyst. Atoms could be generated and transfer their energy to other species, as demonstrated for atoms of mercury or of oxygen [63]. Noyes pointed out to the reaction of molecules, e.g., NO_2, at an irradiated mercury surface, and on the differences and similarity between photochemistry and photo-ionization [64].

A summary of the second general discussion highlighted that, while Plotnikov adamantinely advocated the rejection of the Stark–Einstein law, most of the scientists present in Oxford recognized that the absorption of a light quantum resulted in molecular excitation and obeyed the equivalence law [65]. The problem was what happened next. In fact, while with atoms absorption was "associated with the movement of an electron from one to another Bohr orbit resulting in final expulsion of the electron when the quantum was sufficiently large, . . . with molecules . . . the process was not so simple" as one had then "to deal with both the electronic, oscillatory and rotational quantized energies and the process of physical excitation was thus not necessarily identical with any chemical activation. The recent work by Perrin on fluorescence and chemical action revealed the fact that in complex organic molecules, chemical excitation only resulted in the activation of a particular group or atom within the complex molecule. It followed that molecules may be excited by absorption of light but were not chemically reactive unless one particular energy-absorbing mechanism in the molecule was affected. It appeared that the halogen molecules may readily held about five times the energy necessary for dissociation without that phenomenon occurring." Further points that were underlined were:

- That an "ideal photochemical reaction should possess no temperature coefficient" if the quantum raising the molecule to the reactive state was large enough. The fact that many photochemical reactions were affected by temperature was linked with the operation of a complex mechanism. There was a threshold energy for causing a photoprocess, but this did not necessarily coincide with the maximum of an absorption band.
- The lifetime of excited molecules was in the range 10^{-7}–10^{-8} s.
- The quantum efficiency appeared to depend on the intensity of the irradiation, a fact for which different rationalizations had been offered. Chain processes were at any rate candidates to cause such effects.
- Mercury vapors excited by the resonance line at 2537 Å gave a variety of combination reactions that, although not yet fully explained at the moment, seemed good candidates for mechanistic studies.

It may be concluded that the Oxford conference made a large step forward in incorporating photochemistry in the main field of development of the physics (and by consequence of the chemistry) of the time and indeed gave to this discipline a peculiar role, almost of primogeniture (see the above statement by Luther). A general frame was not yet available, as apparent already by looking at the short report above. However, the basic elements were there, although in part clouded by the complex mechanism of secondary chemical reactions following the primary act. In retrospect, one can understand how difficult it was to rationalize such reactions and their seemingly unjustifiable varied rate and efficiency. Many important factors that plaid a key role had not been identified as yet. When these were, formulating a general frame became possible. This happened two decades later, however, and it came through studies of luminescence, which may well have complications of its own, but certainly less of them than chemical reactions [64].

2.6 Mechanism

In a sense the Einstein law may sound "abstract" to chemists, since important as it may be to know that there were different electronic states and that these could be converted one into another, one had still to understand when chemical transformations happened and how. Einstein may think it obvious that absorption of one quantum of energy produced one excited state and this had a statistically unitary probability of undergoing some decay process. The full adoption of the excited states as protagonists of light-induced reactions by chemists required some time and a better description of the paths followed. In the words by Kögel, "the problem of the primary effect of photochemical absorption is equivalent to the question whether the effect of light is intraatomic, that is play a purely physical role within atoms and molecules, or interatomic, causing a reaction between two atoms or molecules. In the latter case, the chemical change would occur along with excitation, while in the first one the photochemical reaction involved the secondary (purely chemical) effect and would follow the primary, physical effect of light." In such a case, he thought, absorption of the photon would lead to an actual photochemical reaction only under favorable, external conditions.

The words may be different from those used presently, but the idea of investigating the chemical reactivity of excited states and distinguishing purely physical phenomena with no change in the chemical structure from molecular reactions leading to a different arrangement of the atoms had to be the base of mechanistic photochemistry as expressed by the state diagram (see Chap. 3).

Kögel thought that an answer to the dilemma (chemical change occurring simultaneously or after the absorption) could be found by selecting a molecule containing a light-sensitive group that under some conditions reacted thermally and under other ones reacted photochemically in a quantitative way. To this end he compared *o*-nitrobenzaldehyde (highly photoreactive) and nitrobenzene (much less photoreactive). The photolability was attributed to the nitro group even in the case of nitrobenzaldehyde, since the CH=O group did not exhibit a photoreactivity of its own, as he deduced, erroneously as we now know, from the photostability of *o*-nitrocinnamaldehyde. However, both aldehydes became photoreactive in the presence of *p*-phenylenediamine, pyrogallol, and other substances. In fact, there were many cases in which the photoreactivity varied to a very large degree depending on conditions. From this evidence, Kögel concluded that absorption and reaction were separate events. Absorption was a "thermal" (that is not "chemical") phenomenon, where light energy shifted electrons up to higher quantum orbits, from which they came back to the low orbit trough a torsion of the molecule. This allowed a certain time interval to the light-sensitive groups for reacting before coming back to the ground state, not perhaps a fully justified conclusion but a clear picture of chemical *vs.* physical decay of excited state, as we understand them now [66].

2.7 Kinetics

In earlier literature the doubt had been expressed whether the rate of a photochemical reaction depended on the intensity of impinging light (the intensity of the impinging flux in every point of the sample) or rather on the part of it that had been absorbed. The former idea envisages light as a generic activator; the latter points to a precise interaction between light and chemical entities. Actually both points of view were expressed by Gros and, respectively, by Luther and Weigert, only to find that both models gave experimentally indistinguishable predictions [67–70]. Bodenstein, who introduced the name Einstein for a mole of photons (see Sect. 2.5), further suggested that the absorbed intensity should be expressed in Einstein per sec per liter. Thus, by indicating by the letter L (initial of lumen, licht, light, lumière, luce), the number of Einstein involved, one writes the absorbed radiation as:

$$J_{\mathrm{abs}} = dL_{\mathrm{abs}}/dt \tag{2.1}$$

and dividing by the volume

$$[J_{\mathrm{abs}}] = J_{\mathrm{abs}}/V = 1/V(dL_{\mathrm{abs}}/dt) \tag{2.2}$$

and for a simple dissociation reaction

$$\begin{gathered} A_2 + hv \rightarrow 2A \\ -d[A_2]/dt = [J_{\mathrm{abs}}] \end{gathered} \tag{2.3}$$

which, apart from the choice of the symbols, is the form generally used today [50].

Then, for primary processes the simple law below was valid:

$$dx/dt = nI_{\mathrm{abs}} \tag{2.4}$$

or by using the Beer law for the absorption by the molecule M:

$$dx/dt = n\varepsilon b[\mathrm{M}] \tag{2.5}$$

Two limiting cases were important, on one hand almost complete and constant absorption and thus apparent zero order and on the other one low absorption and thus apparent first order. Such “order,” as Bodenstein appropriately remarked, had nothing to do with “what is known as the velocity constant of a chemical dark reaction; it is indeed nothing but the factor for calculating the energy absorbed in terms of the quantity of matter reacting. It is thus of course independent of external circumstances, such as temperature, addenda (if any), catalytic agents and aggregate state” (never heard truer words, which took a long time to be fully accepted by experimentalists, however). Then came the kinetically “extraordinarily complicated” secondary reaction, of which no fully worked-out example was available at the time, despite extensive studies, e.g., for the reaction between hydrogen and chlorine. It had been demonstrated that this was a chain reaction, but then the effect of impurities and of temperature on the intermediates involved had not been determined. The only conclusion was that both parts had to be examined and “investigations on the kinetics of photochemical processes should always go hand in hand” with those of “dark” reactions.

However, disturbing reports continued to appear. As an example, would the simultaneous irradiation with different wavelength ranges cause the same effect as the separate, sequential irradiations? After an extensive investigation, Padoa and Vita had reported that this was not the case for some systems, and indeed in some cases irradiation by a single color led to a more extensive reaction than using non-filtered, white light [71–73]. As an example, in the oxidation of HI, the ratio of the intensity of action of red, green, and violet light was compared with that of the white light and the sum of the ratios was 1.121. Correction for energy absorbed in passing the filter as compared with the energy of the white light from which the colored component was extracted led to the sum of the corrected ratios to be 3.17, i.e., the effect of the separated components was 317 % of that of the white light. This was unexpected and several possible objections were considered by the authors themselves but were eliminated experimentally.

Indeed a similar result was obtained for the reaction:

$$2\,\mathrm{FeCl_3} + \mathrm{H_2C_2O_4} \rightarrow 2\,\mathrm{FeCl_2} + 2\,\mathrm{HCl} + 2\mathrm{CO_2} \tag{2.6}$$

in the presence of quinine bisulfate as sensitizer (212.5 % of white light for the separate light components) and with a different apparatus and method. Possible rationalizations of this peculiarity were proposed. When these and other experiments were carried out in Winther’s laboratory, however, it appeared that the excess was due to a large mistake in the evaluation of the transparency of the filter used for green light and there was no significant difference, provided that the actual absorption of each filter was evaluated when used separately or in series [73]. As in the case above, experimental mistakes due to unsuitable instruments, particularly for distinguishing the different regions of the spectrum, frequently occurred. Obviously having an efficient source and a sensitive measure of the light flux helped.

2.8 The “Laws” of Photochemistry

A couple of years after the Oxford meeting, Taylor pointed out that the quantum theory of absorption and emission of radiation on one hand “amplifies the first law by defining more particularly the absorption act,” but in so far as it “sets a limit to the energy available in a single absorption act, it also sets a limit to the nature of chemical change that can result from such absorption. Thus, for example, if the absorbing system is composed of a single type of diatomic molecules and the light energy absorbed per quantum is less than the energy of dissociation of such molecules, it follows that such dissociation cannot occur as the result of absorption of a single quantum."

Taylor contrasted the most uncompromising form of this law, where an exact equivalence between absorbed quanta and reacting molecules was postulated, with experimental evidence that showed that this was only exceptionally the case. After examining the available data [75, 76], he suggested that "the difficulties inherent in the acceptance of the law of photochemical equivalence as originally formulated would embody the elements of this law which have found support from its study. For this purpose it seems necessary first to avoid entirely the name which has become usual in reference to this matter, since equivalence has been demonstrated only in exceptional cases, rather than as a general rule."

"He concluded that the situation may be met by means of two laws of photochemistry. The first law of photochemistry would be the Grotthuss–Draper absorption law, embodied in the statement that:

- Only light that is absorbed is effective in producing chemical change.

This would be followed by the second law of photochemistry which might thus be expressed as:

- The absorption of light is a quantum process involving one quantum per absorbing molecule (or atom). The photochemical yield is determined by the thermal reactions of the system produced by the light absorption.

Of this second law, the quantum concept of absorption is Einstein's contribution to the progress of photochemistry. The second half is a generalization from the experiments of numerous workers, who, in testing Einstein's original ideas, have added enormously to the quantitative knowledge of mechanism in photochemical processes and demonstrated the factors which determine the yield from a given illuminated system". Essentially, this is the view that has prevailed and the form laws have taken [77–81].

In his talk in Oxford, Allmand had listed *ca* 60 quantum yield measurements in 1926. In 1938, Daniels was able to publish a collection of some 240 measurements and proposed that the photodecomposition of uranyl oxalate that had been investigated in detail was adopted as universal reference.

He stated that "in the early development of quantitative photochemistry it was believed by some that the Einstein relation would apply in many cases not only to the primary process of photoexcitations but to the overall reaction as well. Quantum yields were summarized with the purpose of testing this hypothesis. Any hope of simplicity in chemical kinetics disappeared long ago, and the present table has been assembled not to emphasize the almost universal occurrence of secondary effects which follow the primary process of quantum absorption, but to record the experimental facts of photochemistry in the simplest possible manner. The primary excitation is usually followed by rearrangements and degradation of the energy as heat, by reverse or competing reactions which make the overall quantum yield less than unity, or by continuing reactions which produce a chain and give a value greater than unity. Sometimes it is possible to study these factors from the magnitude of the quantum yield and its response to influences such as temperature, wave length, concentration, and chemical reagents. The amount of chemical reaction produced by the absorption of radiation will change with the duration of exposure, the intensity of the light, the thickness of the optical path, the physical condition of the absorbing material, and other factors. The fundamental simple relation between light and chemical action, however, is the quantum yield Φ, i.e. the number of molecules of substance reacting for each quantum of radiation, or photon, absorbed. When this is known the extent of the chemical reaction produced by the absorption of a given amount of light is easily calculated."

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Chapter 3
The Framework of Photochemistry: State Diagram

3.1 Absorption/Emission

Photochemistry is taught in most universities, whether as an independent course or as a part of an advanced course in chemistry along with other topics (intermediates, advanced synthesis, theory, luminescence, analytical methods, etc.). In most cases, the course begins by giving the definition of electronically excited state as having a different electron distribution with respect to the ground state and by illustrating the radiative and non-radiative processes occurring by means of a monodimensional state diagram, generally referred to as Jabłoński diagram.

The essential feature in such a diagram is the role of non-spectroscopic states, distinguished by the multiplicity different from that of the ground state, in the case of organic molecules triplets rather than singlets. This feature makes reaching triplets by absorption of a photon extremely unlikely (a forbidden transition), and thus, the corresponding absorption bands are not detected in the spectrum, or only under peculiar conditions (very long optical path, perturbing the system through the heavy-atom effect or in the presence of paramagnetic species). The lack of direct evidence about the formation of such states required a long, and somewhat controversial, path to arrive at what is now felt a well-established paradigm.

Indications that there was something more than what absorption spectra indicated came from various sources, first of all from luminescence studies, for the simple reason that instruments, and primarily the human eye, are more sensitive to a weak emission (detected against a dark background) than to a weak absorption (where the transmitted light is almost identical to the blank).

Beginning from “normal” emission, that light was emitted under illumination was early reported (see Sect. 1.2) and was distinguished from other optical phenomena, e.g., reflection or diffraction. In a very important work, Stokes observed that [1] when exposed to daylight, certain materials, solid or liquid, exhibited a peculiar emission. Thus, by looking at the sample in a direction such as the ordinary reflection was avoided, a different emission emanating in all directions could be

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observed, apparently a “false dispersion” or “dispersive reflection.” Thus, examining the decocts of the bark of some trees (e.g., cinchona that contained the alkaloid quinine), as well as some samples of fluorspar, intense emission of a distinctive color was detected in every case and indeed from many other samples. Noteworthy, there was “one law relating to internal dispersion which appeared to be universal, namely, that when the refrangibility of light was changed by [this] dispersion it was always lowered” (in other words, red shifted). No exception to this rule had been found while a great many samples had been examined. He felt “almost inclined” to suggest a single word name for this emission and thought of “fluorescence” from fluorspar, in analogy to the name “opalescence” that had been likewise modeled on the name of the mineral opal that showed this property. The name was accepted and the law (Stokes’ law of fluorescence stating that the wavelength of the emitted fluorescent light is greater than that of the light exciting such fluorescence) holds, except when an anomalous emission from high-lying states takes place, as observed in some classes of compounds, where however such exceptions are well explained by the peculiar excited state arrangement.

Stokes carried out also a different experiment, where illumination by the sun or a lamp was substituted by an electric spark. With a quinine sulfate solution, he noticed that a feeble spark caused an intense blue emission over a considerable part of the solution, much stronger than when the solution was exposed to a continuous source, while a bright spark did cause a strong emission, but this was limited to a thin layer close to the walls of the vessel. Furthermore, interposition of a glass plate (but not of a quartz plate) between the spark and the vessel inhibited emission in the latter case, but not in the former. Thus, those from the spark were merely rays of very high refrangibility (UV), which were “intercepted by a very small quantity of a substance known to absorb such rays with energy.” When the spark was rich in the UV component (bright spark), it was absorbed by a thin layer of solution generating a strong fluorescence, while a visible emission (feeble spark) was less absorbed and penetrated in depth causing a weaker and more distributed emission.

The matter was not as simple, though. Thus, some dyes exhibited a double emission—double in the sense that two emissions at different wavelengths were observed (one, as expected, more or less close to the absorption spectrum and the other one at lower energy) and/or in the sense that it decayed according to a double exponential law. The origin of these phenomena was long debated and required a long work before the various contributions to the complex luminescence were disentangled.

3.2 The Triplet State: Emission

The key issue can be best appreciated with reference to a series of contribution by Lewis and colleagues culminating in a seminal 1944 paper [2], where Lewis and Kasha proposed to explain how a spectroscopic study of phosphorescence (long-lived emission, afterglow) “provided quantitative data concerning an extremely important state of every type of molecule, the triplet state.” They began by excluding from the discussion one of the two classes of light-emitting materials, that is, phosphors such as “mineral phosphors.” These contained some inhomogeneity in the crystals, and in this case an electron was ejected. When this returned, light was emitted as an afterglow. Thus the phenomenon involved chemiluminescence.

Lewis and Kasha focused the discussion on the latter class, where the emission “may be ascribed to a definite substance, whether this substance is in the pure crystalline state, or adsorbed on a foreign surface (including adsorption on the filaments which form the structure of a gel), or finally, dissolved to form a homogeneous transparent solution in a solvent which is usually, through supercooling, in a rigid or glassy state.” Here phosphorescence was obtained by irradiation at a wavelength too long for causing ionization. Photoionization had been actually observed in some cases, as an example with diphenylamine, and could be clearly distinguished, both because it involved a specific intermediate (the radical cation) that could be detected and because of the observed first-order decay of the emission.

The stumbling block for the rationalization of such molecular afterglow had been the existence in some dyes of two long-lived emissions, indicated by Lewis and Kasha as α and β (see Fig. 3.1) [3]. The first one gave an emission spectrum identical with that of the short-lived emission (fluorescence) and had a shape

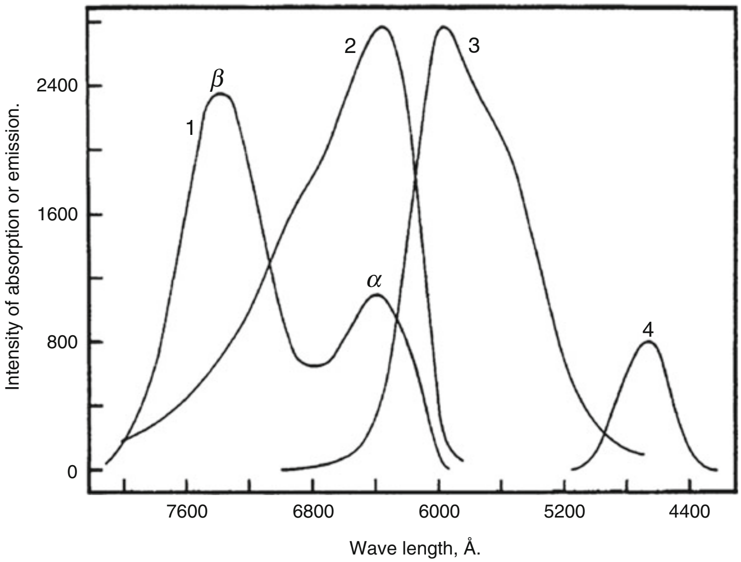

Fig. 3.1 Curve 1: absolute intensity (except for an arbitrary constant) of the phosphorescent emission of crystal violet in glycerol at 178 K, showing the alpha and beta bands. Curve 2: similar absolute intensity of fluorescent emission (plus 5–10 % phosphorescence), at 178 K. Curve 3: for reference, the absorption spectrum. Curve 4: intensity of green phosphorescence band (not corrected for plate characteristics). Reprinted with permission from [3]. Copyright 1942, American Chemical Society

approximated to a mirror image of the absorption spectrum. The speed of the α process increased rapidly with temperature, while the β process seemed to be nearly independent of temperature. The observation of more than a single emission from many dyes, with difference in spectral shape, lifetime (either monomolecular or bimolecular decay), and dependence on solvent nature, temperature, and concentration, worried experimentalists and gave origin to much skilled work. Unfortunately, clear-cut conclusions were not always reached. The very fact that emission may be intense with dyes—including of course those that were present in the sample as impurities—made the purification of dyes, and even assessing the purity of the samples, a serious problem.

Even when impurities were excluded, multiple emission could be observed. Formation of complexes, solvation, conformational equilibria, the intervention of different excited states, and energy transfer were invoked as the possible cause of such multiform emission, and actually all of these mechanisms have been found to participate to various degrees in different cases.

Lewis and Kasha considered as the first step for the rationalization the adoption of a proposal by Jabłoński [4, 5]. This scientist had offered a simple approach to this problem by assuming that in molecules exhibiting a twofold emission, "there must be at least one metastable energy level M, situated lower than the level F reached immediately after absorption. From state F the molecules could pass either to a normal state N, emitting the band F–N (fluorescence), or to the metastable state M" (see Fig. 3.2). Actually, Perrin had previously postulated the existence of a metastable state α below the state formed by absorption (a, see Fig. 3.3). Returning to state a from α would require some energy supply, whether from the medium or otherwise, and two different luminescences would result, the first one direct (from a, receiving no energy contribution from the medium) and the latter one ("retarded") due to the path via α. In the latter case, a lengthening of the emission lifetime upon lowering the temperature would be observed [6, 7].

Jabłoński added to Perrin's hypothesis the further assumption that the metastable state could emit, although the probability of such transition M–N was very small. Therefore when the temperature was sufficiently high, a large majority of molecules were raised thermally from the level M to F and were then able to emit the band F–N (long-lived emission at room temperature). At low temperatures, direct transitions M–N took place (see Fig. 3.2).

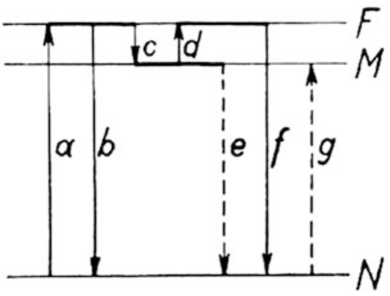

Fig. 3.2 State diagram by Jabłoński. Emission may occur via the metastable state M, generating a second emission besides that from F. Adapted with permission from [8]. Copyright 1984, American Chemical Society

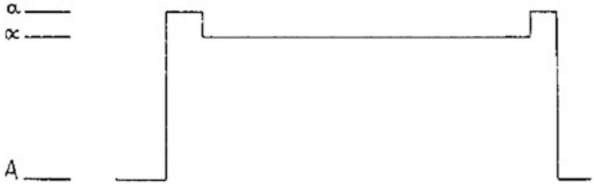

Fig. 3.3 State diagram by Perrin. A metastable state α can be reached via excited state a, and some energy from the medium is required to go back. By permission from [6]

Lewis and colleagues verified this assumption for the case of crystal violet (see Fig. 3.1) [3]. This dye emits fluorescence only when the solvent is highly viscous (e.g., in glycerol at 210 K), and at this temperature or slightly below, the long-lived component, phosphorescence, appears. Lewis measured the spectra by using a photographic plate obtaining the result shown in Fig. 3.1 (glycerol, 178 K). Curve 1 represents the phosphorescence, showing the α and β bands, and curve 2 the fluorescence (plus 5–10 % of phosphorescence) that is a mirror image of the absorption spectrum (curve 3). By using the above hypothesis, Lewis assumed that there was a metastable state lying below the fluorescent state (38.0 kcal mol^{-1} above the ground state), from which a molecule could either decay directly via the β process or be activated thermally to the energy of the fluorescent state (43.8 kcal mol^{-1}) and then return to the ground state by the α process.

Lewis thus adopted the energy level diagram and designed it as the Jabłoński diagram. He added to each level further closely spaced lines, indicating in a schematic way the vibrational levels of each state. In further experiments with fluorescein, Lewis found that upon increasing irradiation intensity, phosphorescence reached a maximum. Under such conditions, *ca* 80 % of fluorescein was in the phosphorescent state, and it was possible to measure the absorption spectrum of such a species. In fact, examination of a sample when irradiated by a strong mercury arc placed at 30° with respect to the tungsten probing light revealed a new spectrum with two bands at 505 and 650 nm, to the red of the 436-nm band otherwise observed. On the basis of experiments where the intensity of the exciting light was varied, it was possible to extrapolate the spectra of the two species involved, the fluorescent (F) and the phosphorescent state (P, apparently a single state in view of the simplicity of the spectrum). The 505- and 650-nm bands were assigned to transition from the lowest phosphorescent state to two levels of still higher energy. It was not possible to reach 100 % accumulation of this metastable state, and the experiment suggested that molecules excited to the higher states P′ and P″ decayed exclusively to P, a remarkable fact when considering that this laid *ca* 50 kcal mol^{-1} above the ground state (Fig. 3.4).

The building of a theory of photochemistry then pursued by assessing that every molecule could have only one phosphorescent state. Examination of a range of molecules (mainly aromatic derivatives) showed that carefully purified samples did give a single emission (see Fig. 3.5). It is true that crystal violet showed a second (green) phosphorescence, which was induced by UV irradiation, not by the visible (see curve 4 in Fig. 3.1), but careful examination showed that this was due to a

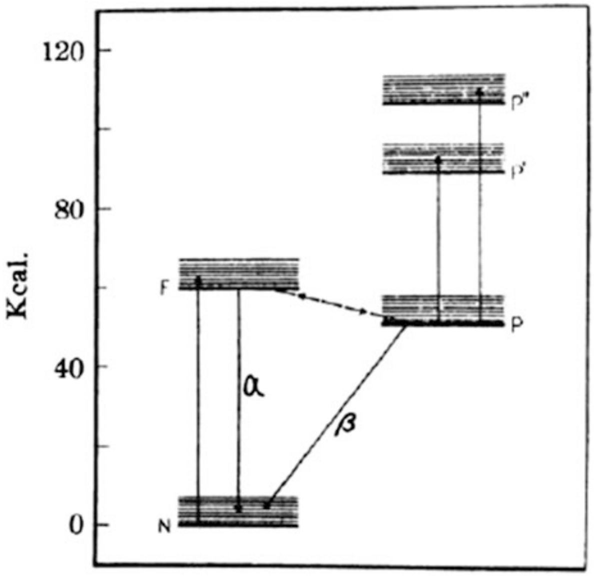

Fig. 3.4 Energy diagram of fluorescein in boric acid. Singlet and triplet manifolds are distinguished. Adapted with permission from [2]. Copyright 1984, American Chemical Society

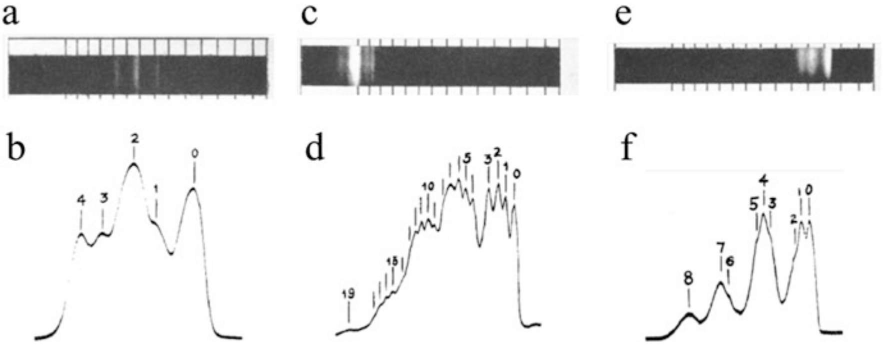

Fig. 3.5 Photographic plates (**a**–**c**) and microphotometer traces (**d**–**f**) of some aromatic compound in EPA at 90 K: (**a**, **b**) naphthalene; (**c**, **d**) phenazine; (**e**, **f**) diphenylamine. Adapted with permission from [2]. Copyright 1944, American Chemical Society

photoproduct however. It was further observed that the vibrational structure of the phosphorescence was independent on the state of the sample (in glass, adsorbed on a matrix) and thus attributable to the decay to different vibrational levels of the ground state, not to vibrational states of the solvent. Furthermore, a different vibrational structure was observed for fluorescence and phosphorescence, though the receiving (ground) states were the same ones, a fact attributed to the different electronic structures of such states that would lead, on the basis of the Franck–Condon principle, to the participation of different vibrational modes for the F and the P states.

The key point now was reached of attributing a chemical structure to the phosphorescent states. A reasonable proposal was that these were distorted forms or tautomers of the ground state that were formed photochemically and were inhibited to come back to the ground state conformation by the rigidity of the medium (a path recognized as viable by Lewis in the 1941 paper; see further below). However, medium rigidity was not an absolute requirement, and furthermore the previously mentioned accumulation of metastable states had demonstrated that when these were in turn promoted to higher-lying states, the last intermediates decayed again to the lowest-lying metastable state, not to the ground state. Since it was difficult to think that molecules of different structure could all become distorted and there was no reason that local heating liberated by vibrational decay would not have permitted decay to the ground state rather than to the metastable state, a geometric change was not the key factor.

This is not to say that the existence of a transient state described in some way as an isomer of excited state has not been established with dyes of the same family. As an example, in the case of ethyl violet, a time-resolved study has shown in 1991 that the initially formed transient (S_1 conserving the geometry of the ground state) decayed (3.6 ps) to an intermediate S_x. This showed a spectrum similar in shape to that of S_1 but shifted to higher energies and was best described as a well-defined conformer resulting from some torsion [9]. Non-radiative decay from S_x involved a 7-ps lifetime. Similar phenomena have been often observed with aromatic compounds. The relatively slow radiative decay leaves time for reaching more stable conformations. Likewise, tautomerism has been demonstrated in many instances.

However, in the case that Lewis was studying, most of the properties listed above clearly indicated that a more general property had to be involved, which allowed a group of transitions and prohibited the other one. Lewis thought that the only possibility that could be applied to complex molecules was a difference in multiplicity that would allow transitions within each set of states, but not between different sets. The metastable state was thus identified with the triplet state.

In this way, the long lifetime of the phosphorescent state was attributed to a quantum-mechanical prohibition, and Lewis later demonstrated that the corresponding excitation from the ground state to the metastable state was also possible, but "quasi-forbidden." The fact that phosphorescence could be much better detected in rigid glass was explained by the fact that return to ground state occurred not only by emission but also by "dissipative processes" in which the energy was given up as thermal energy, as was made apparent by the fact that gradual softening of the glass caused a lessening of the emission intensity along with a shortening of its lifetime.

Thus, the rigid cage did not affect the rate of phosphorescence but rather protected the metastable state from the non-radiative decay, which reinforced the identification of this as the triplet state for organic molecules.[1] "Normal" absorption

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[1] As Lewis recognized, this was true for organic molecules, but in other cases spin labeling might be reversed, as shown by the case of ground state triplet molecules, such as oxygen.

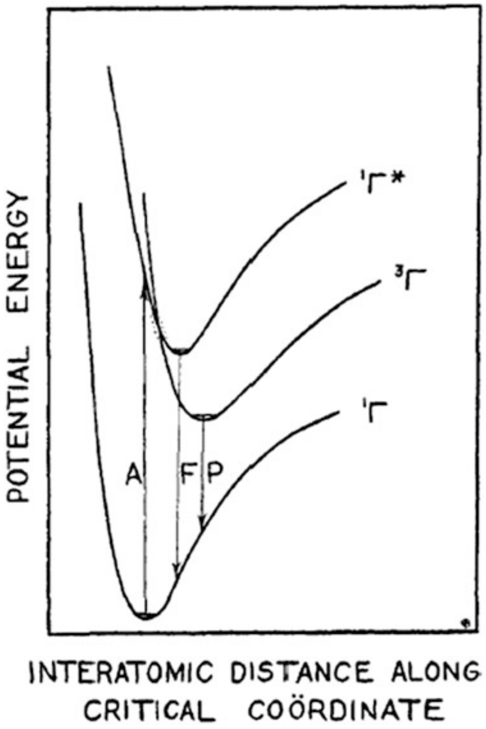

Fig. 3.6 Schematic potential-energy diagram of the three lowest electronic states of a complex molecule, depicting potential hypersurface cross sections along a critical coordinate. After primary absorption, fluorescence may occur and, in addition, radiationless intersystem crossing followed by phosphorescence. Adapted with permission from [11]. Copyright 1947, American Chemical Society

and emission corresponded to transition between two singlet or two triplet states, "abnormal" absorption or emission to transitions between states of different multiplicity. Lewis thus introduced the use of the terms of fluorescence and phosphorescence, not as a generically fast and slow emission, but specifically as involving conservation or change of the multiplicity [2]. The "quasi-forbidden" $S_0 \rightarrow T_n$ absorption was no significant entry to the triplet manifold (Lewis and Kasha suggested that exceptions were some compounds characterized by an unusual color, such as nitroso derivatives and thioketones, but in this case they were in error) [10]. Rather, the triplet was reached via the singlet formed by direct absorption. A potential curve diagram was better suited than the line diagram for explaining the situation. Thus, intersystem "crossing" of potential curves for singlet $^1\Gamma^*$ and $^3\Gamma$ states after primary absorption of light and rapid vibrational cascade led to the vicinity of the zero-point level of the lowest excited singlet (see Fig. 3.6). In turn, $^1\Gamma^* \rightarrow {}^3\Gamma$ intersystem crossing was followed by vibrational cascade to the zero-point level of the $^3\Gamma$ state. Thereafter, spontaneous phosphorescence emission ($^3\Gamma \rightarrow {}^1\Gamma$) may occur [11].

In parallel with Lewis's work, A. N. Terenin had found evidence for the existence of a long-lived metastable electronic state in derivatives of benzene in the condensed state at low temperature, as well as in the gaseous state, and had likewise advanced the view that this state corresponded to the triplet state. He had been able to connect the peculiar emission spectra in the visible that these aromatic compounds exhibited at low temperature with the chemical reactions of such photoactivated states. Furthermore, this explained the property of paramagnetic oxygen to induce forbidden transitions in these molecules, resulting in a "paramagnetic quenching" [12]. The time was ripe also in the theoretic field, where calculating the energy of the triplet state of organic molecules was attempted[2] [13].

Thus, the introduction of the monodimensional diagram of electronically excited state energy for the rationalization of emission(s) is due to Jabłoński, but the introduction of the multiplicity label for differentiating families of states is rather due to Lewis (or Lewis and Kasha [2]) that has(ve) given to this diagram the hermeneutical value it has demonstrated in the following decades and still maintains for the exploration of photochemical mechanisms.[3]

Further support was given by the application of other techniques. In particular, that the phosphorescent state was paramagnetic was demonstrated through a skilled experiment where a very thin-walled tubing was suspended horizontally [11, 19, 20]. The capillary tip of the horizontal bar which held the phosphorescent sample (fluorescein in boric acid glass) was centered in the magnetic field and was illuminated by high-pressure mercury arc. The tip was observed through a microscope. With field = 0, irradiation produced no observable deflection, but the tip moved when a strong magnetic field was applied. Noteworthy, the movement was hindered when the atmosphere surrounding the sample contained oxygen. The experiment gave positive results only with long-lived triplets (lifetime >> 1 s), since in that case triplets accumulated at a high steady-state concentration. With these compounds, such as fluorescein, it was possible to compare the measured force with that expected for a triplet state, and a qualitative agreement was obtained. In order to avoid assumptions on the steady-state concentration of the triplet, a conceptually similar experiment was then carried out by Evans. He used a much more sensitive instrument and was able to measure the decay of the photomagnetic effect, as well as to demonstrate that this followed a first-order kinetics (Fig. 3.7) [21]. The paramagnetic nature of the triplet was then further established by comparing the decay of paramagnetic absorption and phosphorescence [22–25].

This view took some time to be accepted and contrasted with alternative rationalizations sharply refuting the role of a metastable state and its identification as the triplet [26]. In particular, Franck was convinced that "the direct conversion of

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[2] Actually, as indicated in Kasha recollections, Lewis first thought of the attribution of the triplet multiplicity to the metastable state after hearing a talk by Mulliken on the triplet state of organic molecules [8].

[3] Presentations of Jabłoński's contribution to spectroscopy in the frame of the evolution of science and political situation in the 1930s and 1940s have been published [14, 15]. The contribution of Jacques and Francis Perrin, Jabłoński, Vavilov, Levshin, Lewis, and Kasha to the definition of state diagram has been critically evaluated and the originality of each one commented by Nickel [16, 17]. The topic was discussed at the first congress on photoluminescence in Warsaw, May 20–25, 1936 (Pringsheim president, Jabłoński secretary). The lively discussion that took place on that occasion has been retraced in detail by Nickel [18].

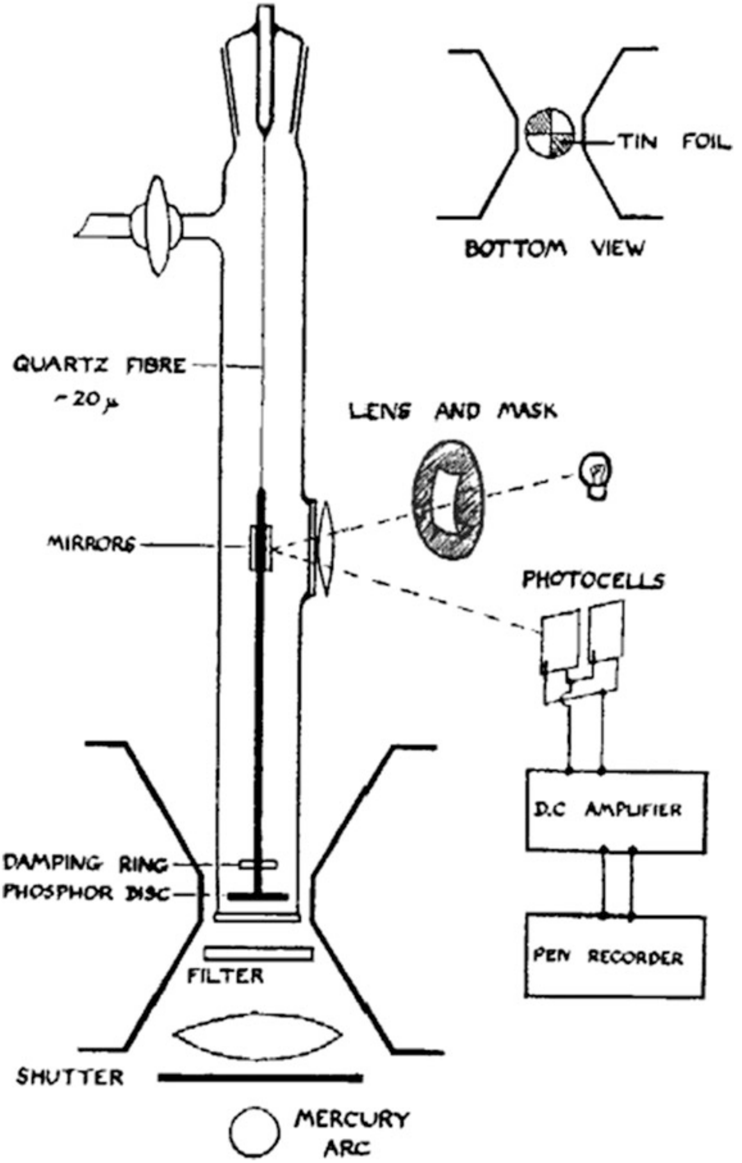

Fig. 3.7 Experimental arrangement for measuring paramagnetism. A thin disk (1 mm diameter, 0.3–0.4-cm thick) of boric acid containing the substance to be studied with alternate quadrants covered by tinfoil is suspended in a hydrogen atmosphere. When the disk is illuminated in the magnetic field, a steady-state concentration of the triplet builds up, and the disk is deflected in a clockwise direction. By permission from [21]

electronic energy into oscillatory energy was possible only under the special condition that the potential energy curves of the acceptor molecule were greatly changed by the forces (electric or chemical) exerted by the excited molecule," and internal conversion (the term that he coined for this phenomenon and was then generally accepted) had a role "only for those complicated molecules whose quantum states are so numerous that their spacing is comparable to their natural width. Internal conversion can occur only when the molecule is in a special configuration which is common to the excited and ground states. In terms of the potential energy diagram, this transition occurs when the system is represented by a particular point lying on the line of intersection of the surfaces corresponding to the normal and excited states." Thus, he concurred with the expectation that internal conversion occurred with a low probability (see Fig. 3.8).

However, he thought that "it is neither necessary nor probable that internal conversion always leads to the complete dissipation of the energy of excitation as heat. Indeed, it is quite probable that the violent oscillations, which are a consequence of internal conversion, lead to the formation of a tautomer of the original dye molecule; the keto-enol transformation being a possible example." If, as is the case in Fig. 3.9, the ground state of the tautomer N′ is lower in energy than the excited state E, but still much higher than N, "then the molecule in the tautometric state will have optical properties which will be similar to those which it would have in a metastable electronic state, with the important difference that the tautomer may have a much longer life." This difference in half-life is likely to be especially great when the dye molecule is surrounded by solvent molecules. It is evident that a

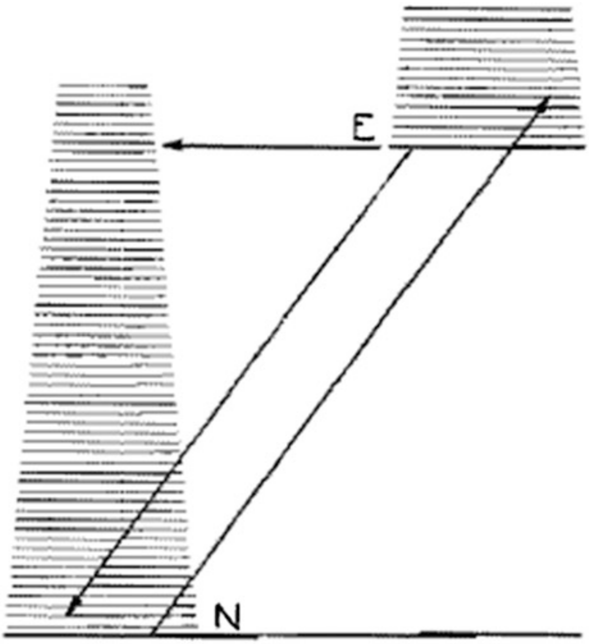

Fig. 3.8 Schematic representation of the energy levels and transitions corresponding to a system where internal conversion from E to N, which results in the degradation of the energy of excitation, is possible. By permission from [26]

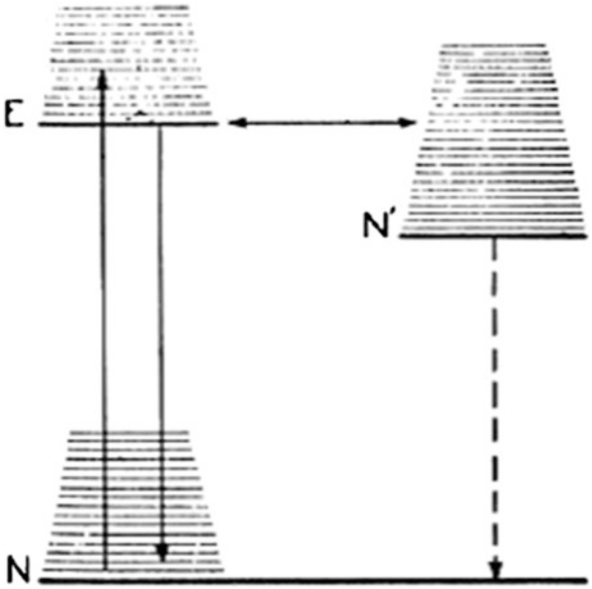

Fig. 3.9 Schematic representation of the energy levels and transitions corresponding to a system where internal conversion leading to tautomer formation is possible. By permission from [26]

tautomeric level, like N′, could be responsible for the phenomenon of phosphorescence. The intensity of the phosphorescence produced in this way should decay exponentially as implied by such a tautomeric change. Franck opposed the role of triplet for several years. When Kasha reported the role of triplet in phosphorescence as the first lecture (20 min) at the Lewis Memorial Symposium in 1946 (as the last student to have completed his PhD with him), Franck presented his arguments against the proposal for 15 min and then called other illustrious scientists, such as Livingston and Rabinowitch, who attested that they had found no indication for the triplet in their photochemical and, respectively, photobiological experiments, and finally by Teller who demonstrated by quantum chemical arguments that the triplet could have no role in molecules containing only lightweight atoms.[4]

3.3 The Triplet State: Reactions

In parallel with respect to studies on the emission of dyes, the role of triplet was demonstrated also in chemical reactions. Protagonist here was the carbonyl chromophore, and the problem was again to demonstrate the participation of a non-spectroscopic state.

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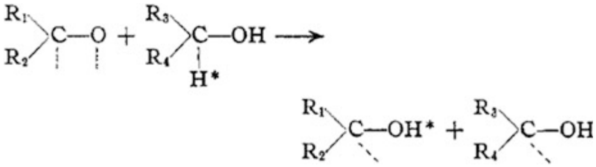
[4] A vivid recollection of that meeting and of other important moments has been published by Kasha [8, 27].

In the period between the two world wars, the photochemical reactions of ketones had been extensively studied both in the gas phase and in solution and the role of radicals ascertained (removal of metal mirrors, trapping by iodine, product structure) [28], but the multiplicity of the reacting excited state had received less attention. However, it was becoming clear that such an excited state had a radical character. In particular, a study of the photoauto-oxidation of aldehydes showed that this occurred with a quantum yield in the order of 10^4 a clear indication for a chain process via radicals, although these did not seem to be formed in the primary act. In his studies on the thermal auto-oxidation of aldehydes, Bodenstein had suggested the intermediacy of an activated "upright" form of the aldehyde (Scheme 3.1) [29, 30]. When studying the ketone-photosensitized aldehyde oxidation, Bäckström applied the same concept and suggested that the primary photochemical process "consisted in setting upright the carbonyl double bond" and the hole in the valence structure of the oxygen caused hydrogen abstraction from alcohols to form semipinacol radicals, "of which it had to be assumed that they were capable of existence as free species," as well as from aldehydes (Scheme 3.1). In the latter case, the acyl radicals formed added oxygen to give an acylperoxy radical that Bäckström identified as the "activated" intermediate of the thermal reaction. Thus, photochemical reactions could be understood as involving the formation of such valence-unsaturated species caused by absorption of a photon, while the slower thermal initiation probably involved the intervention of traces of impurities, in particular transition metals that gave access to the same species. Once arriving at the acyl and the acylperoxy radicals, a chain process followed in the same way, whether thermally or photochemically initiated. The same scheme could be adapted to the gas phase acetaldehyde oxidation [31]. The non-chain photoreaction of aliphatic aldehydes in solution likewise appeared to involve the formation of intermediates with "free valences" [30], and a similar path may be involved in the bimolecular reduction of ketones to pinacols via semipinacol radicals and their statistic recombination [32].



Scheme 3.1 Formation of radicals by hydrogen abstraction. Reprinted with permission from [33]. Copyright 1938, American Chemical Society

As mentioned above, a few years later Lewis and Kasha reported on the phosphorescence in many photochemical systems, not only in rigid media, but also in some cases in fluid solution and in the gas phase and attributed such emission to the triplet state (a forbidden $T_1 \rightarrow S_0$ transition). This was the case, for example, of biacetyl, which phosphoresced, but was also known to abstract hydrogen from various substrates, e.g., from alcohols, and to give radical recombination products. Actually, in their key 1944 paper, Lewis and Kasha present their conclusions by stating that they identified the phosphorescence emitting metastable state as “the triplet or biradical state” and noted that “the physicist speaks of the triplet state, the organic chemist of the biradical state.” The triplet state implies a pair of electrons with spins parallel; a substance that has two “odd” electrons is called a biradical. The two names “are synonymous except that in the organic biradicals their two odd electrons may be sufficiently isolated from one another that their spin is independent of each other” [2]. Indeed, Lewis attempted to picture the chemical structure of excited states and identified a biradical nature as appropriate in several cases, such as alkenes and ketones.

In fact, presenting photoreactions as involving biradical intermediates was natural. The energy of UV photons is of the same order as that of covalent bonds, and in photochemical reactions bonds were cleaved and formed. Thus, with aldehydes and ketones, the light-activated state was not unnaturally drawn as a biradical, with a large or small separation of the radical sites and the reaction pictured as a radical process, e.g., in hydrogen abstraction from alcohols to give pinacols [33, 34].

Bäckström measured the quenching of the emission (called for the moment long-lived fluorescence, although in later papers he used the term phosphorescence) [35] by alcohols, amines, and phenols and obtained quenching constants from 2.6×10^2 M^{-1} s^{-1} (methanol) to 5.9×10^9 M^{-1} s^{-1} (hydroquinone). Recalling his proposal that absorption of a photon led to a “biradical” (indeed the same designation used by Lewis and Kasha) or “bond upright” carbonyl, he suggested that the act of quenching actually consisted in “a chemical reaction between the biradical and the quencher involving abstraction of a hydrogen atom from the latter. This accounted for the general parallelism between quenching power and inhibitory action in autoxidation reactions” [36, 37]. Further support came from a study where triplet biacetyl was generated by energy transfer from benzophenone, as revealed by the appearance of both phosphorescence and photochemical reaction [35]. At the same time, Hammond studied in detail the photochemical reduction of benzophenone (B) by benzhydrol (BH_2), a convenient choice since hydrogen transfer gave a single radical ($BH^{\bullet}$) and coupling of this yielded a single product, the pinacol BHBH [38, 39]. The quantum yield of reduction (Φ_B) was found to depend on the concentration of benzhydrol, and the simplest mechanism accounting for such result involved deactivation of the chemically active excited state by a first-order mechanism. Considering the excited state as an unstable intermediate gave the rate law:

$$\frac{1}{\Phi_B} = \frac{1}{a} + \frac{k_d}{a k_r [BH_2]} \tag{3.1}$$

where a is the yield of the chemically reactive state, k_d is the decay rate constant of such state, and k_r is the rate constant for hydrogen abstraction from BH_2. A doubly reversed plot of $\Phi_B vs$ $[BH_2]$ was actually linear, consistently with competition between thermal decay to the ground state and hydrogen transfer from the alcohol, and the intercept at $[BH_2] = \infty$ was 1, indicating that the yield of the chemically reactive state (a) was unity. The observed slope was too large for admitting that the reactive state was the singlet (estimated to have a lifetime ≤ 0.2 ns), even if hydrogen transfer should occur at diffusion-controlled rate, which seemed unlikely. Thus, it appeared that "even at room temperature, the excited state produced by the n→π* transition of benzophenone underwent quantitative intersystem crossing with the production of a long-lived triplet." The identification of the triplet as the reacting excited state was consistent with the observed quenching by paramagnetic ferric dipivaloylmethide [39].

Starting from these studies, n→π* triplet carbonyls with their characteristic radical chemistry took the key role they have maintained in photochemistry. The "chemical" aspect of the description of such excited states was strengthened by the analogy with alkoxy radicals. Thus, comparing the competitive consumption of different hydrocarbons in the photoreduction of benzophenone led to a reactivity series very similar to that observed with *t*-butoxy radicals. Triplet benzophenone was somewhat more selective and more sensitive to the electron-donating characteristics of the hydrocarbons, but the energetics was very close [40]. As for the "physical" aspect, this received theoretical support by Oosterhoff, who calculated the lifetime of triplet–singlet emission for benzene and acetone and found that although the value obtained was too high in comparison with observed phosphorescence, the calculated ratio for the two compounds agreed with the experiment. Furthermore, the Hammond group could demonstrate that excited states of ketones were able to transfer energy to acceptors, such as dienes, and to cause sensitized cis–trans isomerization in such compounds. Energy transfer occurs with unitary probability when exothermic, at a lower rate when endothermic [41, 42]. Further reactions were identified and inserted in the same paradigm, so that in a consistent picture of the chemistry of n→π* triplet carbonyls and their radical chemistry could be summarized. This included Norrish II fragmentation and hydroxycyclobutane formation, Norrish I cleavage followed either by CO loss and recombination of the fragments or by H transfer leading to a ketene and cycloaddition between α,-β-unsaturated ketones and olefins and between carbonyl and olefins. When the structure allowed it, these reactions were regiospecific but not stereospecific. This was in accord with a path via radical (or diradical when the reaction was intramolecular) intermediates, and the few instances of stereospecific course were proposed to involve the singlet [43].

Furthermore, studies by Kasha on *N*-heterocycles as well as carbonyl and nitroaromatic derivatives had evidenced a transition corresponding to the excitation of a (nearly) nonbonding (heteroatom) electron to an antibonding π* molecular orbital. These had been designed as n→π* transitions and found to differ from π→π* under important respects. Although labeling the starting orbital as nonbonding is too stretched, the different chemistries exhibited by the two types of excited states offered an effective guideline in the exploration (and the prediction) of the photochemistry of these compounds (see Table 3.1) [44].

Table 3.1 General characteristics of n→π* and π→π* transitions

	n→π* transitions	π→π* transitions
(Vapor)	Sharp vibrational structure	Moderately broad
(Solution)	Very blurred	Structure maintained
(Acid)	Strong blue shift	Preserved
	Unique ν_{vib}	Complex vibrational envelope
	$\Phi_P/\Phi_F \geq 1000$	$\Phi_P/\Phi_F \sim 1$

By permission from [44]

3.4 Paradigms of Photochemistry

As stressed by Kasha, the delay in the identification of the metastable states as triplets was mainly caused by the choice of dyes for luminescence studies. This had been an obvious move, in view of the bright emission that facilitated experiments, but in retrospect this introduced a heavy limitation. Dyes exhibit by definition a high oscillator strength of the S_0–S_1 band, which implies as a consequence a short lifetime of S_1 and a low intersystem crossing quantum yield. Furthermore, the weak phosphorescence is submerged under the fluorescence spectrum due to the small S_1–T_1 separation, and return to S_1 had an important role, as seen above. These features, along with the scarce propensity of physicists for admitting spin changes in molecules containing only light atoms, retarded the recognition that an intrinsic property of a *molecule* was involved. Rather, studies of phosphorescence and long-lived fluorescence were directed toward an effect of the environment, such as adsorption on surfaces, frozen solution, and solid state. When these limitations were lifted by passing to different molecules such as aromatics and ketones, with a larger S_1–T_1 gaps, the thermally activated, long-lived emission did not occur any more, and the direct emission from either S_1 or T_1 could be better distinguished.

As Kasha observed, physicists had been too involved in the study of atoms and biatomic molecules and had ignored what could happen with polyatomic molecules, where different mechanisms were available for mitigating the prohibition of the $S_1 \rightarrow T_0$ transition. Thus, spin–orbit coupling that admixed some character of a different state could be predicted by symmetry considerations, when the appropriate interaction Hamiltonian term could be applied. Thus, despite a spin-orbital prohibition factor of the order of magnitude of 10^{-6}, both $T_1 \rightarrow S_0$ emission and $S_1 \rightarrow T_1$ ISC occurred in many classes of organic compounds and indeed in several cases became the predominant processes. This was not due "to an abnormal quantum mechanical enhancement effect, but to the dynamics of excitation" that involved "ultrafast radiationless transitions occurring in internal conversion rates in the 10^{12} s^{-1} range. Even with the highest prohibition factor, $S_1 \rightarrow T_1$ ISC could occur at a rate in the range 10^6 s^{-1}". This did not compete strongly with the fluorescence rate in dye molecules but became quite competitive, e.g., when the S_1 state had a nπ* configuration and thus a limited oscillation strength.

"In brief, a high quantum yield of $T_1 \rightarrow S_0$ phosphorescence emission does not mean a high transition probability for this radiative process, but merely a rate for the spin-orbitally restricted $S_1 \rightarrow T_1$ radiationless process which competes favorably with the $S_1 \rightarrow S_0$ radiative rate" [45].

On the basis of this work, Kasha was able to publish in 1950 a series of paradigms that showed what could be learned from luminescence studies and outlined the processes involved in the photophysics of complex molecules. These paradigms actually allowed to rationalize the photochemical reactions that were discovered in the following decades. The two types of radiationless transitions were clearly distinguished.

- Internal conversion, viz., "rapid radiationless transition between excited electronic states of like multiplicity," with a probability generally high. This caused "the appearance of a unique luminescence, regardless of which state of a given multiplicity was excited" and yielded "a most useful spectroscopic criterion: the emitting electronic level of a given multiplicity is the lowest excited level of that multiplicity" (which became known as the Kasha's rule and is equivalent to the experimental Vavilov rule, establishing that the emission spectrum shape does not depend on the excitation wavelength) [44, 46, 47].
- Intersystem crossing, viz, "the spin–orbit-coupling-dependent internal conversion", distinguished from the former "by a prohibition factor of about 10^6" but probable in many molecules, and strongly affected by the introduction of heavy atoms, as Kasha extensively documented in the following years [44, 46].

3.5 Generalized Use of the State Diagram

The use of state diagrams can be further developed. An example of extended use of this approach is the application to the treatment of the data of photoinduced anisotropy of organic dyes and its dynamics that provides an insight into the nature of interactions between the dye and its microenvironment. The kinetic of the photoinduced anisotropy in liquids is usually described in terms of a rotational Brownian motion of free rigid bodies, yielding an equation of rotational diffusion, but this encounters mathematical limitations. A way to solve the problem is offered by the discontinuous distribution approach (DDA), where molecules are assumed to be oriented in discrete directions only, and rotational diffusion is represented by discontinuous jumps. This approach is conceptually analogous to that used in the Jabłoński diagram, and actually a way to account for rotational diffusion using a DDA-like method has been proposed (see Fig. 3.10) and called polarization-sensitive Jabłoński diagram (PSJD) [48].

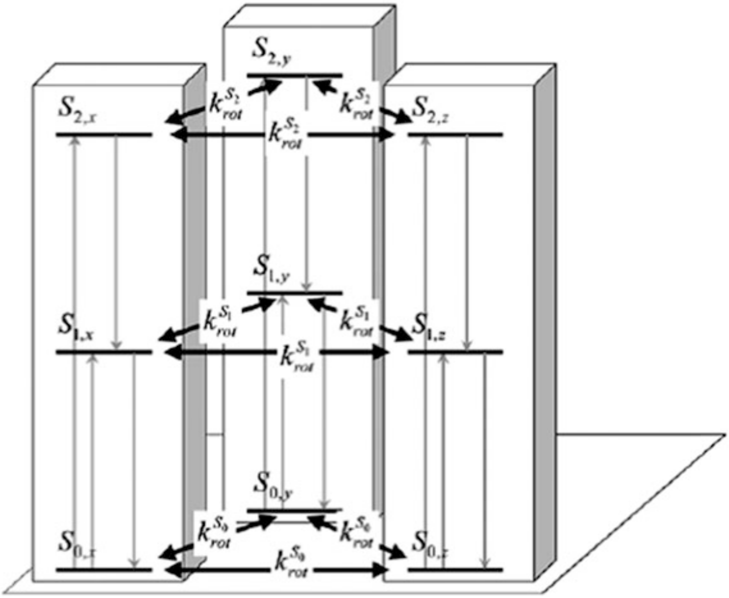


Fig. 3.10 Polarization-sensitive Jabłoński diagram for a spherical rotor: the three sublevels of each electronic states are connected by “rotational” transitions (only the singlet system is shown). By permission from [48]

3.6 Moving Along the States

The use of state diagrams allowed incorporation of previous conclusions about transitions between electronic states. At the 1926 Oxford meeting, it was agreed that the primary process to which the Einstein law applies was the formation of excited states. The conditions required in order that this led to a photochemical reaction was considered in the important contribution by Franck (Sect. 3.4). A necessary condition was that the molecule acquired vibrational energy exceeding the dissociation limit, that is, the energy to break a chemical bond in that state. The likelihood that excitation led to a chemical reaction could be assessed only if the properties of the excited state were known, since the fact that the photon energy exceeded that of fragmentation was not per se sufficient. In solution excited molecules lost excess energy by collision with other molecules, but even in gas phase at low pressure a molecule may take up many times its dissociation energy without dissociating. As mentioned, this point was stressed by Franck, who quoted the example of iodine molecules that absorbed and reemitted as a resonance spectrum an amount of energy five times the work of dissociation when illuminated in the far UV and did not undergo cleavage with unitary quantum yield (see Fig. 3.11) [49].

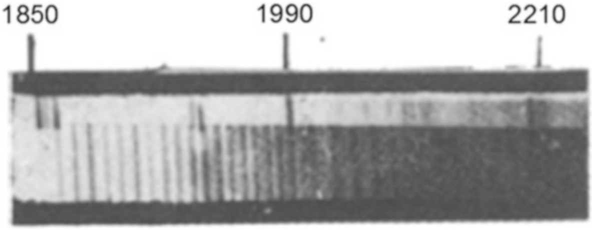


Fig. 3.11 Fluorescence from iodine vapor excited by the Al lines at 185.4 and 186.2 nm. By permission from [50]

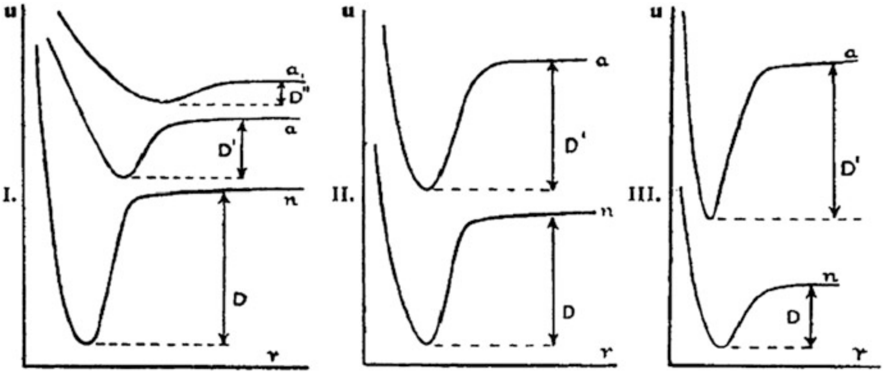


Fig. 3.12 Energy involved in the (photo)fragmentations of the excited state of biatomic molecules. By permission from [49]

Thus, according to Franck, the question whether a molecule would dissociate was "reduced to a consideration of the magnitude of the oscillation and rotation energy changes, which are coupled with the changes which the electron system undergoes upon absorption of light. Only when this amount equaled or exceeded the dissociation energy for the state considered could dissociation take place." Since it was assumed that electron transitions affected only the binding of the atoms, leaving unaltered the relative nuclear separation and the potential well in the excited state had a different shape with respect to the ground state, a nuclei position different from the minimum could be reached. Franck [49] found a correlation between a large change in the oscillation quantum number and a large alteration of the bonding in the excited state. He based a classification of photochemical mechanisms on these characteristics. Thus, promotion from ground state n to excited states a and a$'$ included a vibrational component (the equilibrium distance is longer in both excited states than in the ground state, $r', r'' > r$), and this may lead to overcome the barrier to dissociation. This was no necessary consequence, however, as it depended on the specific case and might still require an energetic contribution ($D' < D$; see Fig. 3.12, left side).

This was the case of halogens. On the other hand, in molecules such as oxygen and nitrogen, the equilibrium distance r did not change, and the dissociation energy was essentially independent on excitation ($D' = D$; Fig. 3.12, center). Finally, the equilibrium distance r' may be smaller in the excited state, as in "molecules" (or rather complexes) that were stable only in the excited state, as it was the case for Na_2 and Hg_2 ($D' > D$; Fig. 3.12, right side).

Franck also recognized that upon direct dissociation, the amount of energy ($h\nu - D$) translated into kinetic energy of the fragments [51]. The communication by Franck at the Oxford meeting spurred the interest by Condon, who developed quantitatively the theory for calculating the amplitude in spectra applied to transitions where the molecule was vibrating in the initial state and assumed further that the nuclear velocities were not changed by the electron transition. In this way, the major aspects of the observed intensity distributions in band systems in emission and absorption were explained. "It is at the two extreme positions that the vibrator spends most of the time, i.e., the electronic transition is most likely to occur when the vibrator is in one of these" positions [52–54]. The equations for the extrema thus give the bands which one expects to be strongest in a band system. This is the basis of the "Franck–Condon principle," asserting that a vibrational transition accompanying an electronic transition is more likely when the starting and final vibrational wave functions overlap to a larger degree. This rationalizes the shape of the absorption bands, the fact that fluorescence is to the red of the absorption spectrum (Stokes' shift), as well as, as seen above, the likelihood that a photochemical cleavage occurs.

In terms of classical mechanics, the Franck–Condon principle "is the approximation that an electronic transition is most likely to occur without changes in the positions of the nuclei in the molecular entity and its environment. The resulting state is called a Franck–Condon state, and the transition involved, a vertical transition. The quantum mechanical formulation of this principle is that the intensity of a vibronic transition is proportional to the square of the overlap integral between the vibrational wavefunctions of the two states that are involved in the transition" [55]. This principle was readily accepted and from the beginning quoted with the names of the two scientists [56–58].

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Chapter 4
Some Paradigmatic Topics

4.1 Photochemistry for Synthesis

The rationalization of the physicochemical framework of photochemistry was relatively slow and controversial, as indicated in Chap. 3, and it could not have been otherwise because this required to come to terms with the radical difference between electronically excited state and ground state processes. However, advancement in the physicochemical aspects was not accompanied by a fast development of preparative organic photochemistry. The conceptual frame based on the state diagram and knowledge of the kinetic parameters range were available to scientists by the end of the 1920s, at least in the main lines. They had relatively few photochemical reactions to test for the application of such schemes, though, despite that in 1908 Stobbe had advocated a fast development of organic synthesis via photochemistry—also as a condition for new mechanistic elaborations [1]. However, while the general paths of chemical reactions, based on the interaction between electrophilic and nucleophilic species, which actually remain to this day the core of synthetic chemistry, in particular of industrial application, were established during the enormous advancement of organic synthesis in the period 1870–1950, no parallel advancement took place in synthetic photochemistry. True, scattered reports of the photochemical *reactivity* of some molecules (not however of the identification of photoproducts) had been very early reported [2].

As an example, this is the case for the photoreaction of santonin that was first mentioned in 1834 or of the transformation of anthracene into a high melting point compound that was reported in 1866 (see below). However, the recognition of the latter product as the 4+4 dimer resulting from an unprecedented cycloaddition was proposed only in 1895 and proved much later. As for santonin, the correct formula of the photoproducts from the crystals, which were formed via a complex rearrangement of the cyclohexadienone ring, was demonstrated only through intensive work by several laboratories that began to be published in 1957! This delay evidences one of the key problems of organic photochemistry. Photochemical

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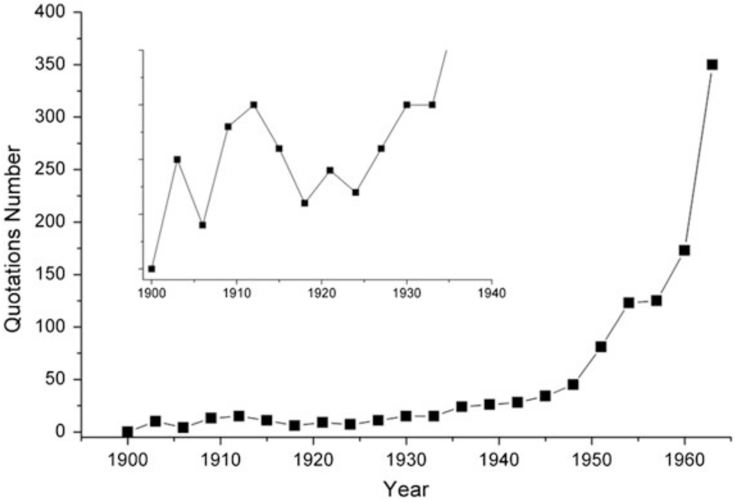


Fig. 4.1 Number of quotations in the book *Organic Photochemistry* by Schönberg plotted vs. the year of publication; in the *inset*: an enlargement focusing on the beginning of the twentieth century

reactions tend to take a completely different course with respect to thermal ones and furthermore often involve a large change in the structure. Thus, it was no simple matter to recognize the structure of a photochemical product and one could not have recourse to analogy with the literature, since very few studies were available.

There was a period where organic photochemistry seemed to take a brisk pace (see Fig. 4.1). At the beginning of the twentieth century, Ciamician and Silber in Italy, Stobbe in Germany and a few other scientists carried out an intensive experimental work that led to the discovery of several classes of organic reactions. This generated a great interest at the time but remained confined to a small number of laboratories. Apparently, after about 20 years devoted to photochemistry, Ciamician felt that no great advancement could be further obtained and left the field for his last work years. As a matter of fact, preparative photochemistry essentially died out with the outbreak of the World War, and for more than three decades (1915–1950), photochemical studies were essentially limited to kinetic aspects of "simple" reactions, with little interest for the synthetic aspect. Or at least research in this field advanced slowly, as indicated by the fact that a book on preparative photochemistry was printed only in 1957. This was the treatise by Schönberg [3], which was followed by the second edition in 1968 [4].

Noteworthy, the latter was much enlarged, and this did not result from a change in the coverage, but from a large increase in the activity in the field. In fact, if the number of papers quoted in the second edition of the book is plotted vs. the publication year, it is apparent that an abrupt surge occurred in the early 1960s (see Fig. 4.1). This is clearly due to the major change in the experimental approach that became common in these years. Thus, chromatography became of general use and was of course much more informative on the course of a reaction than periodical chemical analysis. This is a key advantage for optimizing the yield when consecutive reactions are possible, as it is often the case in photochemistry. And then, obviously chromatographic methods allowed the study of reactions where a mixture of products was formed in a much easier way than at the time when fractional distillation and crystallization were the only separation methods available. Furthermore, and even more importantly, the great progress of spectroscopic techniques and their routine use made it possible to recognize the structure of products much more easily, a decisive advantage when a deep-seated structural change took place, as it was often the case for photochemical reactions that underwent unprecedented processes [5]. After the first start in the period 1900–1915, which remained limited to very few laboratories, the period 1960–1980 represented the true golden age of organic photochemistry. The technical advancement mentioned above made possible to take any bottle from the shelf, dissolve the compound contained, and irradiate the solution to form a product to which a (often novel) structure could be assigned. Or, even if things were not exactly in this way, the advancement was really fast. New processes were discovered and the growing interest for mechanistic investigation found new fuel for advancement also in photochemistry, and indeed in particular in photochemistry.

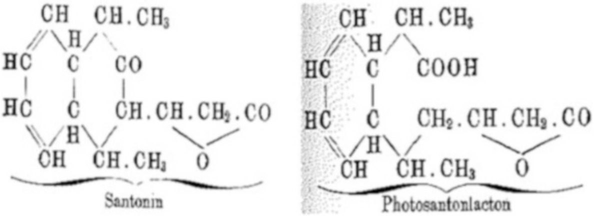
4.1.1 Some Exemplary Cases of Early Reported Photoreactions: Santonin, Anthracene, 2+2 Cycloaddition

Accessing the high-energy level of excited states makes possible for such a complex system as an organic molecule to evolve over a high-lying potential surface and to arrive smoothly at deep-seated bond reorganizations that are not accessible thermally. Thus, new reactions that have no analogy in non-photochemical processes are frequently observed. A few examples may clarify the matter.

4.1.1.1 Santonin

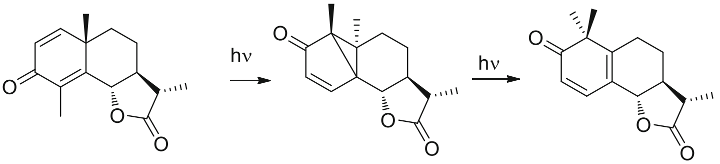
The photolability of santonin, an anthelmintic sesquiterpene lactone extracted from *Artemisia cina*, vulgarly called santonia or levant wormseed, was reported, as mentioned, already in 1834 in the frame of the characterization of this compound by Trommsdorff [6], a few years before that a preparation based on this active principle was introduced on the market (actually this was the first commercial drug in the United States). Trommsdorff noticed that the crystals turned yellow and “burst” into small pieces when exposed to light (more effectively upon irradiation by blue and violet light than by yellow, green, and red light). This is arguably the first organic photochemical reaction reported, and Trommsdorff lamented that he could not pursue more nearly the investigation because of the small amount of compound available (this was obtained in $2\frac{1}{3} - 2\frac{1}{2}\,\%$ yield by extraction from the seeds).

Later, the photoreaction of santonin was studied in solution by Sestini [7] and by the Cannizzaro group [8, 9], in part in collaboration, over several decades, with new impetus. In a typical experiment, *1 kg* of santonin was dissolved into *52 L* acetic acid, poured in several vessels, and exposed to solar light for several *months*. About 1/9th of the solvent was evaporated under reduced pressure and photosantoic acid precipitated upon cooling from the residue. Dilution with water gave further photosantoic acid and from the solution a second product, isophotosantoic acid, was obtained. However, the structure of santonin itself was not known at the time, indeed it took a long time to be demonstrated [10]. At present, a X-ray structure of santonin, available in gram quantities, can be obtained in 1 h, but earlier works had to rely only on chemical tests. These supported the presence of a lactone and a ketone ring, based on evidence such as the solubility in bases, the elimination of water upon heating, the formation of mono- and di-acetyl derivates, and the positive test for a carbonyl, but were not sufficient for arriving at a strong assignment. Several structures could be considered for this diterpene (see Scheme 4.1) and for the product formed upon irradiation, and Cannizzaro had to restrain himself to hypotheses contemplating the cleavage of one of the six-membered rings present [9].



Scheme 4.1 Formulae of santonin and photosantonlacton proposed by Canizzaro; see [9]

When the problem was confronted again 70 years later, the means involved were much better suited and the knowledge about terpenes of this type was much more extensive. A mercury arc was used rather than solar light, thus reducing the irradiation time required and allowing to obtain a better yield of the primary product, and chromatography was available for obtaining pure products starting from 1 g, rather than 1 kg [11, 12]. Furthermore, the irradiation was carried out also in aprotic solvents, obtaining a new product, lumisantonin, that could be converted in the one formed in acetic acid and further chemical characterization was carried out. Spectroscopic (UV, IR) analysis was highly informative for the identification of various structural motifs, which allowed to arrive to a much better supported, but still hypothetical, assignment involving a rearrangement of the cyclohexadienone moiety (Scheme 4.2). Both UV and IR spectroscopy on lumisantonin and some derivatives supported the rearrangement of the cross-conjugated ketone into a cyclopropylvinylketone (see the bands at 1710 and 1770 cm^{-1}; Fig. 4.2) [11, 12].



Scheme 4.2 Photorearrangement of santonin

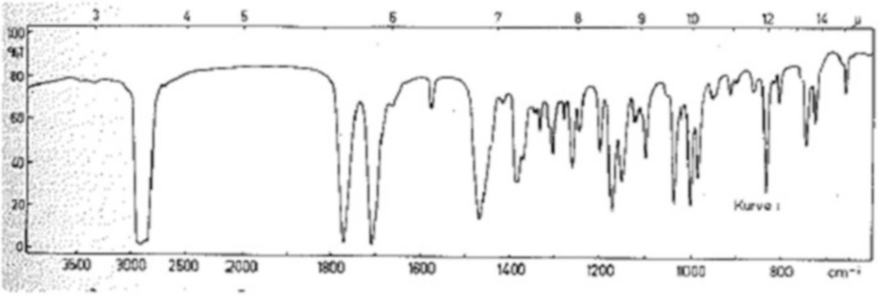
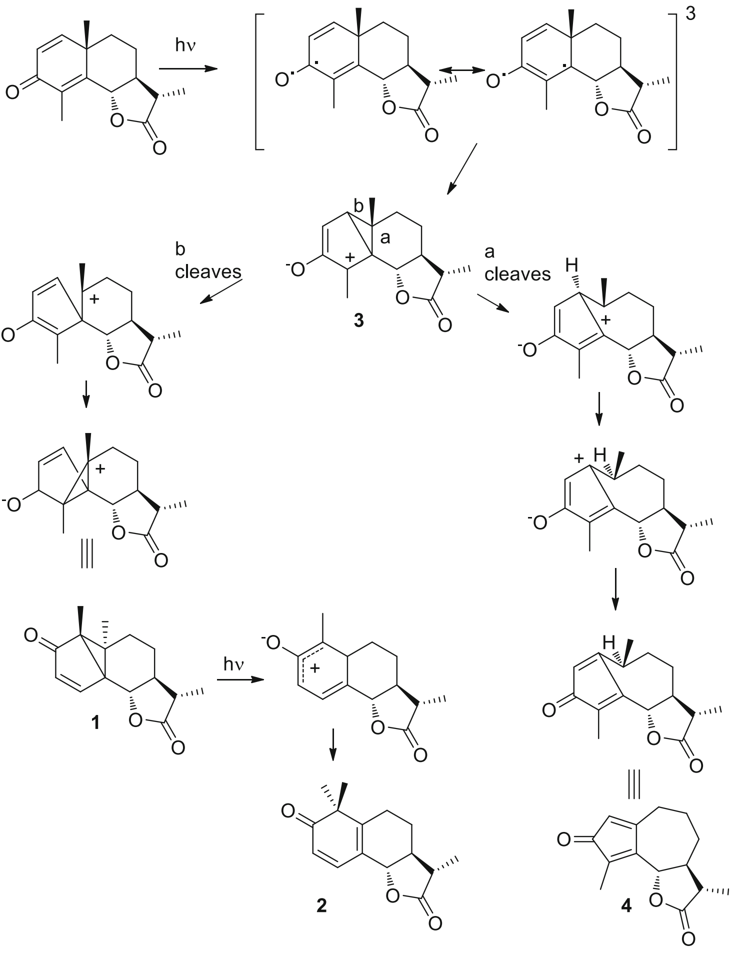


Fig. 4.2 IR spectrum of lumisantonin. Notice, besides the lactone band, the one due to the cyclopropyl ketone moiety; by permission from [12]

Subsequent work on 4,4-diphenyl-2,5-cyclohexadienone showed an exactly analogous pattern and led to the recognition of this rearrangement as a general photochemical reaction of cross-conjugated ketones [13]. Furthermore, the correct structure assignment allowed a rationalization of the chemistry occurring in terms of zwitterionic or biradical intermediates that did fit in the approach organic chemistry practitioners were increasingly using [13–17]. The reaction could now be rationalized as occurring from the triplet nπ* state of santonin that intersystem crossed to a closed shell zwitterionic intermediate that in turn underwent cleavage of either the *a* or the *b* cyclopropyl bond. The latter one predominated in solution and led to a tricyclic ketone (**1** in Scheme 4.3) as the first isolable product in aprotic media, lumisantonin.

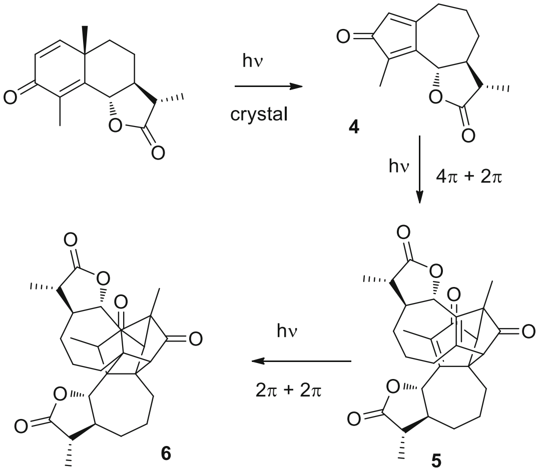


Scheme 4.3 Photorearrangement of santonin: mechanism

A second photochemical step caused methyl group migration leading to cyclohexadienone **2**. Further irradiation led to cleavage of the three-membered ring and to photosantoic acid (actually a lactone), the historically first isolated product (Scheme 4.3) [13]. Examination at a low temperature gave indication of a zwitterionic intermediate, characterized by a strong blue color, assigned as the primary photochemical product **3**, from which rearrangement and methyl or hydrogen shift led to the final products [14–17].

And the tale goes on, because this is the process occurring in solution, while the photochemistry occurring in the crystals, the phenomenon that started all this work in 1834, was clarified still later and found to involve *three* subsequent photochemical steps through a single-crystal-to-single-crystal transformation. In the crystal, cleavage of bond *b* predominates in intermediate **3** and the primary product is cross-conjugated cyclopentadienone **4**. This reaction is followed by two ensuing 4π + 2π and 2π +2π cycloaddition processes involving the cyclopentadienone moiety in two molecules that were appropriately disposed in the lattice (see **5**, **6** in Scheme 4.4) [16, 17].

Scheme 4.4 Photoreactions of santonin in the solid state



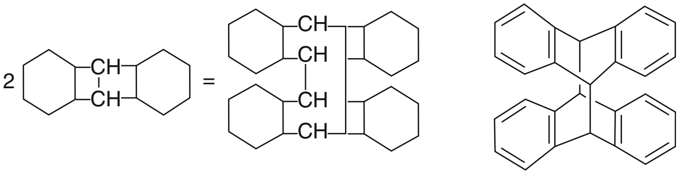
After several studies, a reinvestigation of the reaction with polarizing microscopy, X-ray diffraction, spectroscopic methods, chemical trapping, and product analysis evidenced that the crystal structure determined the course of the reaction and that the external crystalline habit was conserved during the transformation, although the crystals burst when a certain degree of conversion had been reached. Obviously, the use of refined spectroscopic techniques was a must for such a study (see Scheme 4.4 and Fig. 4.3) [18, 19]. The santonin adventure over 180 years demonstrates both the power of photochemistry in disassembling and reassembling molecules, and how difficult is understanding what is going on.

Fig. 4.3 Two molecules of santonin occupy two different sites in the crystals of santonin. Upon irradiation, one of them is more reactive (MR) and the other one much less (LR). The transformation is topotactic (that is guided by the crystal lattice) and, up to 30 % conversion, occurs in a crystal to crystal way. The arrangement of the two molecules before and after irradiation is indicated by filled (0 %) and light bonds (30 % conversion). Reprinted with permission from [18]. Copyright 2007 American Chemical Society

4.1.1.2 Anthracene Dimer

As seen above, interest in the photochemistry of santonin originated during the characterization of this natural product. Accidental observations of photochemical processes were not uncommon. Another case involves a photoreaction first noticed by Fritzsche during the systematic characterization of aromatic hydrocarbons he was carrying out. In a 1867 paper, he remarked that there were a number of new hydrocarbons that had been obtained from coal tar, but had not been fully characterized as yet [20]. As an example, he had isolated a compound for which elemental formula $C_{14}H_{10}$ had been obtained from analysis, but had refrained from giving it a name and proposing a structure, waiting for a fuller characterization. In the meantime, however, the same product had been isolated in other laboratories and had been given the name of anthracene.

Excluded from the official baptismal, Fritzsche then reported several properties of such molecule he had discovered, including the remarkable photochemical behavior. Thus, he found that upon "exposure of a saturated solution to direct solar light, quite early microscopic crystals began to precipitate." Crystals of different habit were obtained from the irradiation in different solvents, but they were identical in most properties, while being strongly different from the starting compound. When melted, or rather brought to a temperature higher than the melting point of anthracene, the photoproduct reverted back to the starting compound (in fact it was later found that the pure photoproduct melted at a higher temperature, but some decomposition always occurred during heating).



Scheme 4.5 Formula of anthracene evidencing the particular valence status of *meso* carbons and dimer of anthracene where carbons have been restored to the normal valence, as reported in [21–23]. The modern formula follows

For the purpose of the work Fritzsche was carrying on, that is, identifying unique properties of various hydrocarbons from coal tar that could facilitate structure assignment, the behavior under illumination was not useful, because reactions under these conditions occurred also with other compounds from the same source. However, one of the first photochemical reacting chromophores had thus been discovered. As for the nature of the chemistry involved, one had to wait some decades until later work demonstrated that the same reaction occurred with several substituted anthracenes, in some cases even more efficiently than with the parent compound, but not from the corresponding dihydroanthracene [21–23]. Thus, the cause of the dimerization (polymerization in the language of the time) was the cleavage of the bond that was thought to exist between the two *meso* CH groups. Such groups returned to the normal valence by reaction with another molecule of anthracene and the 4+4 dimer structure was formed (Scheme 4.5) [21, 22].

Later work lending final proof of the structure of anthracene derivative dimers came at the time where spectroscopic methods, in particular IR, were in general use [24–27].

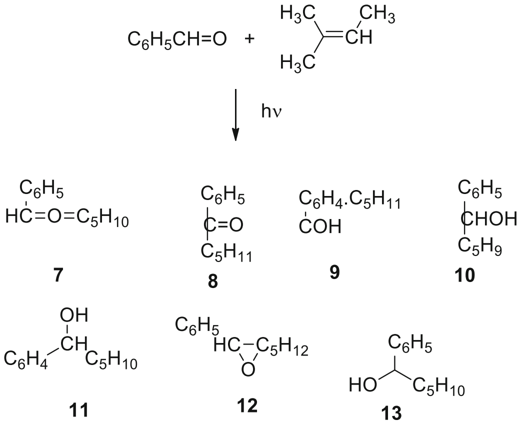
4.1.1.3 Oxetanes and Cyclobutanes

Fortunately, gifts earlier scientists were not in want of were logic and courage. Thus, when experimental evidence, as far as was available, and limpid reasoning led to a conclusion, there was no negative bias toward novelty. This may be well appreciated in the discovery of the 2+2 cycloaddition of carbonyl and alkenes to form oxetanes in 1909. At the time, only a single preparation (by a completely different way, cyclodehydration of propyleneglycol) [28] and very little about the chemical properties of this class of compounds were known. Paternò exposed to sunlight an equimolecular mixture of amylene (43 g) and benzaldehyde (67 g) in a sealed tube for almost 3 months and a half in winter and then the contents of the tube were fractionally distilled [29, 30]. The main product of the reaction was analyzed for carbon 81.6 % and hydrogen 9.6 %, a result that agreed with that of an addition product of benzaldehyde and amylene, $C_{12}H_{16}O$. The cryoscopic determinations in benzene gave a molecular weight of 168.7 ($C_{12}H_{16}O = 176$) and the product boiled at 230–232 °C.

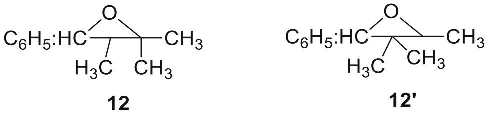
The oxygen atom in this compound did not appear to be present either as a carbonyl, since it did not react with phenylhydrazine and hydroxylamine, in spite of the several experimental conditions used, or as a hydroxyl function, as neither an acetyl derivative nor a benzoyl derivative could be prepared. Furthermore, the product:

- was very stable toward the oxidants, e.g., was not modified in contact with concentrated nitric acid;
- heated in sealed tubes at almost 300°, was split into the starting constituents;
- treated with bromine in acetic acid, absorbed bromine in a large amount with no evolution of hydrobromic acid.

For an adduct between amylene and benzaldehyde, six hypothetical formulas were possible (see Schemes 4.6 and 4.7).



Scheme 4.6 Structures considered for the photochemical adduct between benzaldehyde and amylene

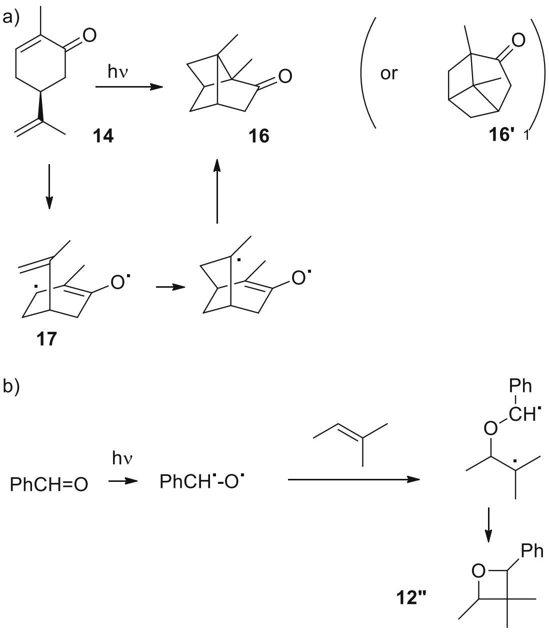


Scheme 4.7 Regioisomeric oxetane structures

Formula **7** could in no way be considered on the basis of what was known on the formation and the properties of oxonium ions, while formulas **8** and **9** were excluded because of the mentioned absence of aldehydic or ketonic properties. Formulas **10**, **11**, and **13** had likewise to be excluded because of the hydroxyl group. The product thus had to correspond to one of the two structures remaining (**12**, **12′**), although the choice between these two regioisomeric formulas was not possible at the time [29, 30].

Several decades afterward, there was still no general access to these heterocyclics, not to speak of a photochemical reaction. Actually, an important report pointed in another direction and showed that the irradiation of aldehydes in the presence of alkenes led to the addition of the RC(=O) group and of a hydrogen atom across the C=C bond with formation of ketones RC(=O)C–CH(via acyl radicals, formula **8** in Scheme 4.6) [31]. Interest for oxetanes increased, because of important applications in some polymer and pharmaceutical compounds of industrial significance. In search of a viable synthetic path, Büchi thus fished out from the literature Paternò's report and concluded that, since "no general procedure has been developed for synthesizing highly substituted trimethylene oxides, it was of interest to reinvestigate Paternò's reaction and to determine the structures of the products obtained." He did so and found, one would say with some surprise, that the assignment was correct [32]. His work confirmed the structure attribution, likewise excluding the presence of carbonyl and hydroxyl functions, now a very fast experiment due to the availability of IR. He found that these compounds did not react with either phenyl lithium or lithium aluminohydride, differently from what previously reported for such heterocycles, but were cleaved under acid conditions, in this way allowing us to recognize the regiochemistry [32].

The 2+2 photocycloaddition of α,β-unsaturated ketones with alkenes has a history in part analogous. Thus, Ciamician and Silber reported the photochemical conversion of carvone (**14**) to a product that was named carvonecamphor (**15**) [33]. This was a solid, smelling exactly like the starting material and likewise contained a ketone function, but no C=C double bond, since it resisted to bromine and permanganate. Rather, it contained a small ring, as suggested by the ready rearrangement to an unsaturated isomer, isocarvonecamphor, under acidic conditions. This reminded the Authors of the intramolecular cycloaddition of cinnamic acid and they proposed that the tricyclic structure **15** was formed through an analogous intramolecular reaction, though explicitly admitting the hypothetical nature of the assignment. The irradiation of carvone was later reexamined in Bologna and on the basis of the results from permanganate oxidation the alternative structure **16** was proposed for carvonecamphor (see Scheme 4.8a) [34, 35]. Fifty years later, Büchi finally decided for Ciamician's structure on the basis of a study where again spectroscopy had an important role, both IR (thus, a carbonyl band at 1727 cm^{-1} supported a cyclopentanone, not a cyclopropyl ketone function; there was further indication of the presence of two methyl groups and the absence of a cyclopropyl methylene) and UV (evidencing that no conjugated carbonyl was present) [36]. Furthermore, the framework of photochemistry had been considerably developed, and the reaction could be rationalized as involving intramolecular attack of the diradical triplet state of carvone to the endocyclic C=C double bond with formation of the most stable diradical (**12**″, see below), similarly to what postulated for the intermolecular carbonyl-alkene addition to form the most stable 1,4-diradical, and of **12** from it (see Scheme 4.8b).



Scheme 4.8 (**a**) Regioselective intramolecular addition of carvone and (**b**) intermolecular addition to amylene

4.1.2 *The Synthetic Potential of Photochemistry*

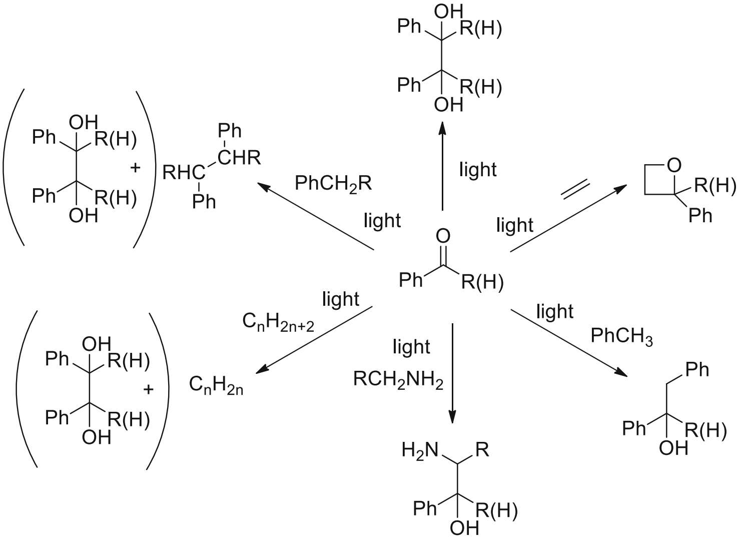
The reactions mentioned above, the rearrangement of cross-conjugated ketones, the 4+4 dimerization of anthracene, and the 2+2 cycloaddition in the Paternò–Büchi reaction and in the enone-diene cycloadditions did not remain isolated examples and in fact pertain to processes of more or less large scope that can hardly be made to occur by alternative thermal reactions. Thus, photochemistry has a potential role in organic synthesis. Modern synthetic and analytic methods allow to overcome the difficulties mentioned in Sect. 4.1, although the role of this method in organic synthesis is still far below what it may be. With regard to this aspect, it is interesting to recall a controversy that took place between two of the "fathers" of photochemistry exactly on recognizing the synthetic role of photochemistry. In a paper published in 1914 [37], Paternò summarized his photochemical work. As he stated in the introduction, this had been essentially completed some years before and "the general processes observed had been communicated in 1909" in a talk before the Accademia dei Lincei and published in the Gazzetta [38, 39], so that the present notes were only the "experimental support of what had been revealed at that time." He now stressed that in the talk he had acknowledged that "the most systematic and complete work" on the chemical action of light, distinguishing it from the effect of any different catalyst, was that by Ciamician and Silber, begun in 1901 and mainly devoted to the reducing action of alcohols on quinones, ketones, and nitro compounds. "Someone may later have felt—he added—that there was some analogy between his own research and that by Ciamician and Silber, who in the meantime had shifted their attention to [photochemical] hydrolysis processes. However, it was obvious to the careful reader that this was due to something introduced in the last papers *after* that those scientists, having heard of his results, had successfully completed the study of some reactions that they had previously considered only because these were accompanied by a reducing effect, interrupting the work when encountering the first difficulties a complete study would have required." In essence, Ciamician had failed, according to Paternò, to grasp the synthetic perspective the theme might offer, and had begun his studies anew only after the early Paternò publications, reaching similar results and omitting to acknowledge priority by someone else.

Then Paternò listed the "reactions of general application" for which he thought credit should be given to himself and highlighted the points of contrast with Ciamician [37]. Apart from the cycloaddition with alkenes [29, 30, 40] that went undisputed, these included some further reaction of ketones, such as that with alkylbenzenes that caused the oxidative dimerization of the latter to form bibenzyls [41]. He was piqued when Ciamician reported a year later the dimerization of toluene and cymene as "experiments begun several years before and reconsidered at that time" [42]. In effect, it seems that Ciamician in this case did not contribute significantly to the development of this reaction, limiting himself to reporting a few results, easily predictable on the bases of what Paternò had previously published.

Further reactions of ketones that Paternò listed likewise involved attack by a ketone at a C–H bond, and all of them were variation of the radical chemistry initiated in this way. The radicals then coupled, in the homogeneous or heterogeneous way and the various products obtained in this way, or at least the easily isolable ones, pertained to different classes of products evolving to different end (isolable) products, according to their structure. Thus, reaction with alkylbenzenes yielded cross-coupling products. As an example, benzophenone coupled with toluene, ethyl- and propylbenzene, and diphenylmethane to give the corresponding phenylated alcohols. This process, which he called the "enolic" reaction because of an analogy between this C–C bond forming reaction and aldol condensation (see Scheme 4.9) [41, 43], was actually extended by Ciamician to aliphatic derivatives, obtaining cross-couplings between acetone and some alcohols [44, 45], "an important result," as Paternò loyally recognized [37].

Analogously, when irradiated in the presence of aromatic ketones, *N*-methylamine, benzylamine, and several alkaloids gave the respective α-aminoalcohols [46, 47]. The reaction of ketones with further aliphatic compounds gave the pinacol from the former and an oxidation (or dehydrogenation) product from the latter (see Scheme 4.9) [38, 39]. A typical example was the reaction with an alkane, as exemplified by that of benzophenone with linear alkanes (such as pentane) that gave ⅔ of the pinacol and ⅓ of the oxetane arising from addition of the ketone onto pentene generated in the primary reaction. Further compounds that participated into this reaction included alcohols, ethers, epoxides. These processes had been studied by either of the two groups and in several cases by both of them, but the products structure had not yet been completely clarified. This elicited some comments by Paternò on the consistence of the rationalization offered by Ciamician and again the reproach of having investigated with insufficient care (and even with insufficient skillfulness) the reactions accompanying the reduction of ketones [37].

Paternò ended his summarizing manuscript by affirming that he claimed credit for the abovementioned reactions starting from the date of the first note, published in 1909 (see Scheme 4.9). Ciamician gave a detailed answer to these remarks and concluded that a new photochemist was welcome in the field, provided that he acknowledged previous work. He further recalled that he had been involved in research on this theme much earlier than Paternò, which is indisputable [48]. The last scientist further stated that he was not likely to pursue the study of this subject, although he did not fully exclude this possibility. As a matter of fact, this remained his last contribution to photochemistry and one of the last significant papers by Paternò, now approaching the age of 70 and involved in collaboration with the Government directed activities during World War I. As for Ciamician, he published only a couple more of papers on photochemistry and then he too left this field and, apart from the activity related to the war he too had to carry out, devoted his last years to a different subject, that is, to the transformations that an exogenous substance underwent in vegetal organisms (glycosylation). Unfortunately, he died only a few years afterward at 64.



Scheme 4.9 Photochemical reactions of aromaticketones and aldehydes reported by Ciamician and Paternò

Summing up, the original contribution by Ciamician and Silber in defining the concept of photochemistry and in demonstrating which were the chemical processes "caused by the action of light and light alone" was acknowledged by Paternò, while what he reproached to the two colleagues was their limited "organic" insight.

They had thought that photochemistry was essentially a way of promoting redox processes and little else. Actually, they considered that the fact that further products had been isolated a variation to the reduction of ketones and quinones they had studied, not the discovery of a new process. On the contrary, Paternò felt that a new method of reduction of ketones was nothing “really new” and was less appealing for the synthetic chemist than the formation of C–C bonds through an oxidative dimerization or cross-coupling process. Probably, even nowadays many synthetically minded chemists would concur with this evaluation in principle, although in most cases mixtures rather than pure products were obtained from such photoreactions. Apart from priority, the fact remains that the two groups had discovered the majority of the present-day known general photoprocesses of aldehydes and ketones (besides those that were the subject of the controversy and mainly involving aromatic derivatives, see Scheme 4.9, some reactions of ketones studied by Ciamician should be added, in particular the fragmentation processes of aliphatic (in particular, alicyclic) ketones, now known as the Norrish type I reaction.

Perhaps, one may see in the controversy a slightly different approach toward chemistry in general and photochemistry in particular between the two scientists, although there are more similarities than differences. If one has to apply a classification, both of them were “organic chemists” that used light as a reactant for obtaining a chemical transformation, an approach that is maintained in modern synthetic organic photochemistry. Both of them surely shared the view expressed by Stobbe in 1908 (see above) [1].

The two Italian scientists were the most prolific contributors of new photochemical reactions at their time. Ciamician was also a physical chemist and took care also of this aspect, e.g., he took pains to demonstrate that his reactions were caused by light, excluding the intervention of other agents, attempted to determine which was the active wavelength, and formulated the hypothesis that the induction by light of a chemical reaction “had something to do with the most recent and profound speculations of mathematical physics” about “a quantity” of light producing a kind of ionization [45]. This mixed approach is possibly reflected in the title of his series of notes, “chemical action of light,” in comparison with the more straightforward organic approach by Paternò, who chose the title “synthesis in organic chemistry by means of light.”

It is possible that the enthusiasm for the discovery of reduction as a general effect of irradiation (the reduction of ketones, quinones, and nitroaromatics has been a favorite theme from the start of their photochemical work) led Ciamician and Silber to focus their attention on this aspect, and indeed some of the products from the photoreduction of ketones are easier to detect than other products formed in the same reaction. However, Ciamician and Silber can in no way be accused either of want of preparative pertinacity (compare, e.g., the painful work for isolating the various reduction products from nitroaromatics and establishing a connecting mechanism they had carried out, or that required for isolating and recognizing such labile compounds as the aldehydes from the α-cleavage of cyclic ketones) [49] or of insufficient “organic flair” (their bold but strictly rational reasoning in assigning the cyclobutane structure to the product from the intramolecular cycloaddition of carvone [38, 39] closely parallels that exhibited by Paternò in assigning the oxetane structure to his cycloadducts [29, 30, 40], the two reactions being the first reported examples of 2+2 cycloaddition). After their work, preparative photochemistry advanced slowly for several decades. Not surprisingly, it started again from the irradiation of ketones (see Scheme 4.9), but appeared quite oblivious of its previous story. A conspicuous indication of this situation is the fact that no photoreaction has been named after the two pioneers. Thus, there is no photochemical Ciamician reaction (although Schönberg proposed that the enone-alkene cycloaddition was named after him) [39]. The α-cleavage of ketones, particularly of cyclic derivatives, thoroughly investigated by Ciamician in the first years of the twentieth century [49] is now known as the Norrish Type I process and has been reported by that scientist (who does *not* quote previous studies) in 1934 [50–52]. Likewise, Paternò's [2+2] carbonyl/alkene cycloaddition is not even considered in the capital review by Schönberg on the photochemistry of non-enolizable ketones (1947) [53], although it is adequately discussed in the following book (2nd edition, 1968) by the same author [4], after that it had been rediscovered by Büchi in 1952 and bears now both names.

4.1.3 A "Green" Synthetic Method

A point that both Ciamician and Paternò evidenced was the peculiar *mild* conditions that characterized photochemical reactions and the fact that freely available and nonpolluting solar light was used [45]. For example, Paternò commented on the easy reduction by alcohols in photochemical—in contrast to thermal—reactions. "This easiness of alcohols to give hydrogen, yielding the corresponding aldehydes", he remarked, contrasted with the drastic conditions under which alcohols were converted to aldehydes under thermal conditions (800–820 °C according to Ipatiew) [38, 39]. Furthermore, both Paternò and Ciamician evidenced that the cross-coupling of ketones and alcohols (see above) led to C–C bond formation in a way similar to the aldolic condensation, but, contrary to the latter reaction, did not require the use of a base.

Indeed, Ciamician explicitly presented his work in photochemistry as the search of a mild synthetic method alternative to thermal methods. The great triumph of the chemistry of his time, now capable of preparing compounds identical to the natural ones, had however been obtained "by displaying an excessive show of force," he noted [54]. Most syntheses in the laboratory required the use of a high temperature or pressure, while nature, and in particular green plants, offered "the wonderful example of great results obtained, at least from what appears, through the least means" [54]. This statement expresses with an astonishing clear-sightedness the modern concept of "green" or "sustainable" synthesis, characterized by the mild conditions and the respect of the environment. More precisely, Ciamician thought that it was the absorption of solar light that gave to green plants this ability and this was the reason, he declared, behind his embarking in an exploratory work for ascertaining whether photochemical reactions may be considered a mild alternative also for synthesis in the laboratory. Thus, the first systematic exploration of synthetic photochemistry carried out by Ciamician and Silber over 25 years originated from an environmental-conscious consideration and in this sense it may be concluded that photochemistry and green chemistry were born at the same time [55–57].

4.2 Born to Measure

4.2.1 o-*Nitrobenzaldehyde and the Equivalence Law*

The formulation by Einstein of the "equivalence law" induced extensive work attempting to reach an experimental verification, as reported in Chap. 2, and the distinction between the primary process—for which the law holds, and secondary processes that led to final products in an *overall* quantum yield that might well differ from 1, as in practice was the case for most photochemical reactions. In this sense, it was perhaps more interesting that the measured value could be a simple number, e.g., 2 or ½, rather than 1, because a round number led to the expectation that a simple rationalization could be arrived at, thus supporting the trust in the theoretical frame that was being built. The most interesting case in this respect is probably the rearrangement of *o*-nitrobenzaldehyde to *o*-nitrosobenzoic acid, a clean reaction that had been reported by Ciamician and Silber in 1901 [58, 59] and occurred in the same way in solution and in solid. The original workers had noticed its efficiency (in part, as we can appreciate now, due to the good absorption of solar light by this yellow compound).

It is thus not surprising that Weigert chose this process as a suitable model for the verification of the equivalence law. This was a mechanistically "very simple photochemical reaction," in the sense that appeared to be an intramolecular rearrangement with a shift of an oxygen atom, involving no interaction with the medium that might introduce a departure from the simplest path. Thus, it closely corresponded to the idea of primary photoprocess as expressed above. The actual measurement of the quantum yield had required detailed studies, in order to establish how precise and dependable were the results and the suitability of the analytical method chosen (in particular, potentiometry for the aldehyde) [60–65], as well as the dependence on conditions. It appeared that wavelength and intensity of light caused little effect, as did the concentration of the solution (though some disagreement with the results by Kaplan occurred) [60, 62–64]. Experiments under different conditions consistently gave a quantum yield close to 0.5 (exemplificative data obtained in various laboratories over several decades, which did not vary much from the accurate study by Bowen and by Leighton and Lucy [66], are shown in Table 4.1). Now the question was, which confidence had to be given to such a fractional value. As always in science, as in any manifestation of the human mind, similar data could be interpreted in opposite ways.

Table 4.1 Measured quantum yields for the rearrangement of *o*-nitrobenzaldehyde[a]

Light, conditions	Measured quantum yield	Year, reference
"Violet light," r T	0.5	1924, [67]
366 nm, 22–24 °C, ligroin	0.52	1934, [68]
366 nm, 22–24 °C, acetone	0.51	1934, [68]
350 nm, acetonitrile, r T	0.50 ± 0.06	1980, [69]
313 nm, water, 20 °C	0.40 ± 0.03	1994, [70]
366 nm, water, 20 ± 1 °C	0.42 ± 0.02	1994, [70]
390–440 nm, crystals r T	0.44 ± 0.06[a]	1934, [68]
366 nm, crystals, 22–24 °C	0.50	1924, [67]
334 or 366 nm, poly(methyl methacrylate) film, r T	0.50 ± 0.06	1968, [71]
313 ± 20 nm, water-ice, *ca.* 25 °C	0.41±0.04	2010, [72]

[a] To be corrected by taking into account the loss of light by scattering

Thus, Bowen et al. [67] studied the photorearrangement of *o*-nitrobenzaldehyde in the crystal state and measured the quantum yield (the amount of acid formed was determined by extraction with water and measurement by conductivity, the light intensity by means of an air thermometer). The results obtained varied between 0.38 and 0.68, in fact again not far from 0.5, but one had to take into account the loss of energy by scattering owing to the irregular disposition of the crystals, difficult to assess quantitatively, but estimated to be <50 % by comparison with a white substance. From these data, the Authors concluded that "when allowance has been made for energy not absorbed and for experimental errors, it appears that for each quantum of absorbed radiation very nearly one molecule of product is formed." On the other hand, Wegscheider [68] found again values close to ½, but opined that it was not appropriate to round off the experimental value, since the actual measurements varied between 0.503 and 0.610, exceeding the experimental error (he also found that the quantum yield in the solid phase was close to unitary). Furthermore, Küchler and colleagues [73] carried out the photolysis in the gas phase and found that even in that case the quantum yield remained below 1. Thus, a mechanism should exist that made deactivation to some extent unavoidable. As can be easily understood, this was disturbing when considering in a simple-minded way the equivalence law.

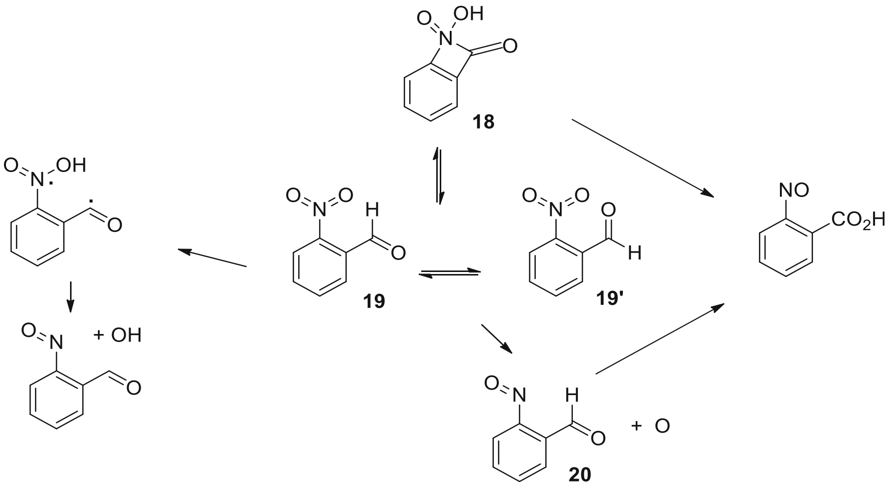
4.2.2 Mechanism: Early Studies

The next question was whether a quantum yield of more or less exactly 0.5 had to do with the physics or with the chemistry of the molecule. Physical mechanisms that were invoked were either a partial absorption or a partial deactivation. Weigert considered the first one a viable hypothesis, in the sense that absorption may depend on the reciprocal orientation of the light beam and molecules. Indeed, Padoa had shown that this was the case in crystals and using polarized light (see Table 4.1 and references therein, [74]). Alternatively, $\Phi = 0.5$ may be the result of mere collisional deactivation that happened to occur at the same rate as reaction, a mechanism preferred by Küchler and Patat [73]. More precisely, these Authors thought that excitation by light essentially involved the nitro group (see further below) and this reaction required previous intramolecular energy transfer from the nitro group, freely rotating between the two planar conformations, to the actually reacting formyl group. They calculated that transfer had to occur within ns, in order to compete with intermolecular deactivation by collision with inactive molecules (N_2) and this may well be the source of the lower than unitary efficiency.

Other scientists, however, found that a straightforward rationalization had to be found for a primary photoreaction with quantum yield one half, not an accidental compensation (perhaps a version of Einstein's "God does not play dice with the universe"). The number of possibilities that were considered is noteworthy. One was that the photoreactive species was not *o*-nitrobenzaldehyde, but an intermediate formed from it that absorbed light and reacted. To this, Tananescu pointed out that no "active" hydrogen was present in the structure of *o*-nitrobenzaldehyde [75] and suggested that some intermediate was formed in equilibrium and absorbed light, as an example formula **18**.

Weigert [76] objected that, were this the case, the quantum yield should be quite dependent on the irradiation wavelength, because the two forms would absorb differently, whereas this was not the case for *o*-nitrobenzaldehyde. Such a dependence was observed for the less reactive 4-nitrophthalaldehyde (quantum yield around 0.1) and indeed the hypothesis of the intermediate was considered in that case [77].

A mechanism based directly on the molecule structure was proposed by Zimmer (Scheme 4.10), who suggested that the reaction involved detachment of an oxygen atom from the nitro group followed by recombination with equal likelihood at the C and N atom [78]. The hypothesis of the liberation of a gas was ill tenable, however, in view of the uniformity of the reaction quantum yield under so many different conditions.



Scheme 4.10 Some of the mechanisms put forward to explain the quantum yield 0.5 of the conversion of nitrobenzaldehyde into *o*-nitrosobenzoic acid. Thus, it may be thought that of the two rotamers (**19**, **19′**), only one absorbed light; or only one had a significant likelihood to react. Or that previous rearrangement to the actually photoreactive species was required (**18**). Or that an atom of oxygen was detached and recombined with the same efficiency at the nitrogen and at the carbon atom (see **20**). Or that the nitro group abstracted a hydrogen atom and that a hydroxyl group was split off and recombined

In the meantime, theoretical chemistry was developing and this mechanism was considered. Actually, the rearrangement of *o*-nitrobenzaldehyde was one of the first photochemical reactions for which a theoretical mechanistic investigation was carried out [79]. It was felt that radiation at the long-wavelength end of the spectrum was absorbed by the nitro group (from the comparison of the UV spectra of various substituted derivatives—the association of a UV band with a specific vibration seemed to be appropriate at the time). The next question was whether the groups were freely rotating. Steric hindrance was expected to have a role, but could not be calculated with the methods available at the time. However, the sum of the dipole, induction, and dispersion effect was calculated and a (ground) energy surface was described (see Fig. 4.4). It resulted that the most stable form was coplanar and rotation was greatly hindered for the CHO group (the ordinate in the figure), but confronted a smaller barrier for rotation of the nitro group (along the abscissa, 1.36 kcal/M). It may be expected that electronic excitation would lead to a state with some vibrational excitation. In particular, a vibration may “swing the oxygen nucleus near enough to the aldehyde hydrogen, so that an hydroxyl group with normal nuclear separation could form by a mere redistribution of the electron cloud…at the same time a chemically saturated nitroso group could form from the remainder of the nitro group, leaving the hydroxyl to react with the carbonyl.” Now, starting from the planar conformation it may be that excitation of the N–O bond pointing toward the formyl group led to reaction, while excitation of the other one led to decay with no reaction, explaining the experimentally observed ½ quantum yield [79]. A model was built, which included transfer and deactivation (electronic to vibrational energy, then to the medium) and predicted a reaction lifetime of ca. 10^{-13} s.

The quantum yield of this reaction thus was a hot topic for a couple of decades and was the ground of several disagreements. Thus, polemics were published between Weigert and respectively Kailan, about the quantitative determination of the photoproducts [60, 62–64]; Jannsen about the role of an intermediate [61, 65, 77]; and Wegschneider about whether the quantum yield was exactly 0.5 and this had a mechanistic significance that required a rationalization [76]. The mechanism was seen as quite important because, as pointed out by Kogel (see Sect. 2.5) [80], this may distinguish at which point the actual chemical change occurred, at the same time as excitation or afterward from an excited state, as yet chemically unchanged.

4.2.3 Mechanism: Modern Studies

When advanced instruments were available after 1970, the mechanism issue was confronted again and some elements of the previously reported hypotheses were incorporated in the new proposals. Thus, the reaction is in fact intramolecular and goes through distinct intermediates. Transients were detected by flash photolysis and it was noticed that, while the quantum yield of photoreaction of the aldehyde was rather insensitive to the nature of the solvent, the transient signals in the same systems were extremely sensitive to the presence of water in the medium. Thus, the initial (photochemical) step was irreversible, but generated further "active" species, the evolution of which depended on conditions. Scaiano [69] proposed that the intermediate was the aci-nitroketene (**21**), an identification that was further supported by experiments in matrix with IR detection (see Scheme 4.8) [81]. In the following years, spectral and time resolutions grew spectacularly, arriving at femtosecond resolution both with UV–Vis detection (see Fig. 4.4) [82] and with the highly structure informative Raman detection [83, 84].

On the other hand, the ½ quantum yield (or rather 4/10, see Table 4.1 and below) seems have no special significance, or maybe it does in the sense that quite often excited molecules funnel down to the potential energy surface of the ground state at a geometry corresponding, or close, to a maximum, and thus the likelihood that the system comes back to the starting configuration (reagent) or to a new one (products) is similar. The state-of-the-art science (see Schemes 4.11 and 4.12) [85] considers that the singlet excited aldehyde decays within less than 1 ps via three channels, viz. internal conversion, intramolecular hydrogen transfer to give the ketene, and (minor) intersystem crossing to the triplet state (that in turn forms a further amount of ketene). The end product, nitrosobenzoic acid, is formed from the ketene via a further cyclized intermediate or directly in the presence of water (and thus its lifetime strongly depends on the solvent, from 13 ps in a 1:1 ethanol/water mixture to 24 ns in acetonitrile) [82, 83, 85–87].

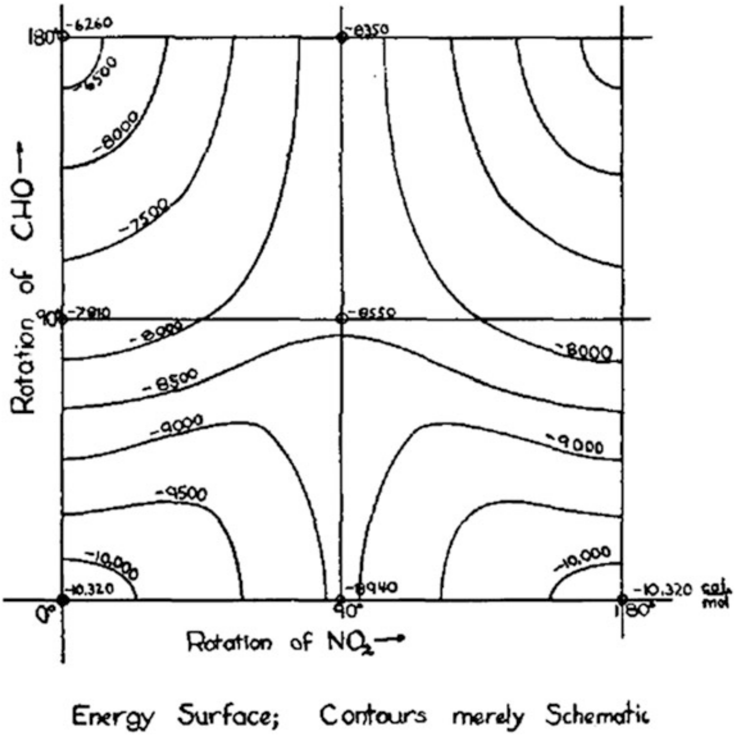
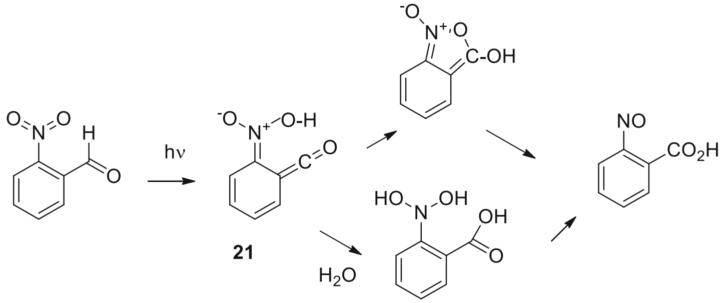
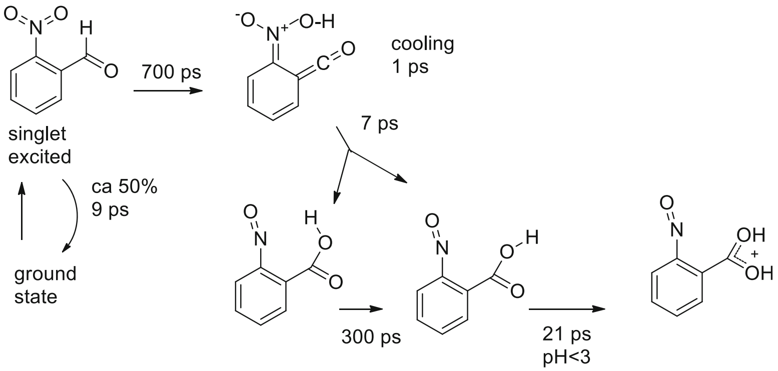


Fig. 4.4 Altitude, energy of *o*-nitrobenzaldehyde; abscissa, angular rotation of nitro; ordinate, angular rotation of aldehyde. By permission from [79]



Scheme 4.11 Photochemistry of *o*-nitrobenzaldehyde



Scheme 4.12 Photochemistry of *o*-nitrobenzaldehyde. Kinetics

The photochemical step is ultrafast (~0.5 ps), which explains the independence of conditions and in particular the fact that Kasha's rule is obeyed (the quantum yield is independent of the irradiation wavelength), since IC from higher singlet states is likewise ultrafast, actually faster (<0.1 ps) than reaction. The ketene intermediate is formed irreversibly, otherwise the quantum yield would depend on the solvent and thus the branching occurs during the decay of the electronically excited state. The decay involves a displacement of the aldehyde hydrogen atom toward the nitro group that brings the ground and excited state surfaces in energetic vicinity opening a path toward internal conversion, leading in part to the starting material, in part to the ketene intermediate. The last species gives the nitrosoacid quantitatively. As a result, only a limited change in the quantum yield is observed when exciting at shorter wavelength (Fig. 4.5a, dark blue line).

In the meantime, the computational contribution became a versatile and relatively easy to use instrument. An example is shown in Fig. 4.5b, where the potential energy surfaces for the intramolecular hydrogen transfer reaction of *o*-nitrobenzaldehyde in ground and singlet excited state are reported [86]. Calculations by the more reliable MS-CASPT2//CASSCF approach have been likewise carried out [87] as well as molecular dynamics simulations [85] (Fig. 4.6).

4.2.4 o-*Nitrobenzaldehyde as an Actinometer*

Apart from the role in mechanistic photochemistry, the scarce dependence on conditions continues to make this compound a convenient actinometer. A recent study has confirmed this fact, supporting its choice as a practical, photochemically sensitive, and thermally robust standard [72]. The study showed that the molar absorptivities of the aldehyde were only weakly dependent upon temperature and that the quantum yield was virtually independent of temperature as well as of the wavelength. This compound was used as an actinometer in field experiments on photochemistry in ice, with excellent results. The value of 0.41 was recommended

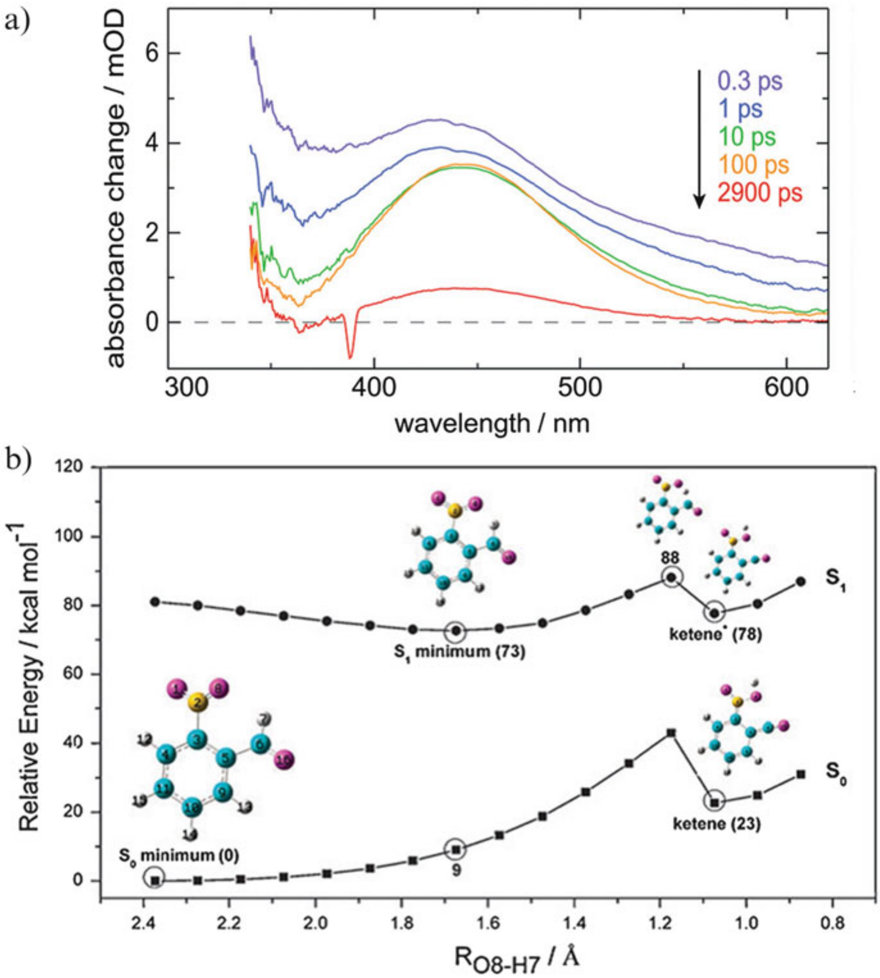


Fig. 4.5 (**a**) Transient absorption data of *o*-nitrobenzaldehyde (48 mM) dissolved in THF. Transient spectra at indicated delay times are plotted. The femtosecond excitation pulse had a wavelength of 388 nm and was in resonance with the lowest excited state. (**b**) Formation of the ketene intermediate. From [81] (**b**) Computed potential energy surface for the rearrangement of *o*-nitrobenzaldehyde. The surface for the S_0 state was obtained from B3LYP/6-311+G(d,p) optimized structures and for the S_1 state were constructed by the TD (time dependent)-B3LYP/6-311+G(d,p) method based on the S_0 optimized geometries. Energy is given in kcal mol^{-1}and bond lengths in angstroms. The solvation effects are included using the polarizable continuum model from [86]

for both solution and water ice [70, 72] and, although this may take away some of the magic of the 0.5 value, this was another of the many applications this clean reaction has found as an excellent actinometer, easy to use and well suited for different conditions, ranging from polymeric films [71], or KBr matrix [71], to TiO_2 suspension [88].

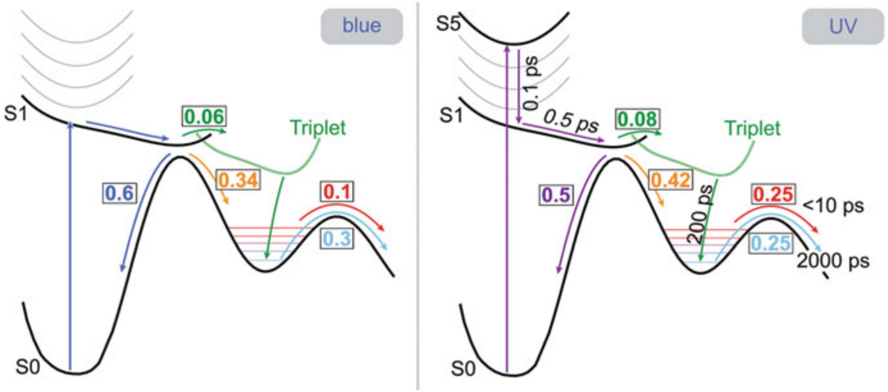


Fig. 4.6 Summary of the approximate branching ratios (numbers in *boxes*) for UV and blue light excitation of *o*-nitrobenzaldehyde. Note that all values refer to the population of the initially excited state, which was set to one. For UV excitation, the relevant rounded time constants are included, where applicable the same values apply for blue excitation. From [81]

4.3 Oxygenation Reactions and Singlet Oxygen

4.3.1 *Photosensitized Oxygenations in Biologic Systems*

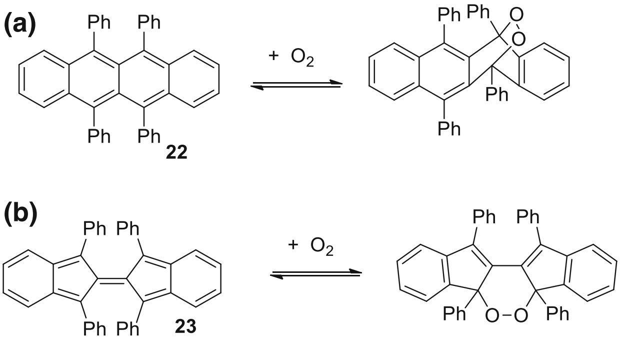
Photosensitized oxygenations are not only one of the most important classes of organic photochemical reactions, but also by far the most significant one in the photobiology. Microbiological studies on biological preparates stained with dyes around 1900 evidenced the photodynamic effect, that is, the death of microorganisms when the preparate was studied at the microscope and thus exposed to a strong light beam. The effect was confirmed and extended, in particular to red globules and vegetal organisms [89]. Noak studied extracts of plants that contained reduced (leuco) forms of dyes and under irradiation were oxidized (or better dehydrogenated) to the colored form. Experiments were carried out in the presence of various fluorescing sensitizers (eosin, Bengal rose, anthraquinone derivatives, and others) by exposure to solar light through an iron sulfate solution in order to minimize the heating contribution. Noak found that oxidation was accelerated in the presence of $MnSO_4$ and compared the effect he observed with the action of recently discovered peroxidase, suggesting that dyes formed peroxides. He also suggested that basically the same photochemical mechanism was involved in both the chlorophyll action in photosynthesis and in the photodynamic effect [89, 90].

4.3.2 Oxygenation Reactions

That the action of light could lead to the combination with oxygen was known through very many examples, already in early studies, in particular in inorganic chemistry. In a typical case, wetting a strip of paper with lead nitrate solution and drying it under a bell in the presence of hydrogen sulfide caused the formation of the brown color of the sulfide PbS_2. When dry, half of the sample was conserved in the dark and the other part exposed to the sun. A couple of hours of irradiation were enough to recover the white color of the oxide PbO_2 [91].

More specifically, oxygenation reactions (involving addition of a molecule of oxygen) were also early individuated, although only in sparse instances. Thus, Fritzscke, the discoverer of anthracene photodimerization, also found that tetracene added oxygen to form what is now known as a cyclic peroxide and the reaction was thermally reversible [92].

Several decades later, Dufraisse came across the photooxidation reactions in his large-scope investigation on rubrene and derivatives, now known as tetraphenyltetracene (22), but then thought to have a different formula (**23**, Scheme 4.13) [93]. This aromatic compound added oxygen under the influence of light, as first reported by Moreau in 1926 [94], again through a thermally reversible process.



Scheme 4.13 Photochemical addition of oxygen to rubrene (**a**). Early proposed formula (**b**)

Dufraisse was impressed by the peculiar thermodynamic properties of the process. Thus, the oxidation was markedly exothermic, consistent with the idea that "light had only a catalytic activity and could be substituted by an appropriate catalyst." On the other hand, the adduct dissociated spontaneously—and thus the addition had to be reversible, a fact not that common for reactions with oxygen in view of the strength of the C–O bond. Heating to induce cleavage caused also emission of light. This, he thought, was *not* to be considered an effect of the dissociation, there was no light energy stored along with the oxygen molecule in the adduct, and he rather considered this a side path with respect to the main reaction, the cleavage. As a matter of fact, the 23 kcal mol^{-1} liberated when the adduct was formed could be considered either a small or a large amount, depending on the point of view chosen. It was a small amount when compared with the ca. 100 kcal mol generally involved in the combination of an organic molecule with two atoms of oxygen, but it was too large if compared to the stabilization involved in the formation of a weak complex, that seemed all that can be allowed in view of the easy reversal of the addition. “Thus, oxygen donates itself to the rubrene molecule to some degree, but it is far from giving itself fully, and this surely was the reason of the easy separation.” On the basis of these somewhat erotic considerations, Dufraisse proposed the formula of a cyclic peroxide, some features of which well fitted with the observed easy detachment of an O_2 molecule. Thus, the two atoms of oxygen remained bonded one to another and were linked to benzylic positions, known for the easy fragmentation. However, this was not enough for justifying a cleavage occurring much more easily than with other peroxides and, having no other piece of evidence, Dufraisse suggested that the key was the fact that both bonds fragmented in a single process by stretching both of them in opposite senses within the same vibration. This resulted in a smaller “damage” to the molecule stability (in fact, he remarked, analogous fragmentations yielding separate entities that could not compensate themselves—consider bis-triaryl peroxides as an example—did not occur since in that case the barrier was too high and the peroxides did not cleave; see Fig. 4.7).

As it appears in Fig. 4.7, a bond cleaved biradical is indicated as the intermediate in the cleavage of the peroxide. At the same time, Schönberg suggested a “radicalic peroxide” as the first formed product of the reaction between rubrene and oxygen [95]. This either evolved to the non-radicalic peroxide, or liberated oxygen going back to rubrene. In the presence of oxygen acceptors, such as thiosinamine, the latter were oxidized, while again rubrene was reformed. Schönberg found that the

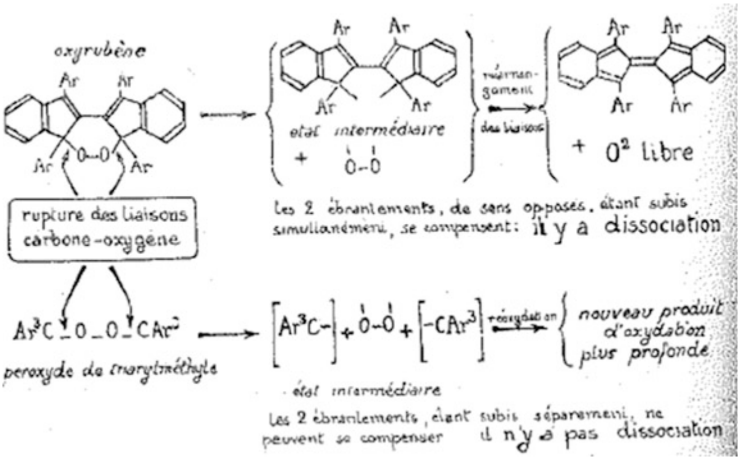


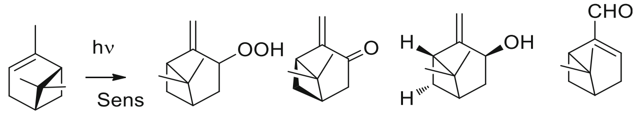
Fig. 4.7 Thermal cleavage of (supposed) rubrene oxide and of bis-trialkyl peroxide. The difference was thought to reside in the simultaneous breaking (ropture, èbranlement) of the two bonds in opposite direction in the first molecule. Reprinted with permission from [93]

biradical structure formed upon light absorption well explained the easy oxidation of other compounds, such as chromanorufene he was studying himself, as well as other oxygen additions photoinduced by chlorophyll, in particular that to amines to form hydroperoxides that Gaffron had being studying in the meantime [96]. Thus, a diradical state could add oxygen to give a (hydro)peroxide reversibly. Actually, a dispute arose over the priority of the diradical intermediates hypothesis—that was felt as being generally applicable in photochemistry—between Schönberg and Dufraisse [97, 98].

The reaction of aromatics later had an important role in defining the mechanism of the photochemical reactions with oxygen, but had a limited synthetic significance. From this point of view, a big step forward was the development by Schenck of the wide-scope photosensitized oxygen addition to dienes to form 1,2-diox-4-enes and to alkylalkenes to form propenyl-3-hydroperoxides [99–101].

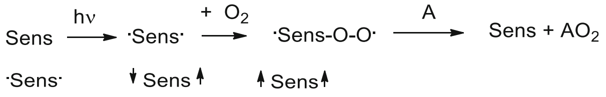
4.3.3 Mechanism

In the Dufraisse/Schönberg scheme (1933), a biradical adduct between oxygen and the rubrene molecule is indicated as the intermediate and results from oxygen trapping of the excited molecule, itself indicated as a biradical. This did not sound inappropriate considering the large amount of energy conferred by the absorption of a photon, well in the order of a chemical bond, that justified the broken bond representation of the excited state on one hand, and the well-known ability of trapping of organic radicals by oxygen in combustion processes. The diradical/triplet nature of molecular oxygen ground state explained the efficient quenching and thus a "chemical" activation of oxygen by forming a bond with the excited aromatic molecule. The same rationalization was then adopted by Schenck when he later discovered the photo*sensitized* oxygenation of alkenes and dienes (see Scheme 4.14) [102–105].



Scheme 4.14 Photosensitized oxygenation of carvene

He invoked the intermediacy of a weakly bound peroxide biradical resulting from trapping of the biradical excited state of the sensitizer by oxygen. This was able to transfer oxygen to the substrate. In the same years, Lewis had identified the metastable state as a triplet, or, by adopting a term more often used by organic chemistry practitioners, a biradical (see Chap. 3). Thus, no wonder that such an intermediate may enter in radical reactions, and in fact a number of photochemical reactions of aldehydes and ketones had been explained exactly via such biradical properties of the excited (triplet) state (see Sect. 3.2). In the extreme view, this corresponded to the representation that the two unpaired electrons of an excited state were independent one from another, in particular with regard to the spin, and dispensed with the notion of triplet, or, in a later formulation, this could be considered accessorial (what was formed was a biradical “from the chemical point of view” and formed an “adduct with biradical structure $^\bullet$SensSOO$^\bullet$”). Schenk considered that the sensitizer was “electronically photo-excited by unpairing two electrons, thus forming “photobiradicals $^\bullet$S$^\bullet$ (1S, 3S)” [103, 105] (see Scheme 4.15).[I]



Scheme 4.15 Biradical mechanism for the photosensitized oxygenation of organic molecules

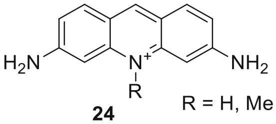
However, another rationalization was possible. This involved the excited states of oxygen. The low-lying excited states of molecular oxygen were actually lower than the triplet state of most dyes, because they were singlet states of the same orbital occupancy as the ground triplet state. These states of oxygen that had been theoretically predicted were actually characterized in the atmosphere by spectroscopists in the 1930s (Scheme 4.16) [106–108].

$$^3\mathrm{Sens}^* + {}^3\mathrm{O}_2 \rightarrow \mathrm{Sens} + {}^1\mathrm{O}_2$$

Scheme 4.16 Sensitization of oxygen

Thus, it may be thought that the triplet state of the sensitizer would transfer energy to gaseous oxygen and activate it in a *physical* way. In this mechanism, no bond formation was involved and the actual reagent were molecules of oxygen excited to the singlet state by energy transfer from the sensitizer. The reagent had thus to be a gas. As pointed out by Kautsky, experiments in solution were ill suited for investigating this point, because it would have been difficult to disentangle different effects [109, 110]. Kautsky thus devised to use spatially confined sensitizers and prepared separately gel granules on which were absorbed either the sensitizer or the substrate to be oxidized so that the influence of molecular oxygen upon their fluorescence could be examined with no disturbance. He adsorbed dyes such as Trypaflavin (see formula **24** in Scheme 4.17, actually used as disinfectant), chlorophyll, or porphyrins on solid silica gel or aluminum oxide gel, to which they remained firmly fixed. The materials formed were quite transparent and when carefully evacuated showed both normal and long-lived (in the order of seconds) fluorescence at room temperature and phosphorescence at low temperature (compare Chap. 3) (see below for the effect of oxygen).

Scheme 4.17 Trypaflavin, a mixture of two dyes



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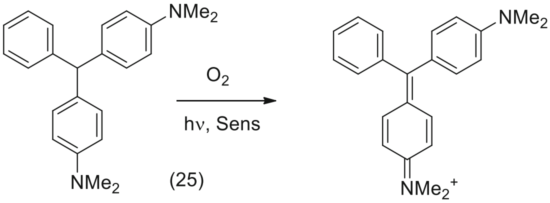
Colorless leucomalachite green (**25**) was likewise adsorbed and shown not to react when irradiated under these conditions, while when this adsorbate was mixed with that of the sensitizer in the presence of oxygen and irradiated the greenish-blue color of the oxidized dye appeared (the experiment was positive only for a small range of oxygen concentrations, however). This proved that an activated gas had been generated by the sensitizer and migrated from the place where it had been formed to where it had reacted. It could thus concluded that the sensitizer acted on oxygen, not on the substrate (Scheme 4.18).

Scheme 4.18 Photosensitized oxidation of Leucomalachite Green (25)



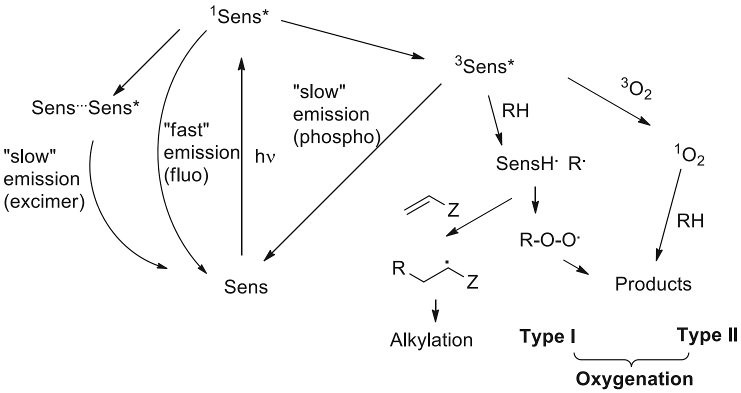
Candidates for this role were only the singlet oxygen states, $^1\Sigma_g$ (37.3 kcal mol, 766 nm) and $^1\Delta_g$ (22.5 kcal mol, 1270 nm), that thus must be the actual reagents. This conclusion was refuted by Gaffron, who studied the sensitized oxidation of different substrates, in particular allylthiourea and isoamylamine, and found that the rate was virtually independent of oxygen partial pressure. The reaction occurred with unitary quantum yield even under excitation at 760–800 nm and indeed even when bacterio-chlorophyll was used as a sensitizer, at 820 nm, where he thought energy was not sufficient for arriving at the excited state (incorrectly for the $^1\Delta_g$ state) [111–114].

But in which way acted the sensitizer? As Kautsky observed, if energy transfer to oxygen was implied, then this occurred in competition with monomolecular decay from the excited state and one would expect that emission of the dye should be quenched by O_2 [109, 110] Actually, for a unitary chemical quantum yield it had to be quenched by 100 % or thereabouts. This was clearly not the case, and the fluorescence of hematoporphyrin and chlorophyll was only marginally quenched. The conclusion was valid for the case of dyes (such as uranin) for which fluorescence was a main path, while the most effective oxygenation photosensitizers fluoresced weakly [115]. The fact that such a minor process was not quenched was thus not decisive for the mechanism. In the last group of sensitizers, the short-lived fluorescing state had little to do with oxygenation and the largest fraction rather converted to another, invisible, “quantum state.” It was this metastable state that lived long enough to be 100 % quenched by oxygen [116]. In fact, Kautsky found that several dyes showed a long-lived afterglow in very diluted solutions (up to 1/100 s) and this was quenched by oxygen, but not by the acceptors [117, 118]. In the adsorbed state, the afterglow lasted up to several seconds, and was quenched already by a 10^{-3} mm pressure oxygen, whereas with the short-lived emission ($<10^{-8}$ s) quenching was barely observed at 10^{2} mm oxygen pressure. Thus, excitation mainly led to the metastable state that sensitized oxygen quite efficiently, and for this reason was detected only in carefully deoxygenated solutions.

Gaffron preferred the alternative rationalization that an excited dye molecule reacted with a ground state one and the excited dimer was the effective (long-lived) sensitizer. In studying the photoxidation of rubrene, Gaffron found that the oxygenation rate was largely independent of oxygen concentration, but increased with a quadratic dependence on the hydrocarbon concentration, according to his postulate [106–108].

Both Gaffron and Kautsky concluded that some long-lived species was involved, but the former scientist attributed the quadratic dependence on the "increasing formation of double molecules" (an excited rubrene molecule + a ground state one) [106–108], while the latter one refused the dimer hypothesis and rather thought that in concentrated solution "a quantum oscillated between two molecules in close vicinity and these did not separate until they found the opportunity to interact with an oxygen molecule" [117, 118]. This, thought Gaffron, was changing horse when a difficulty arose [96].

In retrospect, it is clear that photooxidation is a multifaceted phenomenon and different dyes under different conditions follow different mechanisms- and energy transfer to oxygen by the triplet sensitizer, excimers, the lengthening of excited state lifetime when adsorbed all may have a role, as well as hydrogen abstraction from the substrate by the sensitizer reactions followed by trapping of the radical by oxygen and the ensuing chemistry via peroxide radical and the hydroperoxy radical $HOO^{\bullet}$ (initially proposed by Weiss [119]). (Chemical) activation of the substrate and (physical) activation of oxygen came to be known as the type I and type II photooxidation respectively (Scheme 4.19).



Scheme 4.19 Different mechanism for photosensitized oxygenation reactions

What Kautsky was proposing, with the physical activation of oxygen indeed applied to many dye-sensitized processes but was not accepted by the large majority of influential scientists of that period, mainly due to the still not recognized role of triplet sensitizers up to the 1930s. Furthermore, this mechanism perfectly suited the oxygen addition to alkenes and dienes developed from 1940 on by Schenk; indeed, these reactions are now felt as perhaps the most typical singlet oxygen reactions. Schenck, however, long resisted the introduction of the triplet energy transfer mechanism and insisted on the chemical activation [120].

Somewhat ironically, the Type II (physical) mechanism was strongly advocated by scientists such as Hammond and Turro, who recognized energy transfer sensitization as the most diagnostic test of the role of triplets (in the early 1960s) [121]. However, these scientists mainly studied the photochemistry of ketones, where in the presence of oxygen the short-lived triplets are in part physically quenched by oxygen, but some oxygenation may well occur via the Type I (radical) mechanism due to the efficient hydrogen abstraction from the substrate by the $n\pi^*$triplet (and in fact, the two unpaired electrons are orthogonal one to another, while this is not the case for dyes Schenk was using for the sensitized oxygenation of alkenes). Furthermore, the formally analogous addition of radicals to $C{=}C$ double bonds sensitized by ketones strengthened the proposal [122, 123].

The Kautsky mechanism's physical activation was a wonderful intuition, perhaps just too early for people to use, as Kasha later commented [124], but experimental support by the two-phase experiment and competition in solution was relatively weak. Further experiments based on the same idea, the physical separation of sensitizer and acceptor, were later carried out by other authors, and supported the role of a gaseous intermediates, but the products were not unambiguously identified, or were not diagnostic for singlet oxygen [125–127], or different rationalizations were put forward, e.g., invoking the role of vibrationally rather than electronically excited oxygen states [128].

However, a really solid demonstration of the singlet oxygen role was reached when Foote demonstrated on one hand that thermally produced singlet oxygen (from the reaction between sodium hypochlorite and hydrogen peroxide, ca. 10 % yield) gave the same product distribution as the photosensitized reaction [129], and on the other one performed a three-phase "Kautsky test" under better defined conditions that eliminated any doubt [130]. In this case, a well-investigated singlet oxygen reaction, such as was in the meantime become the ene reaction [131], was used, and products identification and separation of the reagents were ensured by having both the sensitizer and the alkene covalently bound onto polymers. Under these conditions, the hydroperoxide was formed both under 10 and 25 mmHg oxygen pressure (where the singlet oxygen lifetime was 0.56 and 1.4 s, respectively), but not in air (lifetime 0.088 s) or in carbon tetrachloride (lifetime 0.007 s) where $^1O_2$ was too short-lived for migrating from the sensitizer site where it was formed to the alkene site. Thus, the various mechanisms can be distinguished, although in photobiology it may still be convenient to add up all of the effects as being due to "reactive oxygen species" (ROS).

4.4 Inorganic Photochemistry

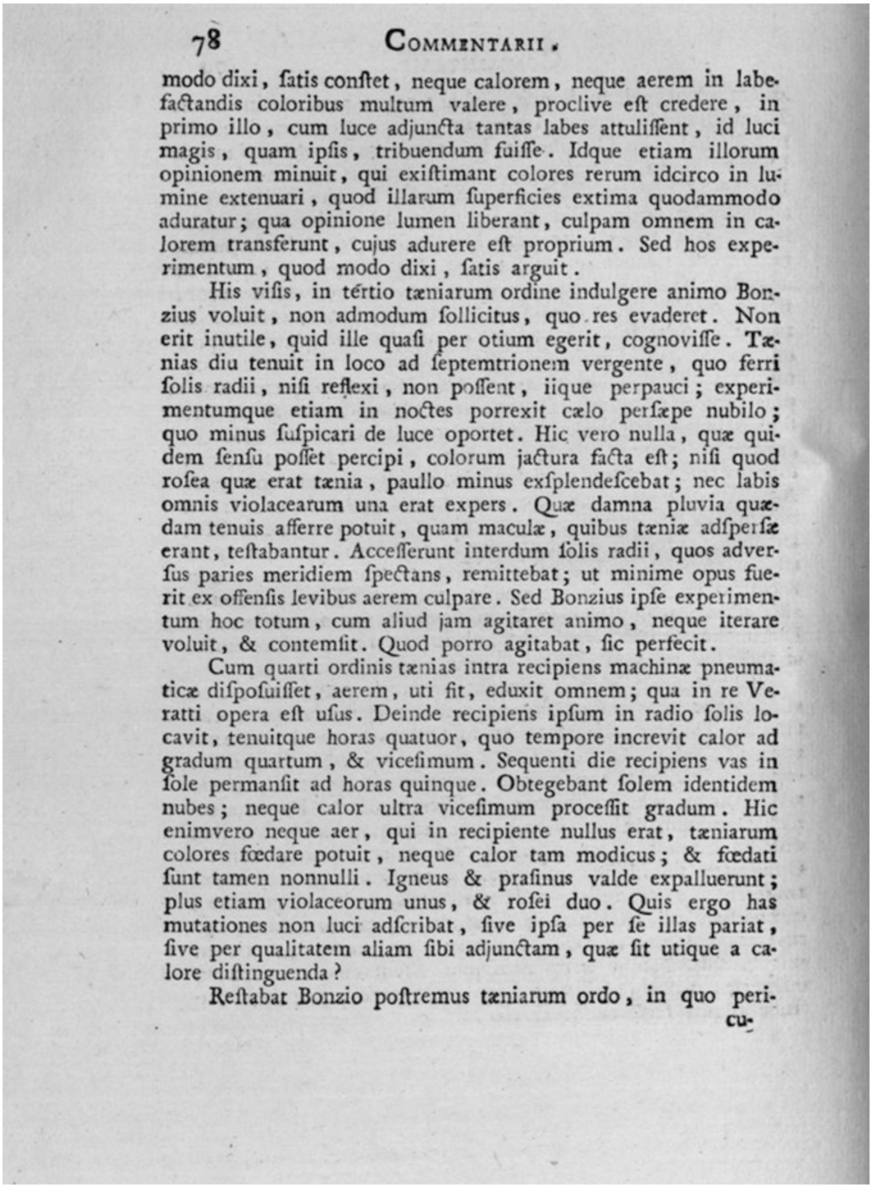
4.4.1 Early Work

The chemical action of light was noticed much earlier among inorganic compounds than in organic chemistry. This is not surprising, since here change of color or formation of precipitates make the occurring of photochemical reaction more immediately apparent. As an example, Count Bestuscheff reported in 1725 the medical action of a "Tinctura toniconervina," actually a gold-yellow ethanolic solution of ferric chloride, and noticed that the color bleached when exposed to light [132]. Scopoli noticed in 1783 that the red solution of potassium ferricyanide became blue when exposed to light and a blue solid precipitated [133]. Even more apparent is the light sensitivity of silver compounds. In his history of photography, Eder mentions that the light sensitivity of silver nitrate was reported by Albertus Magnus in his "Compositum de compositis" at the beginning of the thirteenth century [134]. That silver chloride was decomposed by light was demonstrated by Beccari in 1757 [135] in one of the first recognizements of the specific action of light (similar to the Grotthuss law, likewise formulated for inorganic systems; see Fig. 4.8).

This scientist observed that a freshly prepared sample of "luna cornea" (silver chloride) was white, but that after some time it tended to yellow and later almost to violet. The cause of this change was to be attributed first to air and second to light (see Sect. 4.3).

Furthermore, the luminescence of many minerals has always been a favorite subject of research, as in the case of fluorite. As Clarke reported in 1819 [136], crystals of this material appeared emerald green when observed by transparence, but at angles smaller than 90° a sapphire blue emission appeared. Indeed, luminescence is often important also in modern gemology. A very detailed account of early studies of luminescence, many of which referring to inorganic materials, has been published in the 900 pages treatise by Newton Harvey in 1957 [137]. Furthermore, some photochemical reactions were found to be really useful for preparative purposes. As an example, when the combination of carbon monoxide and iron to give liquid $Fe(CO)_5$ was discovered in 1891, its photosensitivity was immediately noticed. In 1905, the reaction was studied in depth and the bright orange crystals obtained were characterized as $Fe_2(CO)_9$ [138–140]. Quantum yield and mechanism of CO liberation were investigated from the 1960s on. The reaction remains the preferred method for the preparation of the diiron enneacarbonyl and the prototype of ligand substitution of metal carbonyls, a class of reactions that, in view of the mild and versatile conditions, has been largely applied for the synthesis of mono- and polynuclear complexes, besides allowing in-depth mechanistic studies of general interest [141].

By 1830, the photochemistry in solution of complexes such as ferrioxalate and ferricyanide was known, and in the following decades most of simple inorganic compounds were explored. Summing up the knowledge available by 1920, Plotnikov concluded that "the photoactivity depended on the change in the electron configuration that occurred as a consequence of light absorption, and not only the free electrons



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modo dixi, ſatis conſtet, neque calorem, neque aerem in labefactandis coloribus multum valere, proclive eſt credere, in primo illo, cum luce adjuncta tantas labes attuliſſent, id luci magis, quam ipſis, tribuendum fuiſſe. Idque etiam illorum opinionem minuit, qui exiſtimant colores rerum idcirco in lumine extenuari, quod illarum ſuperficies extima quodammodo aduratur; qua opinione lumen liberant, culpam omnem in calorem transferunt, cujus adurere eſt proprium. Sed hos experimentum, quod modo dixi, ſatis arguit.

His viſis, in tertio tæniarum ordine indulgere animo Bonzius voluit, non admodum ſollicitus, quo res evaderet. Non erit inutile, quid ille quaſi per otium egerit, cognoviſſe. Tænias diu tenuit in loco ad ſeptemtrionem vergente, quo ferri ſolis radii, niſi reflexi, non poſſent, iique perpauci; experimentumque etiam in noctes porrexit cælo perſæpe nubilo; quo minus ſuſpicari de luce oportet. Hic vero nulla, quæ quidem ſenſu poſſet percipi, colorum jactura facta eſt; niſi quod roſea quæ erat tænia, paullo minus exſplendeſcebat; nec labis omnis violacearum una erat expers. Quæ damna pluvia quædam tenuis afferre potuit, quam maculæ, quibus tæniæ adſperſæ erant, teſtabantur. Acceſſerunt interdum ſolis radii, quos adverſus paries meridiem ſpectans, remittebat; ut minime opus fuerit ex offenſis levibus aerem culpare. Sed Bonzius ipſe experimentum hoc totum, cum aliud jam agitaret animo, neque iterare voluit, & contemſit. Quod porro agitabat, ſic perfecit.

Cum quarti ordinis tænias intra recipiens machinæ pneumaticæ diſpoſuiſſet, aerem, uti fit, eduxit omnem; qua in re Veratti opera eſt uſus. Deinde recipiens ipſum in radio ſolis locavit, tenuitque horas quatuor, quo tempore increvit calor ad gradum quartum, & viceſimum. Sequenti die recipiens vas in ſole permanſit ad horas quinque. Obtegebant ſolem identidem nubes; neque calor ultra viceſimum proceſſit gradum. Hic enimvero neque aer, qui in recipiente nullus erat, tæniarum colores fœdare potuit, neque calor tam modicus; & fœdati ſunt tamen nonnulli. Igneus & praſinus valde expalluerunt; plus etiam violaceorum unus, & roſei duo. Quis ergo has mutationes non luci adſcribat, ſive ipſa per ſe illas pariat, ſive per qualitatem aliam ſibi adjunctam, quæ ſit utique a calore diſtinguenda?

Reſtabat Bonzio poſtremus tæniarum ordo, in quo peri-

cu-

Fig. 4.8 Page of the Commentaries of the Bologna Institute of Science and arts where Beccari begins to report his experiments with AgCl solid and solar light [135]. The text reads: "*…dixi, satis constet, neque calorem, neque aerem in labe sactandis coloribus multum valere, proclive est credere, in primo illo, cum luce adjunta tantas labes attulissent, id luci magis, quam ipsis, tribuendum fuisse. Itque etiam illorum opinionem minuit, qui existimat colores rerum idcirco in lumine extenuari, quod illarum superficies extima quodammodo aduratur; qua opinione lumen libera, culpa omnis in calorem transferunt, cuius adurere est proprium. Sed hos experimentum, quod modo dixit, satis arguit…' 'as I said, it is apparent that neither heat, nor air have a main role in changing colors, and I think rather that it has to be attributed to light, first of all because of the* of the outermost shell, but also of those of the unsaturated or tensioned states that participated." Looking at the periodical system, he observed that the elements at the center, that is, those that had more free electrons, were also the most reactive, while those at the borders were less reactive, and those of group 0, which had no free electrons at all, showed also no photoreactivity. Plotnikov [142] generalized these observations in the rule that the more valence electrons had an element, and the bigger was the atomic weight, the more photoreactive it was (see Chap. 2 and Fig. 2.5).

4.4.2 Photochemistry and Photophysics of Transition Metal Complexes

Rationalization could not proceed further at the time, and actually inorganic photochemistry, in particular the all-important photochemistry of transition metal complexes, entered its modern age somewhat later than the organic part, starting from the 1960s, when the ligand field theory and thus the spectroscopic assignments of the various transitions had been fully developed. The state diagram is here more complicated, because of the different types of transition possible in a complex ML_n (involving metal-centered orbitals, d–d transitions, as well as metal-to-ligand charge transfer, MLCT, and vice versa ligand-to-metal LMCT and finally intra-ligand transitions) and of the effect of symmetry and of the chemical nature of ligands. These affect the energy ordering and the interconversion rate of the states. Furthermore, spin–orbit coupling has an all-important role and the presence of a heavy atom introduces a major difference with respect to molecules containing only light elements and enables also "forbidden" transitions [143, 144].

The photochemical reactivity of metal complexes is quite varied. As an example, Cr(III) complexes such as $Cr(NH_3)_6{}^{3+}$, $[Cr(NH_3)_5X]^{2+}$, and related species undergo photosolvolysis, often with a quantum yield as high as 0.4 or more, in contrast to their great thermal stability. Taking into account the short lifetime of the excited state, the pseudo-first-order rate constant for reaction is in the range 10^8–10^{11} s^{-1}, which contrasts with the ground state rate constant of $8 \times 10^{-6} S^{-1}$ at 25 °C. Thus, an increase in rate by a factor of 10^{14}–10^{17} makes possible an effective reaction from the short-lived excited state, revealing how deeply changed is bonding in electronically excited states. As for the mechanism, both doublet and quartet states may participate in a chemical reaction or in luminescence (depending on conditions, in particular on temperature) and transfer between different manifolds is possible in both directions, which makes analysis of the system not easy (see Fig. 4.9) [145, 146].

Fig. 4.8 (continued) *strong damage occurring when light is added. This is against the opinion of those that think that the color of things is as much weakened in the light, as much as their surface is damaged, an opinion that frees light and transfers the blame onto heat, the nature of which is to damage. But this can be understood from the experiments...*"

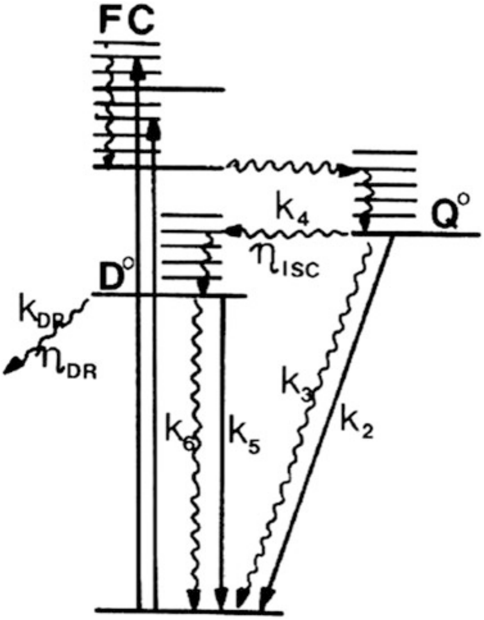


Fig. 4.9 State diagram for an hexacoordinate Cr(III) amine complex. Excitation leads to Franck Condon states that decay by internal conversion. Both direct and reverse intersystem crossing to the lowest quartet state Q° occur. This state emits or decays non-radiatively (k_3, k_2). The lowest doublet D° may be formed by this way. From [145, 146]

Noteworthy, these complexes phosphoresce at room temperature in fluid solution. In contrast to what happens with organic molecules, phosphorescence may exhibit a well-resolved vibrational fine structure when the emitting state and the ground state have similar molecular geometries and vibrational modes of certain symmetry types couple with the electronic transition to relax the symmetry forbiddance [147].

In the case of the hexacyanochromate anion, doublet and quartet states are more far away and back ISC is negligible, while phosphorescence is observed. In this case, it is possible to enter either of the spin manifold by selective sensitization, depending only on the sensitizer energy (spin selection prohibition is softened by the presence of the heavy atom). Thus, sensitizers with energy higher than Q°, such as naphthalene, pyrazine, xanthone, and acridine, cause $Cr(CN)_6^{3-}$ photoaquation, while those that are below that level, such as Michler's ketone, 2′-acetonaphthone, $Ru(bipy)_3^{2+}$, and erythrosine, do not. However, phosphorescence from $Cr(CN)_6^{3-}$ is sensitized by $Ru(bipy)_3^{2+}$ and erythrosine (see eq. 4.1 and Fig. 4.10). This proved that an energy transfer process involving the population of the lowest doublet state of $Cr(CN)_6^{3-}$ did occur, but caused no sensitized photoreaction, only emission (see eq. 4.2). Thus, none of the doublet states is involved in $Cr(CN)_6^{3-}$ photochemistry, nor back intersystem crossing to the quartet state occurs [148].

Sensitization offers also a way for increasing the yield of the desired reaction, when the limit is a low value of the intersystem crossing efficiency. This happens, for example, for $Co(CN)_6^{3-}$, whose reactive lowest *triplet* is populated with efficiency $\eta_{ics} = 0.4$. Sensitization via triplet biacetyl (that has $\eta_{ics} = 1$) leads to an increase in the quantum yield up to a factor 2.5 times [149] (Fig. 4.10).

$$^{*}\mathrm{Ru(bipy)_3}^{2+} + \mathrm{Cr(CN)_6}^{3-} \rightarrow \mathrm{Ru(bipy)_3}^{2+} + (^2E_g)\mathrm{Cr(CN)_6}^{3-} \quad (4.1)$$

$$(^2E_g)\mathrm{Cr(CN)_6}^{3-} \rightarrow \mathrm{Cr(CN)_6}^{3-} + h\nu \quad (4.2)$$

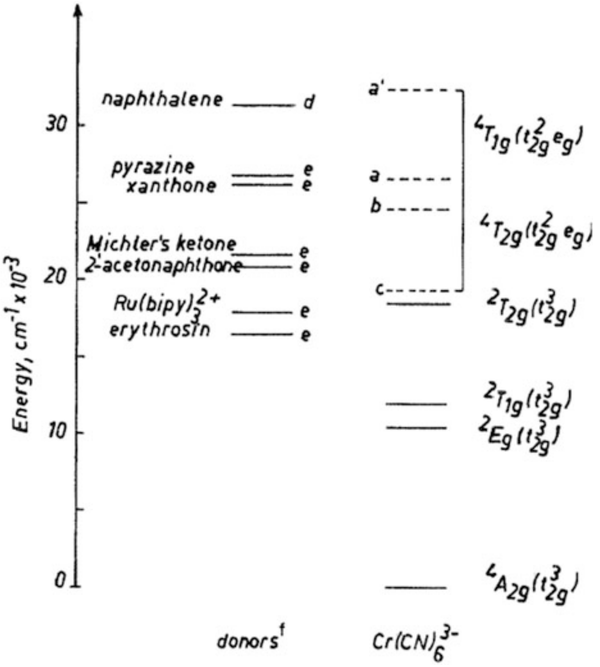


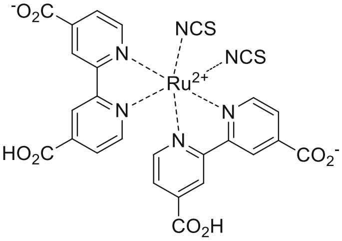
Fig. 4.10 Energy level diagram showing the energies of the electronic excited states potentially involved in the energy transfer from the donors used and $\mathrm{Cr(CN)_6}^{3-}$ a and a′, energies of the absorption maxima; b and c, upper and lower limit values for the zero vibrational level of $^4T_{2g}$ as deduced from the half width of the absorption band and the Stokes shift between absorption and emission, respectively: d, energy of the lowest singlet excited state; e, energy of the lowest triplet excited state: f, acridine does not appear in this diagram due to the uncertainty of the energy [148]

4.4.3 Transition Metal Complexes as Sensitizers

Photochemical ligand exchange is highly interesting from the mechanistic and preparative inorganic photochemistry, but for photochemistry in general, perhaps still more interesting are other compounds that are rather photostable, since these can be used as sensitizers and their properties can be finely tuned by exchanging the central ion, by modifying the ligand structure, by building supermolecular complexes based on several ions, and so on. These characteristics have given to transition metal photochemistry a key role in practically every application where conversion of light energy in any other form is the target.

Actually, the single chemical species most studied from the photochemical point of view very likely is ruthenium (II) tris(bipyridyl) cation (Scheme 4.20), due to the highly favorable properties it exhibits in this respect.

Scheme 4.20 Tris (bipyridinium) ruthenium (II) cation



Despite the fact that the presence of the heavy atom causes a large singlet–triplet mixing, it is still convenient to class the ground state, a closed shell species where the $\pi M(t_{2g})^6$ orbital is the HOMO, as either singlet or triplet. Various types of transitions are observed. In particular, since Ru^{2+} is easily oxidized and difficult to reduce, while the bipyridine ligand is easy to reduce and difficult to oxidize, the MLCT excited states are expected to lie at relatively low energy. In fact, an intense band centered at 450 nm has been assigned to spin-allowed MLCT $\pi_M \rightarrow \pi_L{}^*$ transition. This complex emits a beautiful red-orange luminescence that has been assigned to a spin-forbidden ^{3}MLCT transition, a phosphorescence [150, 151]. The complex undergoes only a slow solvation upon irradiation, leaving room for energy transfer or electron transfer, whether oxidative or reductive (see Scheme 4.20), conforming to the postulate that electronically excited states are both stronger oxidants and stronger reductants than the corresponding ground states. Notice further that in the presence of a sacrificial donor/acceptor, Ru^+ or Ru^{3+} species are generated that can further act as electron transfer sensitizers. The energy of the excited state and the redox potential are tuned over a large span by varying the ligand structure (or the central cation). Electron transfer was documented, e.g., by using cobalt amine complexes [152] or by paraquat. One of the key issues of early photochemical studies had been whether irradiation led a system to a position different from the thermal equilibrium (see Sect. 2.5). Under conditions in which the paraquat monocation was efficiently quenched by a donor, a clear-cut experiment demonstrated that the energy of the photon was used to push the system in the non-spontaneous direction [153].

The wealth of information that has accumulated on ruthenium complexes make them the ideal substrate for studying energy and electron transfer in a variety of applications, and were not ruthenium a very limited resource, one may think of a large-scale use of such complexes, e.g., for solar energy conversion.

A further property that makes transition metal ions tremendously useful in photochemistry is obviously the possibility of complexing several mono- or polydentate ligands around a number of metal ions and thus to assemble sophisticated structures where electronic and geometric factors drive the photochemical processes. This principle has been largely applied in artificial photosynthesis for optimizing light collection and make migration of excitation toward a specific site preferred.

4.5 Energy from the Sun

4.5.1 Ciamician in 1912

Virtually all of the photochemical experiments carried out until the first decades of the twentieth century were carried out by using solar light. That the fact that the irradiation from the Sun had a basic importance as a source of energy was rarely evidenced. Energy for the industrialized society of the last centuries was primarily identified with the highly concentrated form of fuels derived from fossil materials and their elaboration under anaerobic conditions, coal and oil. The fast development of the Belle Époque was obviously accompanied by an even faster expanding demand of energy and some worry about how long this could last began to surface among scientists. That photochemistry had a role in this field was apparent, since all of the living organisms ultimately depended on solar irradiation, which continued to flow over the Earth, while fossil fuels were the nothing else than a warehouse where solar energy of distant times was stored as chemical energy, and was rapidly depleted with no hope of recovery. This point was clearly expressed by some contributions of that time. A case to hand is a talk by Ciamician [154]. Having received the invitation to be one of the four plenary speakers at the 8th Applied Chemistry Congress in New York in 1912 [45], he thought he should not only present his recent work but also stress the applicative side of his research. The topic he had pursued almost exclusively in the last 20 years was the chemical action of light (as mentioned only solar light at the time). Thus, he decided to change the perspective and to evidence the contribution solar irradiation may give to cope with the increasing energy need of contemporary society. On the basis of recent assessments, he calculated that solar irradiation amounted to ca. 1×10^{24} J per year. Solar irradiation was exploited by green plants and stored as a resource, evaluated as dry organic matter, corresponding to 6×10^{20} J per year. A part of the energy that had flooded the Earth surfaces during the previous eons was now under the planet crust and was available as coal and oil. The extraction of oil was rapidly increasing in these years, but coal still gave the main contribution and was extracted to the extent of 1×10^{9} tonnes per year, an amount capable of affording 3×10^{19} J per year, but this could not go further. Ciamician thought that one of the main tasks of science was to ensure that the energy needs continued to be satisfied when coal was no more available. This could be obtained through two paths, that is, (1) by enhancing the amount of energy-rich chemicals produced by plants and (2) by converting sun energy through artificial devices.

The role advanced agriculture could have for an increased supply of resources had been already demonstrated at Ciamician's time. A clear case had been apparent to everybody when the development of the daily press had caused a large demand for wood pulp in a sufficient quantity and at low prices. What was then required, and was found, was having trees that grew more rapidly and thus afforded cellulose faster. As Ciamician remarked, this actually fulfilled a desire Faust had manifested when making a bargain with the Devil for a new youth [155]:

Und Bäume die sich täglich neu begrünen!
(and trees that every day become green)

Mephistopheles had not considered a similar task impossible and had answered:

Ein solcher Auftrag schreckt mich nicht,
Mit solchen Schätzen kann ich dienen.
(such an order does not bother me,
I can supply you with such treasures)

This increase in the plant grow had been obtained by modern science and "*since Liebig, and largely by adopting the methods proposed by him, the production has been at least quadrupled.*" Therefore, it was reasonable to expect that this source of energy would grow further.

"*The harvest, dried by the sun, ought to be converted, in the most economical way, entirely into gaseous fuel, taking care during this operation to fix the ammonia (by the Mond process for instance) which should be returned to the soil as nitrogenous fertilizer together with all the mineral substances contained in the ashes [. . .] The plants are unsurpassed masters of—or marvellous workshops for—the photochemical synthesis of the fundamental substances, building up from carbon dioxide with the help of solar energy." Furthermore, plants are a source of materials for further elaboration to secondary substances that are usually found in small quantity and are of value for special reasons. "The alkaloids, glucosides, essences, camphor, rubber, coloring substances and others are of even greater interest to the public than the fundamental substances on account of their high commercial value*".

At Ciamician time, it was known that chlorophyll sensitized "*assimilation*," that is, formation of carbohydrates from carbon dioxide, but the chemistry underlying to such a transformation was essentially not known (these were the nature "*guarded secrets*" science had yet to discover; see Chap. 12). Certainly, this was not quite simple. Ciamician tested chlorophyll as well as other dyes for a possible effect on the photochemical reactions he was studying, that is, those of ketones, and, not surprisingly in hindsight, found that these had no effect, but couldn't go farther. In the 100 years that have elapsed since then, studies on chlorophyll photosynthesis have enormously progressed and the mechanism involved has essentially been understood. This has resulted to be extremely more complex than could be figured out a century ago. However, the nonnatural approach could likewise be taken and several other processes were discovered, which were caused by ultraviolet radiations and potentially might take place by using visible light, provided that suitable sensitizers were found. Ciamician quoted the synthesis of ozone, of sulfur trioxide, of ammonia, of the oxides of nitrogen, as well as organic processes, particularly reciprocal oxidation and reduction as systems suitable for accumulating chemical energy in sun factories.

"*Where vegetation is rich, photochemistry may be left to the plants and by rational cultivation, as I have already explained, solar radiation may be used for industrial purposes. In the desert regions, unadapted to any kind of cultivation, photochemistry will artificially put solar energy to practical uses. On the arid lands there will spring up industrial colonies without smoke and without smokestacks; forests of glass tubes will extend over the plains and glass buildings will rise everywhere; inside of these will take place the photochemical processes that hitherto have been the guarded secret of the plants, but that will have been mastered by human industry which will know how to make them bear even more abundant fruit than nature, for nature is not in a hurry and mankind is. And if in a distant future the supply of coal becomes completely exhausted, civilization will not be checked by that, for life and civilization will continue as long as the sun shines! If our black and nervous civilization, based on coal, shall be followed by a quieter civilization based on the utilization of solar energy that will not be harmful to progress and to human happiness. The photochemistry of the future should not however be postponed to such distant times; I believe that industry will do well in using from this very day all the energies that nature puts at its disposal. So far, human civilization has made use almost exclusively of fossil solar energy. Would it not be advantageous to make better use of radiant energy?*"

As a matter of fact, the importance of exploiting solar energy had been addressed also previously. For example, Lüther devoted his inaugural lecture at the Leipzig university to the "tasks of photochemistry." In the introduction of his talk, he estimated that the earth received 200 billion horse power from the sun in the form of radiant energy, but only three millions of it were used. Thus, he added, the man who could convert radiant energy into mechanical energy would be able to control the word. This was a pure speculation, he added, and in the rest of the presentation he discussed the photochemical reactions he had carried out [156]. Also, Schaum stressed the role of solar energy conversion at General Meeting of the German Chemical Society in 1910 in München [157].

4.5.2 Bodenstein in 1915

It may be appropriate to refer in some detail to another important talk, given by another leading scientist of early photochemistry, Max Bodenstein. Confidence in the progress of mankind and the interest for solar energy were not lost a few years after Ciamician's talk, despite the outbreak of the war, when he addressed the German Illuminating Engineering Society (Deusche Beleuchtungstechnischen Gesellschaft) on January 30, 1915 [158]. He first of all remarked that the choice of a theme strictly related to the war was obvious for a chemist "in this mighty time" and stressed the importance that the technical equipment of the army and the navy, and here chemistry had a large place, had for the success. "When our mighty guns hurl their projectiles at an unbelievable distance" and are able to make them explode when still in the air, when they hit their target, or after that they have penetrated to a certain depth, the success is due to chemical reactions. And when the crew of a U-boat is able to survive for hours in a narrow space, it is again chemistry that makes this possible by making oxygen available. Thus, Bodenstein found tempting to connect his theme, "The source of energy for our engines," with the war, thinking of the fuel that allowed to transport guns and torpedoes and to the explosives, where after all, again chemical energy substitutes muscular force. He refrained from making this connection, however, on two grounds, first that he did not want to discuss openly such things, according to the instructions by military authorities, and second because only a few people were admitted to the knowledge of the extent to which one source of energy could be—or perhaps had already been—substituted with another one, and he was not among that restricted circle. Therefore, he discussed his theme with reference not to the war, but rather to the mankind of the future, in perpetual search of energy for its engines. Energy came from coal and to a small amount from oil, nonrenewable sources that were bound to end, a situation not previously occurred as long as renewable sources as those found in nature had been used. Besides its own muscular strength and that of his animals, man had used to a limited extent the motion of air and water. These sources could never afford the amount of energy required. Bodenstein took under consideration further possibilities. An improvement was obtaining electricity rather than heat from the combustion of coal, through a fuel cell where coal would dissolve in the anode compartment and oxygen would be consumed at the cathode (fuel cells were developed at this time by Emil Baur [159]). He added that hydroelectric power and coal are ultimately deriving from solar energy and proposed to use directly light. Thus, he remarked that when the surface of a metal kept in vacuum was irradiated, or when the same was done with a sheet of surface-oxidized copper immersed in an aqueous solution, electricity was produced, and connecting the illuminated electrode with the second one electric current was passed and thus work was produced, demonstrating the most direct and clear transformation of light into chemical energy.

Two further ways for obtaining work from light were (1) the transformation by light of a substance in another one at a higher energy and collecting the work generated when the product spontaneously reverted back to the starting material and (2) the photoelectric effect. Bodenstein, however, thought that neither process was anyway close to such target. Although scientific photochemistry was still in its infancy, he thought that it was possible—though by no means certain—that in future all of the energy required for fuelling engines and for heating was taken from solar irradiation, and coal produced by solar irradiation of previous era was not wasted as fuel, but rather used as a material, e.g., in the reduction of oxides for the production of metals, and perhaps even for the production of food [158].

4.5.3 The Beginning of Photocatalysis

After the war, the development of photochemistry lost some impetus, but the problem of energy from the sun continued to receive some attention. A few years later, Spoehr again stressed that chlorophyll photosynthesis was the only way solar light was used on the Earth, but it was too an inefficient and slow process for supplanting "the supplies which have been stored for centuries and are now being depleted" [160] Any other form of energy, e.g., hydroelectric power, was not available in a sufficiently large amount for the present time request, so that one was forced to have recourse to photosynthesis. The success the use of liquid fuels had brought some to think of ethanol from plants as a convenient alternative, but "in order to supply food for our increasing population, no encroachment on agricultural industry would be permissible. Theoretical speculations of the nature of what might be accomplished if, for instance, all the arable land were cultivated were of no consequence to the problem." "*Conditions, economic and social*," he concluded, "*must be faced as they exist. The inertia of our civilization is such that great changes are induced only by the labored movements of evolution or by catastrophe. What part, then, can science and engineering play in the solution of this problem? First of all, it is the function of scientists to exercise foresight in matters regarding the material welfare of humanity for this work, there will be required an enormous amount of patient labor, which naturally should be begun long before the situation becomes acute*" [160].

Research and interest for solar energy utilization continued during the following years and found support in some case, as in the $ 647,700 donation for this aim to MIT by philanthropist G L Cabot in 1930. However, the activity in the following decades involved all of the modes of exploiting solar energy, in particular conversion into thermal and electrical energy, not chemistry in particular. The book by Daniels published in 1964 well represents the many practical possibilities that were available. That book achieved an increasing success when the 1973 oil crisis dramatically indicated the delicate balance of political and technological factors that determined the availability of energy, supporting the recourse to new sources [161].

Photochemical research then mainly centered on photocatalytic water splitting for the generation of hydrogen as a fuel. Various oxides and sulfides, in particular the inexpensive and highly effective titanium dioxide, were used. The photoactivity of this material was already known [162, 163], but the scientific development intervened in catalysis, electrochemistry, and photochemistry, along with the above historic situation, formed the background where the finding that solar light could be exploited for the production of hydrogen received the attention it deserved.

Thus, Fujishima and Honda built an electrochemical cell where a TiO_2 electrode was connected with a Pt black electrode [164, 165] (see Fig. 4.11, Scheme 4.21). Oxygen was evolved at the (rutile) TiO_2 surface upon illumination with light of wavelength shorter than its bandgap 415 nm, ca. 3.0 eV. This was proved to involve promotion of an electron from the valence to the conduction band (1.23 V) leaving holes (h_{VB}) and electron transfer from the water molecules adsorbed on the surface to the semiconductor. Current flowed in the external circuit to the Pt electrode, where water was reduced (via e_{CB}) and hydrogen was liberated.

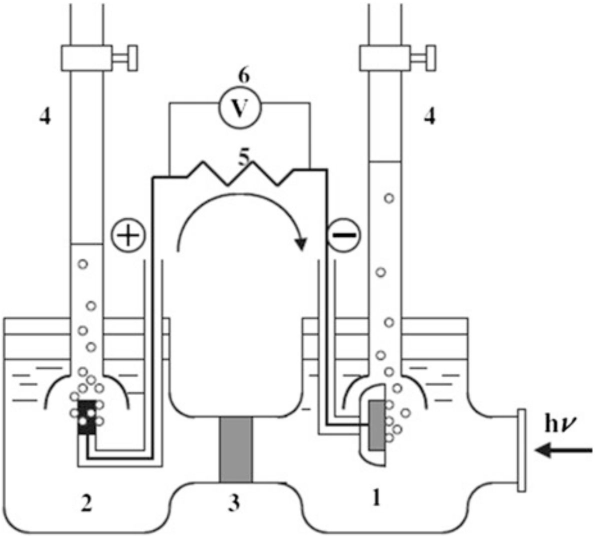


Fig. 4.11 Illumination of a titania electrode (1) causes evolution of oxygen. Hydrogen is evolved at the Pt black electrode (2, in a proportion 2 to 1 with respect to oxygen, as measured by gas burettes 4). A conducting membrane (3) connects the compartments and the electrodes are connected through an external load (5) and a voltmeter (6)

Scheme 4.21 TiO_2 photosensitized water hydrolysis

$$\begin{array}{l}
TiO_2 + h\nu \rightarrow TiO_2(e_{CB}, h_{VB}) \\
2\,H_2O + 4\,h_{VB} \rightarrow O_2 + 4\,H^+ \quad \text{(at the } TiO_2 \text{ electrode)} \\
2\,H^+ + 2\,e_{CB} \rightarrow H_2 \quad \text{(at the Pt electrode)} \\
\hline
2\,H_2O + 4\,h\nu \rightarrow O_2 + 2\,H_2 \quad \text{(overall)}
\end{array}$$

Thus, a (seemingly) simple and robust system offering an artificial alternative to the extremely complex natural photosynthesis was introduced. Clearly, this was far away from the performance of chlorophyll photosynthesis, to begin with for the limited absorption of the solar emission, but the positive features of this really versatile photocatalyst have ever since remained under close scrutiny.

4.6 Cursory Elements of Photobiology

Photobiology is a discipline separated, if strongly connected, with photochemistry. Extending the discussion to that topic would go beyond the proposal and the space available. Attention to this issue will thus be limited to a very cursory glance to the historic development of four major topics, chlorophyll photosynthesis, vision, vitamin D and photomedicine, in order to have at least a rough comparison with photochemistry along the time coordinate.

4.6.1 Photosynthesis

As it is well known, the history of the chemistry occurring in chlorophyll photosynthesis [166–168] is intimately bound to that of chemistry itself, in particular to the discovery by Priestly, Scheele, Lavoisier, and others that air contained a gas, oxygen, that was necessary for life of animals and burning of a candle, and was produced by green plants. The photoinduced activity of leaves was studied in detail by Senebier in the eighteenth century [169–171]. He measured the gas development when green plants were illuminated, depending on the "quality" of air used (in modern terms, oxygen—dephlogisticated air—was evolved and CO_2—fixed air—was absorbed), and ascertained that this phenomenon was due to light, not to heat. He further attempted to determine which range of visible light was more effective by coloring the water bath with dyes that filtered a part of the spectrum, but had not sufficient pieces of evidence for drawing conclusions (Fig. 4.12).

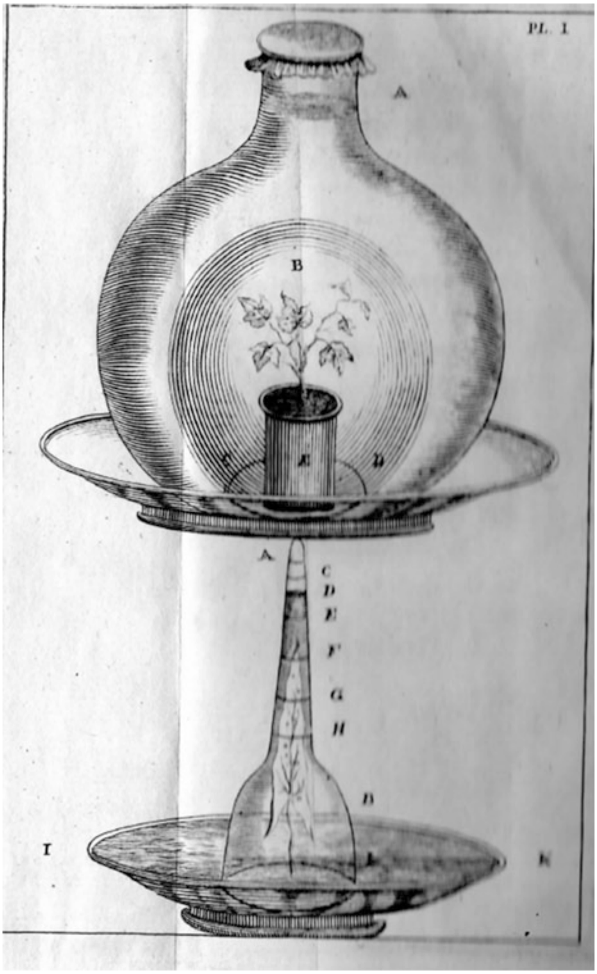


Fig. 4.12 The experiments by Senebier [169], who measured the quantity and quality (allowing or no respiration) of air liberated around a leaf illuminated by light

In the following decades, the absorption of carbon dioxide was demonstrated by several scientists and was generally referred to as “carbon assimilation.” In 1862, Sachs [170, 171] observed the formation of starch in the granules of chlorophylls. However, in 1893 Barnes pointed out that in animal physiology the term “assimilation” was largely used with reference to the transformation of food into tissues. To eliminate any confusion, he proposed the use of new terms for designing the function of green plants and proposed photosyntax or photosynthesis. Although he preferred the first, the latter one came into general use [172, 173].

In an advanced work, Timiriazeff in 1877 exposed five reversed test tubes to light dispersed by a prism, respectively, to the furthest part of the red, to red in correspondence to the chlorophyll absorbance maximum, to orange, yellow, and green [174]. The green organs to be examined were placed in the tube, along with a measured volume of air added with 5 % CO_2. After exposure to dispersed solar light, the amount of CO_2 consumed was determined and shown to increase in passing from green to yellow, orange, and the red light corresponding to the chlorophyll maximum, whereas extreme red (that was not absorbed) showed no consumption, but rather some formation of CO_2, due to respiration. Thus, provided that it was absorbed, light energy was converted into chemical energy via reduction of carbon anhydride.

As for the active pigment, extraction with alcohols of dried leaves gave a dark green, resinous material. The properties of this material (soluble in alcohol, ether, alkalis, cold sulfuric acid, reacting with chlorine, nitric acid) suggested that this had little relation with vegetal resins and rather resembled vegetal dyes. In view of “its properties and the role that it plays in plants economy” such a compound deserved “to be considered as an immediate principle of plants” and the name “chlorophyll” was proposed in 1818 by Pelletier and Caventou [175]. That different dyes were present in leaves was later recognized, but separation was no easy task. An in-depth study by Willstätter based on preferential distribution of the colored compounds present in organic solvents vs. acids of various concentration led to the isolation of chlorophyll a and b and to a reasonable attribution of the chemical structure [176]. The significance of chlorophyll photosynthesis in global energy exchange was clearly evidenced by Mayer in his formulation of the first principle of thermodynamics [177]. Nature, he thought, has given itself the mission to capture solar light and to transform this, which is the most rapidly moving force in a solid form. With this target, it has populated the Earth surface of organisms able to transform this force into a chemical difference. These are *plants*. “The plants word builds a reservoir, in which the solar rays are fixed and are transformed into forms suitable for their use. An economical preoccupation, to which the physical existence of manhood is necessarily linked, and that causes an instinctive good feeling when anyone looks to a rich vegetation,” testifies how deeply mankind recognizes the importance of chlorophyll photosynthesis. The question has to be confronted, whether plants during their life transformed chemicals or were able to create them must be answered, and it was actually clear that the whole of the matter plants accumulated arose from the environment. Every gram of a tree weighing several tons has been taken from there. Matter could not be generated, but only transformed. More precisely, carbon dioxide was reduced. Plants were able to exert their chemical function only under the influence of light, and no such result could be obtained by heating. Light, he thought, seemed to be the only physical force (perhaps along with electricity) able to be transformed into a difference in chemical work.

By using the experimental setup shown in Fig. 4.13, it was found that the amount of carbon dioxide "assimilated" at equal light intensity falling on the same surface was the same for leaves of different plants [178, 179], but this value increased with temperature, more or less rapidly for different leaves. This fact was attributed to the intervening of some thermal activated process. In every case, an optimal value of assimilation was attained and was not overcome by a further increase either in light intensity or in CO_2 concentration.

The way in which carbon anhydride from the atmosphere was absorbed and chemically transformed was the subject of many studies. The reactions involved could be rationalized as redox processes, as was demonstrated by Wurmser [180], but the chemical reactions actually involved required much work for the

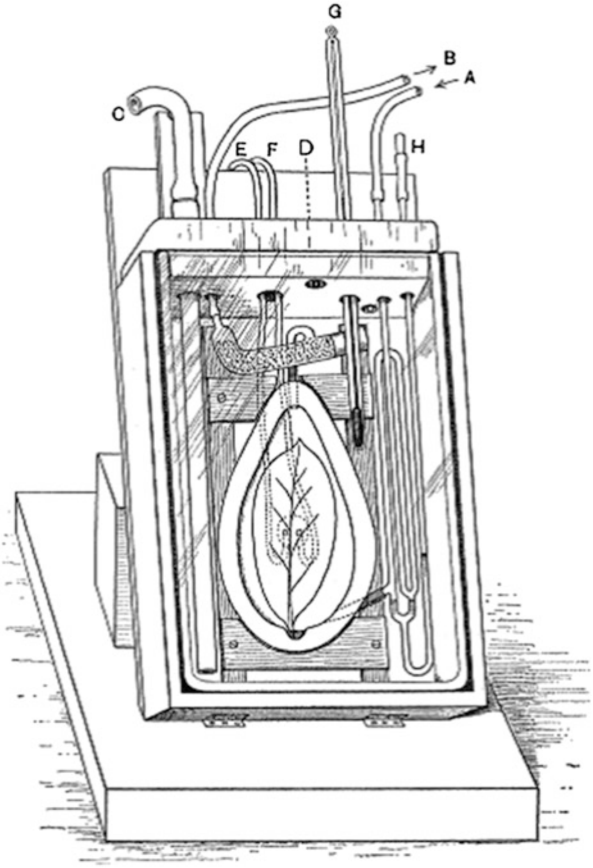
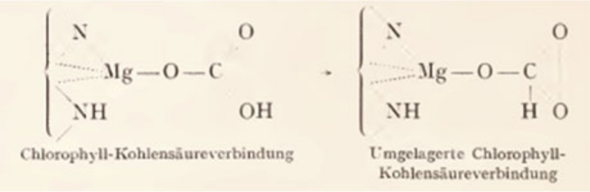


Fig. 4.13 The energy exchange was assessed by Blackman and Matthaei in an thermal bath [178, 179]. This was exposed to solar light on the roof of the institute. The temperature was controlled by running water (entering through C and outflowing from D) and measured by thermometer G. Carbon dioxide from a generator and air were introduced from A, which led to a thrice bent tube ensuring that it equilibrated the temperature with the bath. The gas leaving the chamber through B was dried through a tube of calcium chloride and the CO_2 present was determined by passing through a baryta tube

identification. A rationalization was presented by Willstätter and was based on the reaction of a complex that carbonate anion formed with chlorophyll. Irradiation was proposed to cause a rearrangement to a peroxidic structure that then decayed spontaneously with production of oxygen and formaldehyde that then polymerized to sugars (Scheme 4.22) [181].

$$H_2CO_3 \rightarrow [CH_2O] + \tfrac{1}{2}\,O_2 \rightarrow \text{Sugars}$$



Scheme 4.22 Proposed mechanism for photosynthesis involving bonding of carbon dioxide and rearrangement to a peroxidic species

In Willstätter's mechanism, this would have required that chlorophyll was constantly associated with carbon anhydride; otherwise the short lifetime of exited state would have caused a large loss. Traces of formaldehyde were detected from illuminated leaves, but a relation with oxygen developed was not demonstrated, and at any rate the process occurring in chloroplast was not duplicated in solution, suggesting a role of something more complex than a single molecule of chlorophyll in chloroplasts function.

The way in which carbon anhydride from the atmosphere was absorbed and chemically transformed was the still quite far from rationalization. The reactions involved could be rationalized as redox processes, as was demonstrated by Wurmser [180], but the chemical reactions actually involved required much work for the identification. Scientists had to confront the problem of how one of the most stable molecules, carbon dioxide, came to be reduced and from where the required hydrogen came. Discarded, after 1850, the role of "vital force," various hypotheses were put forward. Liebig [182] proposed that various organic acids, such as oxalic, malic, tartaric and citric acids, were the intermediates in the stepwise reduction of CO_2 to carbohydrates: "If one considers that unripe fruit, for example, grapes, cannot be enjoyed due to their high acid content; that in sunlight these fruits behave in the same way as leaves, namely, that they are capable of absorbing carbonic acid and releasing oxygen (de Saussure); that at the same time as the acids decrease, the sugars increase: in view of these points, one cannot reject the idea that the carbon of the organic acids in unripe fruit becomes part of the sugars in ripe fruit; that, therefore, the acid is transformed into sugar, effected by the release of oxygen and the components absorption of water" [183]. Another great chemist, Baeyer, opposed this view and suggested that rather "when sunlight strikes chlorophyll, which is surrounded by CO_2, the carbon dioxide appears to undergo the same dissociation as at higher temperatures: oxygen escapes and carbon monoxide remains bound to the chlorophyll (or rather forms a chlorophyll–CO_2 complex). The simplest reduction of carbon monoxide is to the aldehyde of formic acid—it only needs to take up hydrogen, $CO + H_2 = COH_2$.

Under the influence of the contents of the cells, as well as through the alkalines, this aldehyde is then converted into sugar. [...] Glycerol could, in addition, be formed by the condensation of three molecules and the subsequent reduction of the thus formed glyceric aldehyde" [184]. As Baeyer observed, direct conversion of CO_2 to sugars was to be preferred to the other hypothesis, because actually organic acids were not accumulated in plants, or at least their content varied among different species and type of cells. The direct conversion of carbon dioxide into formaldehyde seemed to find support with the development of the chemistry of sugars by Emil Fisher and others at the end of the century, with the demonstration that homologation by reaction with formaldehyde was indeed possible for forming the most abundant sugars, hexoses [185]. However, repeated attempts definitely demonstrated that enhancing the formaldehyde content in the plant environment did not cause any increase in the rate of photosynthesis. Furthermore, formaldehyde was strongly toxic, and, at least in retrospect, it is difficult to understand why this mechanism, clearly too simplified, was universally accepted. As for the oxygen atom detached at the beginning of the process, this may lead to a peroxide: unfortunately, again a toxic compound.

After the war, important advancements took place. In particular Otto Warburg introduced new experimental techniques [186]. The use of a sensitive manometer allowed us to measure microliters rather than milliliters of gas and thus to examine much smaller samples, over which it was easier to control the spatial and temporary uniformity of irradiation. The manometers were mounted on a thermostat, so that the vessels could be illuminated with light bulbs from below and were oscillated by an electric motor. Rather than leaves or whole plants, he used the easily grown unicellular green algae Chlorella. This allowed a much better control of experimental conditions, the use of small samples (the proportion of photosynthetic material was higher in this alga), and dispensed with competing paths, such as reflection and filtering of light by other tissues generally occurring with leaves. Under such controlled conditions, suspensions of cells were illuminated, the light intensity measured by a sensitive vacuum bolometer (developed by the father of Otto, Emil Warburg [187, 188]), and the development of oxygen was measured. The actual photochemical aspects were explored in a new perspective, in particular the use of rotating sectors allowed us to study reactions where light intensity was the rate-limiting step, the action of inhibitors was recognized, as well as the dependence on carbon dioxide concentration and lamp intensity and wavelength. On the basis of such experiments, Warburg proposed that the primary photochemical process involved the pigments of the cell and produced a strongly reducing agent. Other thermal reactions occurred at the surface of cells and caused the formation of transients complexes with CO_2 and liberation of oxygen [186] (Fig. 4.14).

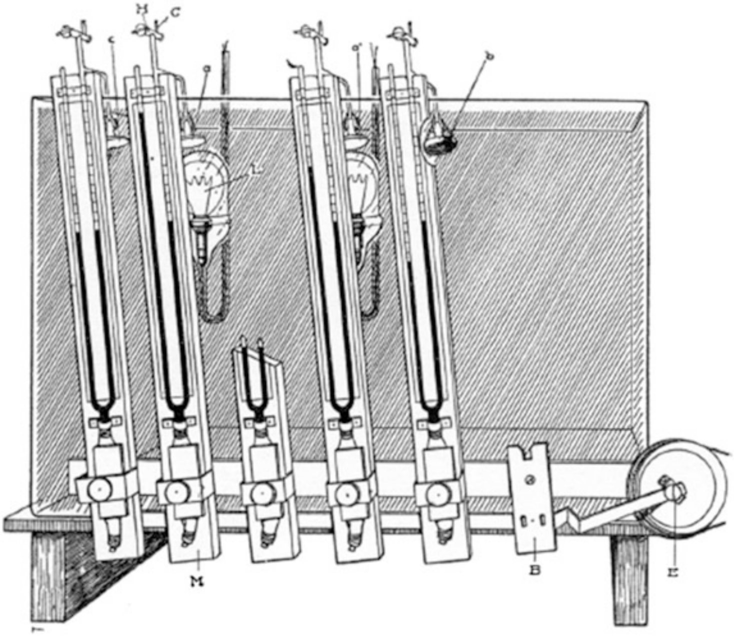


Fig. 4.14 Apparatus used by O. Warburg for measuring oxygen evolution during photosynthesis

Consideration of the energy involved in the process and of the energy of the quantum absorbed by chlorophyll showed that interaction with at least three excited molecules was required for each molecule of CO_2 formed [186]. The investigations by Emil Warburg, fostered also by the formulation of the Einstein equivalence law (1905 in the first formulation; see Chap. 2), and by his son Otto gave a quantitative framework to photosynthesis substituting well-defined chemical measurements to qualitative observations [188].

The path toward the full rationalization was still long, however, key problems being whether chlorophyll not only absorbed light but participated into the reaction (e.g., by forming initially a hydrogenated, or dehydrogenated, form, both hypotheses were considered) that complexed carbon dioxide, the role of water as hydrogen source, the mechanism of oxygen liberation (generally assumed to result from enzymatic splitting of hydrogen peroxide), the number of quanta required for the liberation of one molecule of oxygen, and how the energy could be stored. The measurement of quantum yield of photosynthesis became one of the most investigated quantities, and the object of a long controversy between Warburg (who found 4–5 quanta to be required for the reduction of one molecule of CO_2, and Emerson, who found 8–12) [189, 190], a controversy that was resolved only when Emerson showed that, contrary to naïve expectation, the proportion of CO_2 and O_2 formed was not 1 and not constant during photosynthesis, so that the amount of gas evolved could not be directly used for measuring of quantum yield. Actually, their proportion varied according to the time of irradiation and intensity of the light beam, and

Fig. 4.15 Light cabinet used for the artificial illumination of plants

futher flashing experiments proved that a high number of chlorophyll molecules (2400) were involved in such a reaction [189, 190] and the participation of a second quantum of light. This extraordinary work that required the combined effort of biologists, physiologists, chemists, and physics and was concluded in mid-twentieth century is well known and cannot be summarized here, but detailed accounts are available.

Studies on organisms different from green plants showed that assimilation of carbon promoted by light could proceed through different reactions (in Fig. 4.15 a "light cabinet" is shown where illumination is ensured by four incandescent lamps, which made easier to carry out experiments under uniform conditions).

Thus, in purple and green sulfur bacteria the photosynthetic reaction occurred according to the general equation 4.3 (A, sulfur or a sulfur compound)

$$CO_2 + 2\,H_2A \rightarrow CH_2O + H_2O + 2\ A \tag{4.3}$$

Green bacteria dehydrogenated hydrogen sulfide to sulfur, while under favorable conditions purple bacteria dehydrogenated hydrogen sulfide, sulfur, sulfite, and thiosulfate all the way to sulfate. This suggested that, if photosynthesis conformed to a single scheme, in green plants oxygen was liberated from water, not from CO_2. (see eq. 4.4)

$$CO_2 + \ H_2O \rightarrow CH_2O + O_2 \tag{4.4}$$

The all-important issue of the timescale involved was confronted by various scientists by using intermittent irradiation. By using a neon arc pulsed by rectified current at 50 Hz, Emerson and Arnold showed that "photosynthesis involved a light reaction not affected by temperature, and capable of proceeding at great speed (in less than 10^{-5} s), and a dark reaction dependent on temperature," which required less than 0.04 s for completion at 25 °C and about 0.4 s at 1.1 °C. The light reaction was shown to depend on carbon dioxide concentration and to be inhibited by narcotics, neither of which characteristics were observed with the dark reaction, which was rather inhibited by cyanide. In subsequent experiments using cells varying in chlorophyll content, it was found that "the amount of chlorophyll present per molecule of carbon dioxide reduced per single flash was about 2480 molecules" and "the time required for one unit in the photosynthetic mechanism to complete the cycle of photochemical" and thermal reaction was about 0.02 s at 25 °C. These findings were the basis from which the "trick" nature uses for capturing short-lived excited states via a multiple molecules antenna was discovered [189, 190] and over the years developed into the system based on two photosynthetic units as is presently envisaged [191, 192].

4.6.2 Vision

The physical function of the eye, fully similar to that of camera obscura, had been understood from the time of Aristotle. Furthermore, that rods and cones in the retina functioned as terminals of the optic nerve was proposed by anatomists, but no proof of their role was available until 1877 when Boll studied the structure of (unfortunate) frogs eyes with high experimental skills. He observed that when dark-adapted animals were examined and the retina was pulled away from the basement with fine tweezers, it looked intensely red and maintained this appearance for about 10 s [193, 194]. This color faded to yellow within 20 s to give place to a satin sheen and then to become transparent in the next minute. The red color was not observed when the animals had been exposed to bright light, but it was there again after that they had been kept in the dark. Thus, the color was destroyed by light and reformed when nutrients were supplied for a sufficient time. The bleaching was faster in bright light than under a low light intensity. If the frog was exposed to a narrow stripe of light, examination after 10 min showed that a colorless stripe was formed on the retina. Furthermore, Boll observed that epithelial pigments that were not uniformly distributed along the rod layer were not stationary, but changed position under illumination, suggesting that these pigments were related to the vision of colors [195]. The brain recomposes and rationalizes the images through different filters, again, in the same way of color photography.

The studies were expanded by Kühne, who accurately investigated the effect of different colors [196, 197]. He extracted different pigments from the oily droplets in the cones and compared them with the solar spectrum. The dye called chlorophane (Figs. 4.16 and 4.17) showed two absorption bands in the visible, with maxima

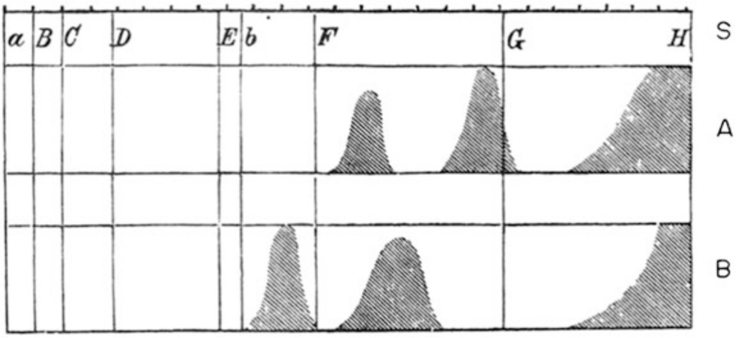


Fig. 4.16 The sun spectrum (S) (Fraunhofer lines are indicated as reference wavelengths, G, 431 nm; F, 346 nm; b, 517 nm) compared with the spectrum of the pigment chlorophane in ether or petroleum ether (A) and in carbon disulfide (B)

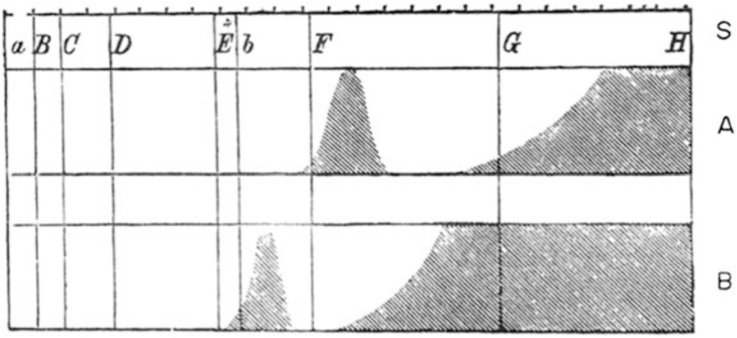


Fig. 4.17 Same as Fig. 4.16 for the dye xanthofane

depending on the solvent, the other dye xanthofane (Fig. 4.16) a single one. Such pigments showed some photosensitivity, but much less than the retina visual purple, not as the photoactive compound originating the nervous answer to the stimulus. This was in accord with their role as light filters, able to provide the brain with information at different wavelength, that is, on color. That it was a photochemical reaction that bleached the visual purple was demonstrated by forming on the retina different images (optograms) that under appropriate conditions could be conserved for some time, like a photographic negative. The conditions for the recovery of the red pigment were likewise studied. What remained to do was to understand the chemical nature of the visual pigment, or rhodopsin, and of the photochemical reaction occurring. This was clarified 70 years later, in a large part due to the work by G. Wald and his wife R. Hubbard [198], establishing that in rhodopsin the polyunsaturated aldehyde retinal is covalently bonded to the protein opsin and that photochemical bleaching involves cis–trans isomerization of the C=C bond in position 11. This is the only photochemical step that is followed by several changes in the structure and separation of the prosthetic group along with neuronal

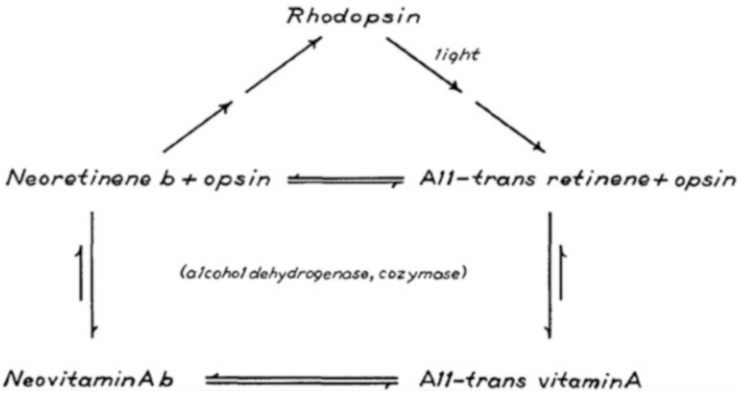


Fig. 4.18 The rhodopsin cycle. The bleaching of rhodopsin yields all-trans retinene (now more currently indicated as retinal), which must be isomerized to neoretinene *b* before it can regenerate the visual pigment. Alternatively, having been reduced to all trans vitamin A, the latter in turn must be isomerized to neovitamin A*b* before it takes part in rhodopsin synthesis. Rod vision thus depends on the continuous stereoisomerization of all-trans retinene or vitamin A, or on the continuous replacement of these substances by new supplies of vitamin A*b* from external sources (adapted from [196, 197])

excitation (Fig. 4.18). A thermal process then reverts back the C=C bond configuration and couples again the protein.

4.6.3 Vitamin D

Another key role photochemical reactions have in human organism is the protection against rickets [199]. Cod liver oil has been prescribed since the beginning of the nineteenth century for the treatment of this disease, but only 100 years later it was recognized that both the absence of some accessory food factor, and precisely a fat-soluble factor [200], and insufficient exposure to solar light were the cause [201]. Furthermore, irradiation of some foods, in particular of whole milk, gave to it a high antirachitic potency, favoring both children's growth and bone calcification. It was demonstrated that the compound involved was the non-saponifiable part of fat. The main component of this fat is cholesterol, but later studies showed that pure cholesterol is not active nor is it activated by light, while a further sterol that contains two conjugated bonds and is present in a very low amount actually has the vitamine activity [202]. A systematic examination of dienes with steroid skeleton [203] evidenced that one of them, first isolated from ergot, had a clear-cut antirachitic effect and this compound (ergosterol) was recognized identical with an impurity accompanying cholesterol from butterfat that was the actual provitamin [204] and was converted by irradiation into calciferol, which was named vitamin D_2 [205] It remained the problem of how could light alone have an antirachitic action even in the absence of ergosterol, but it was later demonstrated that

7-dehydrocholesterol was present in animal tissues and could likewise be considered a provitamin, transformed by light into cholecalciferol, or vitamin D_3 [206] The study of photochemistry of provitamin and vitamin D and its physiological consequences are one of the triumphs of photochemical science [207–210]. From the purely chemical point of view, this combined novel theoretic advancement with the obvious importance of the substances considered and the ability to overcome the large experimental difficulty. The electrocyclic and sigmatropic reactions connecting the compounds of this group probably remain the nicest example of opposite course of photochemical and thermal reactions, the actual basis of the Woodward Hoffmann rules [207–210]. Havinga gathered the interconversion of the various derivatives in Fig. 4.20a. Below room (or body) temperature, vitamin D practically does not form and the isomerizations occurring are shown in the upper part of the scheme. Thus, previtamin D (or D_3, indicated as P) undergoes cis–trans isomerization to tachysterol (T, more efficiently by direct irradiation than by sensitization), while ring closure to either lumisterol L or ergosterol E is inefficient. At a higher temperature, a smooth sigmatropic shift gives vitamin D from P (at 20 °C the equilibrium ratio D/P is ca. 9–1). At still higher temperatures, further thermal isomerizations occur (lower part of the scheme) and under prolonged irradiation subsequent photochemical processes also take place (not indicated).

In vivo experiments on skin preparates at 37 °C showed that previtamin D was likewise formed by UVB irradiation and was specifically translocated from the skin to the blood by the vitamin D-binding protein, subtracting it from the equilibrium with the previtamin and resulting in essentially quantitative isomerization (see Fig. 4.19).

4.6.4 Medicinal Applications of Photochemistry

That exposure to solar light is pleasant and may improve one's health (provided that it is not too prolonged) is a general opinion and has been a recommended practice from ancient times. What was known up to 1900 in medicine was summarized by the Danish physician Finsen, himself one of the most active contributors to the field [211]. There were positive and negative effects. Thus, a study of the erythematic effect of solar light led to the identification of "chemical" light (that is, chemically active, blue, violet, and particularly ultraviolet light) that caused the largest effect, and the characterization of the increased protection by pigmentation of the skin. Not surprisingly, he remarked, if light was able to cause damage to the healthy skin, it was to be expected that this would be even more damaging in the case of illness. Thus, a protection should be envisaged for diseases that made skin more sensitive. Finsen proposed to keep patients who had eruptions from small pox in a room where active light had been excluded by heavy red curtains. The adoption of this

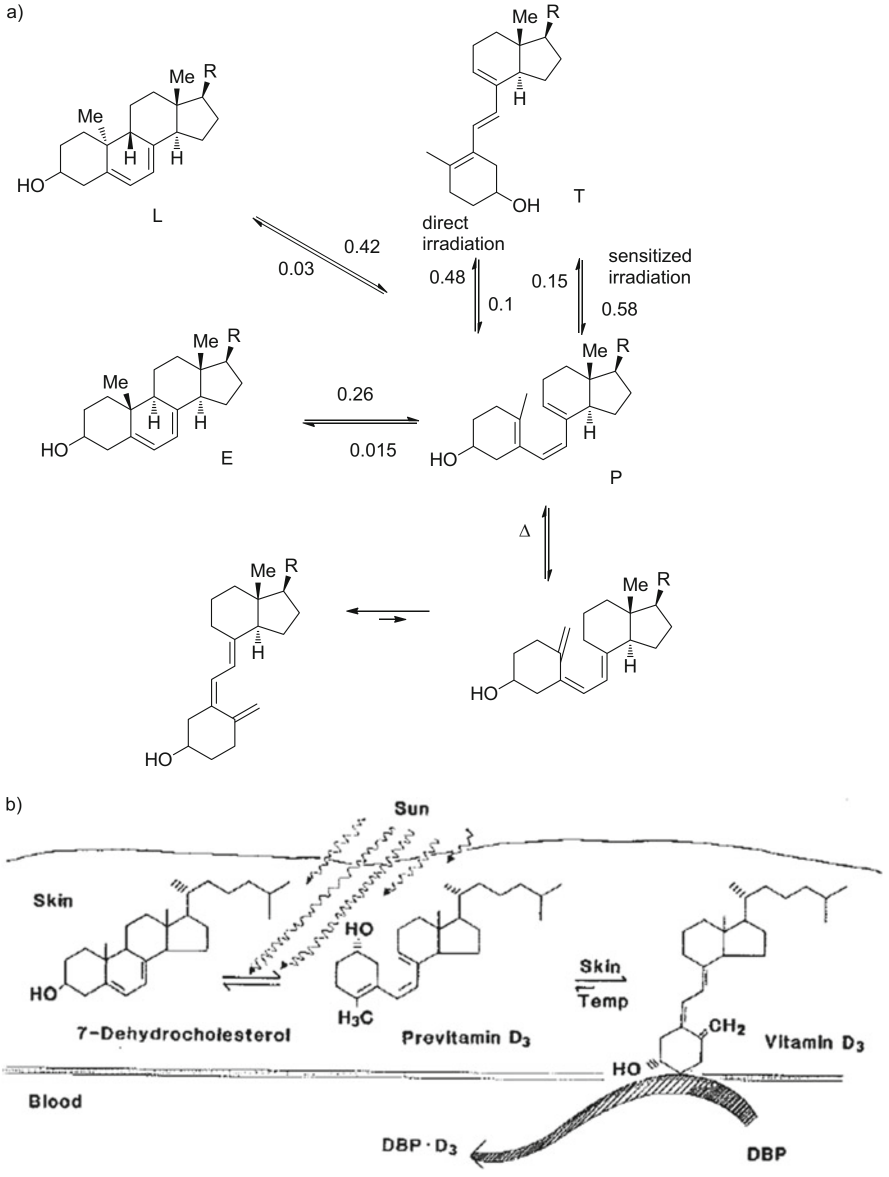


Fig. 4.19 (**a**) Photochemical and thermal reactions occurring with previtamin D at a temperature >20°. (**b**) Schematic representation of the photochemical formation of previtamin D3 in the skin ant the subsequent thermal conversion to vitamin D3. In turn, this is bound to the vitamin D-binding protein (DBP) in plasma and transported into circulation

precaution, provided that it was applied sufficiently early, avoided worsening of the lesions and made healing faster. Thus, the vesicles did not develop into suppurating pustules, or, if they did, they dried faster and left a less apparent scar.

The action of light was multiform, though. Thus, light, and again more intensely violet and ultraviolet light, stimulated animals, e.g., the movements of fetus of frogs. Furthermore, the same light had a bactericidal action and was effective for the treatment of different skin diseases, in particular lupus vulgaris. In fact, this disease is caused by Bacillus tuberculosis and it was already known that such bacteria were killed by light. In order to obtain an effect one had to concentrate the rays (from the sun or from an arc source, not from an incandescent lamp, poor of the "chemical" component) and filtering away the other parts of the spectrum, which would otherwise have caused a burning. The problem with this treatment was its slowness. In fact, a real improvement was obtained only after 3 or 4 months (although the picture of the patients before and after the treatment leaves no doubt about the appropriateness of the choice) (see Fig. 4.20).

A big step forward was done when the use of a xenobiotic sensitizer was introduced in the place of direct irradiation of untreated skin. This appears to have been resulted from a serendipitous observation. In the winter semester 1897–1898, Oscar Raab was assigned by his tutor at the Dermatology Clinic in Munich, professor von Tappeiner, a subject for the "Promotion." The question was whether acridine would have an effect on infusorians, based on the fact that chemically (vaguely) related phosphines had been shown to be active [212, 213]. Raab used a culture of Paramecium and found that these monocellular organisms were killed upon addition of an acridine hydrochloride solution, but the experiment was not reproducible in the sense that the time required for obtaining the effect varied [214]. After 1 week of useless attempts, he observed that the effectiveness depended on the weather, luckily (in retrospect) quite variable in that season in Munich, and found that death of Paramecia was faster in sunny days. Pursuing this work, he concluded that solar light—that excited the fluorescence of the dye used in microscope preparations—was transformed into some chemical energy and killed the Paramecia. Professor von Tappeiner was quick in understanding the implications of this serendipitous finding and immediately proceeded to test the effect of illuminating various dyes on various substances and on cells [215].Tappeiner further demonstrated that oxygen was also required for having the chemical and biological effect and introduced the term "photodynamic effect" for this phenomenon (compare Sect. 4.3). Of particular importance, he found a specific effect on tumor cells [212, 213]. Thus, the initial reports were soon followed by the exciting news of a therapeutic application, viz. that the treatment was able to destroy large tumors and to heal patients disfigured by cancer (again, pictures of patients are quite convincing). The experiments involved tumors on the skin and consisted in *brushing* the part with a 5 % aqueous solution of the dye and exposing to sunlight, while repeating brushing from time to time. As an example, treatment of a skin carcinoma in a 70-year-old woman first interrupted the growing of the tumor and then led to its disappearance, leaving a healed skin, although some trace remained.

These early observations that might be considered a beginning of photomedicine along with the use of ultraviolet light to treat cutaneous lesions did not raise such an extensive interest as it may be expected. Indeed, only a couple of reports appeared

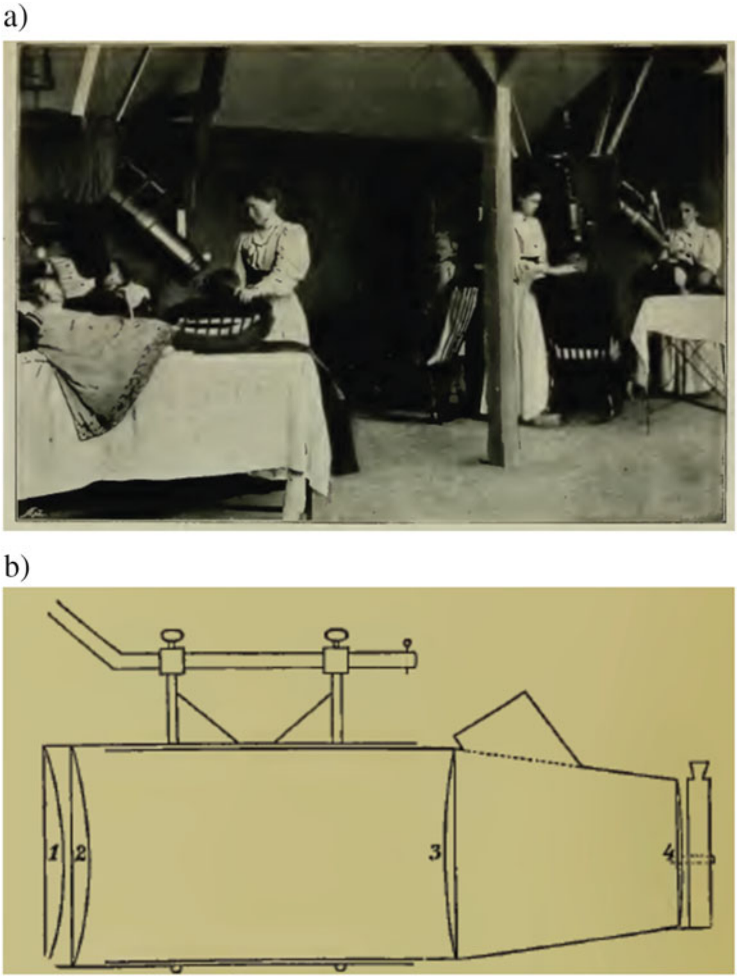


Fig. 4.20 Treatment with concentrated electric light. The concentrating system of lenses is schematically shown. The tube is filled with an ammoniacal solution of copper sulfate in order to filter off the long-wavelength part of the spectrum

during the following decades and the topic found again attention and actual therapeutic application only much later [216]. Thus, in the 1950s, fluorescing dyes were again used and it was found that purified porphyrin was preferentially adsorbed into, and exhibited fluorescence from, tumors, thus offering a method of localization [217, 218], while one had to wait until the 1970s for an actual revamping of studies on therapeutic applications [219, 220].

Porphyrins were found to be powerful photodynamic agents which damaged cells when exposed to light. In particular, malignant tumors took up and retained hematoporphyrin to a greater extent than did normal tissue. When irradiated after hematoporphyrin administration, glioma cells were killed in culture as well as when transplanted subcutaneously in rats. Importantly, treatment with light or hematoporphyrin separately were ineffective. It is generally accepted that this effect involves the excitation of oxygen to the singlet state, well known for its reaction with DNA bases. The progress of PDT from the first proposal to bedside medicine required an even longer time, the first drug with this activity having being approved for clinical use only in 1993. It is expected that further applications to cancer and other pathologies will follow.

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Chapter 5
The Role of Photochemistry in Chemistry

5.1 Photochemistry in Chemistry Meetings

A high point in the history of photochemistry corresponds to the first years of the twentieth century. As it may be seen in Chap. 3, most elements of the theoretical framework of this discipline were available and a consistent picture was beginning to take form in these years, although it would require at least 20 years to arrive at a satisfactory formulation [1]. However, as it happens not rarely in chemistry, it seemed that the discovery of reactions and their application may precede theory. In fact, intense work, though carried out in a small number of laboratories, called attention by the international community to this discipline and by 1910 photochemistry seemed well established as one of the most promising fields of chemistry.

This happened in a time of vigorous economic development (of Western world at least), to which chemistry certainly gave a major contribution, and the use of artificial materials began to become an alternative to those that mankind had traditionally obtained from nature to such a large extent as to change everyday's life [1]. Indeed, many chemistry practitioners felt that chemistry had now reached the first of its targets by unambiguously demonstrating in the previous century that it could produce the *same* compounds as nature did, even on an *industrial* scale. Some clear-sighted scientists thought that this made it possible to confront a further more difficult task, that is, to obtain the same products in a *better* way.

This concept was perhaps most clearly expressed by Paternò, who addressing the 7th International Symposium on Applied Chemistry (the precursor of IUPAC series) in 1909 in London (where the section on photochemistry was one of the best attended [2]) declared that now chemists should concentrate on getting the same results, indeed better ones, through a shorter, easier, cheaper path [3]. This new approach should start once again from the study of nature. After having understood *which* compounds nature produced, it was now time to understand

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how it accomplished this task and to apply what would have learned to artificial methods. In particular, it appeared likely that inspiration would be given by the study of the transformations carried out by *light*, *microorganisms*, *enzymes*, and *catalysts*.

Likewise, Ciamician pointed out in a talk before the French Chemical Society in 1908 in Paris [4] that the task to be confronted was to achieve the best results under mild conditions and avoiding the "show of brute force" presently used in the chemical laboratory (compare Sect. 4.5). This was possible, he thought, by using either of the two means, *enzymes* or *solar irradiation*. In particular, plants appeared to be able to carry out a variety of chemical transformations under mild conditions provided that they were exposed to light. Learning the way this was possible should give artificial photochemistry a central role in the future of chemical synthesis, as indicated by the number of surprising chemical transformations that had been discovered in the last years and were indeed obtained avoiding the use of heat or of aggressive chemicals. As a first demonstration, in his 1908 talk Ciamician presented the photoreactions he had himself found, including H-abstraction and α-cleavage of ketones, 2+2 cycloaddition of enones, reduction to various degrees of nitro compounds, isomerization of X=Y bonds, various oxidations, and other processes [4]. In the 1909 talk quoted above, Paternò similarly advocated the development of photochemistry and presented the 2+2 addition to alkenes and several further reactions of ketones and aldehydes he had discovered [3]. Likewise, the German chemist Stobbe devoted his presentation before the Bunsen Society (Physical chemistry) in 1908 in Wien to a review of the photochemical reactions recently reported (including the photochromic reactions of fulgides) [5] and expressed the belief that photochemistry had a great synthetic potential, provided that a sufficient number of chemists were active in the field.

Thus, there seemed to be a consensus that photochemistry was destined to be one of the main approaches for new—and convenient—synthetic methods.

Besides synthesis, another area where photochemistry was expected to give a major contribution was energy supply (compare Sect. 4.5). Thus, at the General Meeting of the German Chemical Society in 1910 in München [6], Schaum pointed out the importance of photochemistry in this field, since learning how to exploit solar radiation would have solved a key problem for the development of mankind and supplied a sufficient amount of energy [6]. He further noticed that light could be easily converted into other forms of energy, an important result and an excellent theme for teaching chemistry.

Likewise, Ciamician had evidenced the role of the sun as a source of clean energy in the 1908 talk, but elaborated more fully his view on the matter in the well-known talk at the 8th International Congress of Applied Chemistry in 1912 in New York (see further Sect. 4.5) [7]. As he remarked, one may leave nature go on in its own way and modern agriculture should be developed on suitable land. Where this was not possible, however, solar energy should be trapped by converting low-energy into high-energy chemicals. Note that Ciamician's was one of the four plenary speakers and the other three talks bore a marked applicative character (these were presented by G. Bertrand, on small in agriculture [8], C. Duisberg on the advancement in chemical industry [9], and W. H. Perkin on fire-proofing of cotton [10]). Ciamician remarked in the preface to the printed version of his talk that photochemistry had no practical application as yet—except of course in photography-but this was possible in the future, both with large-scale applications, such as the conversion of solar light, and with small-scale ones, such as the use of phototropic dyes for dresses that would change color when passing from sunny to shadowy spots.

5.2 The Role of Photochemistry, 1912–2013

One may wonder whether such targets have been reached and photochemistry has fulfilled the expectation. Probably not yet, or at least not to a full degree. An appreciation of the advancement of photochemistry can be obtained (besides as by the comparisons in Chap. 6) by comparing the program of the 8th International Congress in September 1912 with the corresponding meeting a century later, the 44th International Pure and Applied Chemistry Congress, held in Istanbul in August 2013. In 1912, photochemistry was one of the ten sections. The presentations included, among many others, a series of reports by Bancroft [11] on Grotthus law and on the rationalizations proposed for the chemical action of light and photochemistry. A variety of specific topics were treated and fully occupied one of the 29 volumes of the printed edition (see Sect. 2.3). These included a discussion on the permanence of paintings [12], where it was pointed out that different chemicals caused the decolorization of painted materials in conjunction with light, from the oxidation of gum used in oil painting to the effect of sulfur-containing gases from the atmosphere. The photochemical oxidation of benzene, leading to phenol under full solar light but not in diffuse light when heating in the presence of phosphorous, was investigated [13]. A study of the chemical effect of UV light on gases was presented, including redox reactions, halogenations, and the attending kinetic issues with catalytic and retarding effects [14]. The progress of both photochemistry [15] and photography [16] since the previous congress was reviewed, in the latter case including a further discussion on the chemical nature of the latent image, as well as the formation of different colors, possibly due to silver subhalides and the rationalization of the effect of gelatin—many specific communications about photography were also presented. A plea for teaching "photography or photochemistry" at universities (outside chemical curricula) was presented [17], because of the great dependence on these methods for the advancement of all of the sciences for which photography offered an invaluable documentation.

One century afterward, the picture fully changed [18]. In 2013, the list of disciplines was in part different with the introduction of interdisciplinary themes that in a large part substituted traditional classifications. The topics presented stressed the target or the properties rather than the chemical method, or broad categories such as life science, (nano) materials science, and so on. Photochemistry contributed to most of these themes, starting from clean energy through chemistry [19]. Repeatedly treated were topics such as photocatalytic hydrogen production [20], solar cells [20–26], chemical analysis (sensors, in particular fluorescent chemosensors) [27], chemical synthesis [28], photoaddition to C_{60} [29], photoinitiators for cross-linking [30], photoluminescent polymers [31], photochromic materials [32], photoswitchable chromophores [33], physical chemistry (including photochemistry as a specific topic) [34], photoactuators [35], smart polymers [36–39], photodynamic therapy [40], and innovation and chemical industry [41]. Thus, photochemistry as such has been declassed as a subdiscipline of physical chemistry, but the topic is pervasive and is actually present in most if not all of the sections, the more so in multidisciplinary subjects, consistently with the frontier role that is probably its very nature. The "special relation" with photography, which had predominated during the early times of photochemistry, was no more present, but photophysics and photochemistry had a big role in the development of imaging [42–45] and more generally in the conversion of light into signals with the development of sensors (fluorescent, photoswitchable), of smart materials (D-A conjugated polymers), of optically activated actuators, and so on.

The mere reading of the titles of the presentation gives an idea of the role photochemistry has of making "dreams come true" by creating actual molecules and systems that embodies ideas from biology and physics and make them actually work.

In particular, the photochemical component is large in the case of clean energy, actually the key theme of the entire congress, including topics such as the molecular chemistry of renewable energy, heterojunction photovoltaic energy harvesting by using appropriate dyes, the preparation of nanoparticles (often titania), or organized materials for dye-sensitized solar cells. On the other hand, it should also be noted that thematic meetings on photochemistry, particularly the three series of the IUPAC Symposium of Photochemistry (started in 1964, the 25th edition in Bordeaux, 2014), the International Photochemistry Conference on Photochemistry (from 1952, the 26th edition in Leuven, 2013), and the Gordon Research Conference in Photochemistry (from 1964, the 27th edition in Easton, MA, USA, 2013), are more and more evidencing the contribution this discipline gives to other sciences rather than an advancement in the basic skeleton of photochemistry itself [46].

5.3 Publications in Photochemistry

The role of photochemistry in the advancement of science may be appreciated with reference to the number of publications on this topic. Figure 5.1 shows the number of papers retrieved by Scifinder under the heading "photochemistry." It may be appreciated that the number increases steadily and maintains roughly the same

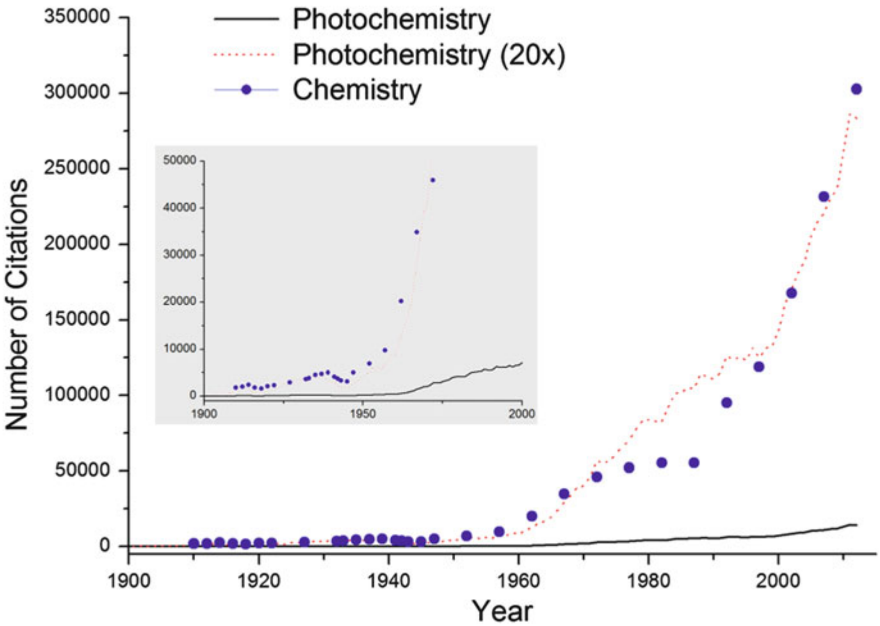

Fig. 5.1 Yearly number of documents on photochemistry (*dotted*: the same number ×20) vs. that on chemistry. In the *inset*: same data on an expanded scale

proportion to the papers in chemistry in general. It corresponds to ca. 1/20th of the whole of the scientific output in chemistry. It may be further observed that in the period 1975–1995 photochemistry increases more steadily, while in 1950–1965 the fraction of photochemical papers is slightly larger. The increase may be a consequence of the oil crisis that led to intensive investigations on water splitting by solar light photocatalysis as an alternative energy source. On the other hand, the inset in Fig. 5.1, where the same data are reported with an expanded scale to allow for detecting the variations in the early times, evidences the strongly negative effect of the two World Wars. This is more conspicuous with an advanced discipline such as photochemistry, which suffers more than chemistry in general the negative effect of the loss of personnel and funding (specific researches were financed for strategic reasons, but this is scarcely reflected in the open literature, or at least not in the short term). The photochemistry production thus arrives three times at a relatively maximum value in chemistry, soon after 1910, with the actual discovery of photochemical reactions and the hope that this was to become one of the main paths in synthesis, soon after 1930, with the debate on the laws of photochemistry and the development of gas phase photochemistry, and after 1975, with photocatalysis and the availability of new instruments.

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Chapter 6
Photochemistry, a Powerful Science

6.1 Harry Potter Meets Photochemistry

Chemistry is a powerful science and the one that actually continuously produces new compounds that can be applied for performing a variety of functions and allows testing the ideas that physics on one hand and biologists on the other hand think of. Within chemistry, photochemistry enjoys a peculiar status, due to high energy and short lifetime of excited states. The properties of such states open a wealth of possibilities, but that means entering a new word and confronting new problems.

Take synthesis as an example. Photochemistry certainly has a wide synthetic potential, but the fact that photochemical reactions take a course completely unrelated to thermal ones has given some annoyance to synthesis practitioners. Consider what opined such an authority as Georg Büchi, one of the most influential participants to the renaissance of photochemistry in the 1950s, the scientist who rediscovered the [2+2] cycloaddition to form oxetanes (now indicated with his name along with that of the original discoverer, Paternò), as well to form cyclobutanes (originally reported by Ciamician). He confided in an interview [1] that he had left the field because he thought that "*[...] useful applications were not forthcoming, and because the course of the transformations could rarely be predicted, thus robbing the investigator of the pleasure derived from designing new reactions*." In fact, the in-depth skeletal transformations occurring in a molecule upon irradiation are not often easily predicted and it seems difficult not to concur with the idea that photochemistry has some magic in it ("*the somewhat mysterious effect that, by simply absorbing a UV/Vis photon, a molecule becomes something different, and in many cases behaves in a way completely opposite to that of its ground state*", as it has been commented) [2]. However, rationalization is perhaps not impossible. The heavy modification occurring upon irradiation in the carbon skeleton of testosterone has been quoted as an example of "magic" [3]. "*A well-trained chemist will have a reliable notion of reactions that may result from*

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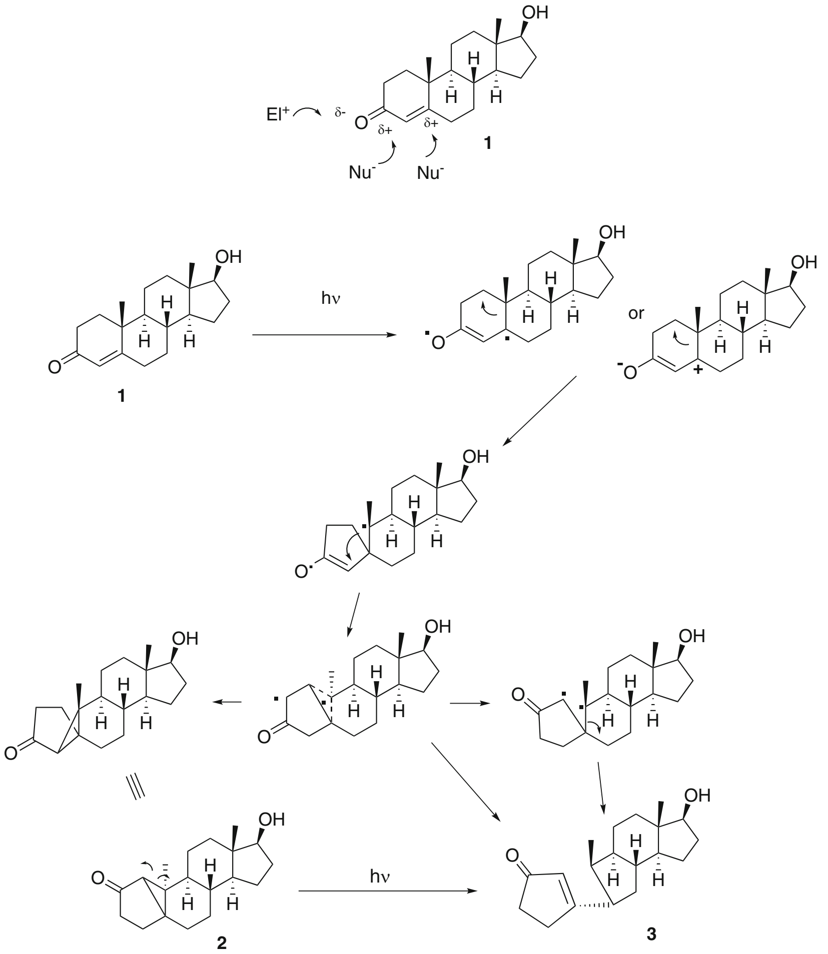
*the addition of, say, sodium borohydride to a solution of testosterone (**1**)—but would he or she dare to predict or make an educate guess about what will happen when a solution of testosterone is irradiated?"*

What actually happens is depicted in Scheme 6.1.

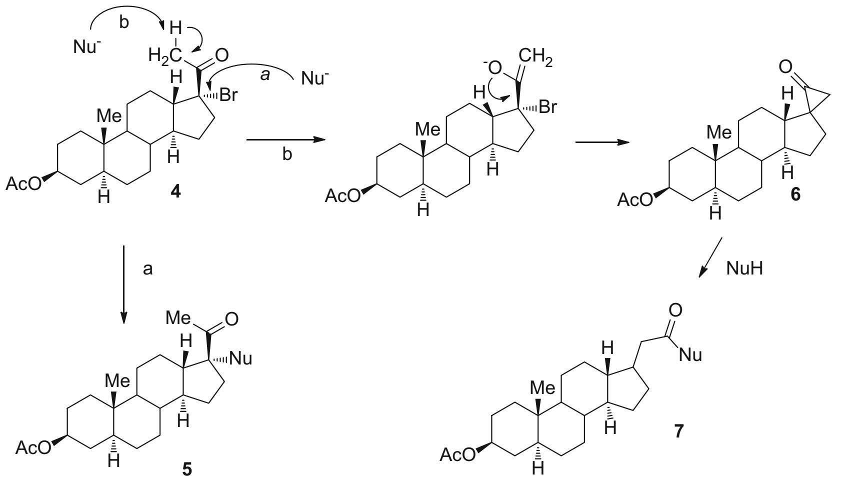


Scheme 6.1 Photochemical reaction of testosterone **1** compared with reduction by sodium borohydride (Nu$^-$ in the scheme)

At first sight, the photochemical reaction involving a deep rearrangement of the cyclohexenone ring (ring A for steroid derivatives) does appear a bit disconcerting. However, chemists are nowadays trained to recognize the site of preferred reaction on the basis of the electronic structure. As for the thermal reaction, the electronegativity of oxygen displaces the electrons toward it and the more easily so when π electrons are concerned (a polarization results, δ^+, δ^-). Thus, in a conjugate ketone, there are two electron-deficient sites. Addition of nucleophiles will occur either on the carbonyl or on the β-carbon position according to their nature, hard or soft, as well as on conditions. As an example, (Lewis) acid catalysis increases polarization and thus the rate of nucleophilic addition. Borohydride, as in general charged nucleophiles, will add onto the carbonyl.

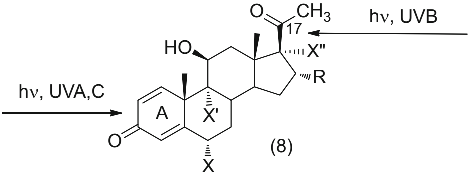
Things change upon irradiation [4, 5]. The activated moiety (the light-absorbing chromophore) is again the unsaturated ketone. The change occurring upon excitation is very large, not a limited displacement of electrons, but the actual *cleavage* of a bond, since the energy supplied is of the same order of covalent bonds (no partial displacement δ; rather, the C_α-C_β π bond is fully broken in the excited state). Thus, let us begin by cleaving a bond and draw a diradical or zwitterionic structure as an appropriate description of the excited state. Once that this postulate has been accepted, no wonder that there is a shift of an alkyl group leading to a different tertiary diradical and return to the ground state via regeneration of a bond between non-saturated positions (compound **2**). It may be difficult to predict which will be the actual path chosen, but the one observed is among the processes one should consider, and this holds also for the secondary photoreaction leading to a β-substituted cyclopentenone **3**. Thus, photochemical reactions can be discussed by using the same concepts used for rationalizing thermal reactions via high-energy intermediates (that is, displacing electrons and passing through intermediates such as radicals, cations, anions), in the same way one usually makes for thermal reactions. This allows to predict if not the preferred one, at least some processes that are possible and compete, including of course chemically unproductive return to the starting material, whether with re-emission of a photon or not.

But let's just complicate slightly the issue by considering another steroidal ketone, compound **4** in Scheme 6.2. Here, a nucleophile (MeO^-, K_2CO_3 in MeOH) may behave as such and substitute the leaving group bromide (Scheme 6.2, *path a* to give product **5**), or behave as a base and abstract a proton from the position α to the carbonyl group (*path b*).



Scheme 6.2 Favorskii rearrangement of ketone **4**

In the latter case, the enolate displaces the bromide and rearranges via a spirocyclopropanone **6** to ester **7** in a Favorskii rearrangement. An educated guess here requires someone more versant in organic chemistry, though certainly this will not surprise anybody accustomed to synthesis. Noteworthy, essentially the same processes can be obtained under irradiation, rather than by adding a base, and these are affected in the same way by geometric factors [6]. Notice also that when both functions are present in the same molecule (see compound **8** in Scheme 6.3), with a ketone function in position 17 and the unsaturated ketone in ring A, the reaction can be directed toward either of them by simply changing the wavelength of irradiation. Clearly this is a lucky case, since not necessarily two chromophores absorb at a wavelength sufficiently different, and when this happens, energy transfer may obliterate the initial selective excitation, but this is not the only example in the literature [7].



Scheme 6.3 Selective photochemical activation of functional groups when present in the same molecule

With time, synthetic chemists will become better accustomed to high-energy intermediates typical of photochemical reactions and this discipline is not bound to remain in the land of magic. Certainly, it adds new dimensions to chemistry and requires a larger contribution of a mechanistic consideration, but then this holds for the whole of chemistry.

Summing up, it is certainly true that photochemistry will widen the scope of synthesis, even without the spell of magic.

6.2 This Is How It Happens: Time-Resolved Spectroscopy in Photochemistry

Much of what we know about how photochemical reactions occur arises from two experimental methods, matrix photochemistry and flash photolysis, which are based on the peculiar possibilities this kind of reactions offer for following their course. Fast thermal reactions are followed by stopped flow methods, with a resolution of a few tenths of millisecond. This is well suited for what is demanded for most reactions of biological relevance, such as enzyme catalysis, protein folding, signal transduction, ligand or drugs binding to a protein or DNA, and kinetics of coordination chemistry. But excited states react many orders of magnitude faster than that, over a very small activation barrier, which led to the minimal temperature

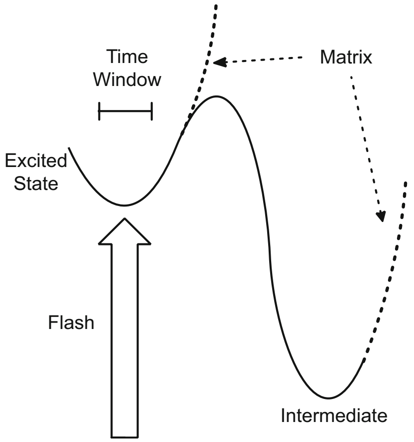


Fig. 6.1 Highly reactive intermediates may be detected either by creating a high local concentration by a strong flash and probing it within a short time window or by hindering further evolution by confining it in a matrix

coefficient that since the initial studies appeared a peculiar characteristic of photochemical reactions.

This very fact opens also peculiar means of study of such species, though. There are two approaches. One is based on the "instantaneous" generation of a large amount of a fleeting intermediate, so that it is possible to take a picture of it before it is further converted, and the other one on blocking at some stage the reaction, by limiting the movement and the reactivity of the primary products and thus allowing their accumulation. The key point is that excited states react very fast, and quite often decay to form further short-lived species, but on the other hand are themselves formed even faster (within 10^{-14} s) and thus a strong, short-lived pulse of light can generate a relatively high local concentration of any transient formed so that it is possible to obtain, by an appropriate interrogation source, its absorption spectrum, whether it is an excited state or a further intermediate arising from it (see Fig. 6.1).

The time window is determined by the length of the source pulse (initially discharge flash lamps, then pulsed lasers, then pump-probe spectroscopy, viz. from ms to fs) and the sensitivity and rapidity of the monitoring system (photographic plate, photodiode, photomultiplier, streak camera). This has progressively permitted the detection of different intermediate types, from those relatively long-lived (radicals, ms) to shorter and shorter excited states (triplets, μs and below; singlet, ns and below; upper singlets, ps and below), and to follow their interconversion [8–13].

6.2.1 Flash Photolysis with Lamps

The history of flash photolysis is essentially that of increasing time resolution. As Lord Porter remarked in his Nobel address [14], science and technology have steadily extended the strict limits of man senses, "*so as to enable him, despite the* *very limited sense with which he was endowed, to observe phenomena with dimensions very different from those he can normally experience* [. . .] *Thus, in the realm of the very small, microscopes and microbalances have permitted him to observe things which have smaller extension or mass that he can see or feel. In the dimension of time. . .most of the fundamental processes and events, particularly those in the molecular word that we call chemistry*", occur in ms or much below that time, although the fastest event perceived by human eye is around 1/20th s. Entering in the realm of the short times thus had meant obtaining a better understanding of the way molecules form and react.

Immediately after World War 2, the flash photolysis method was elaborated in England. Millisecond flash lamps were developed at that time and absorption of a flash caused a dramatic perturbation. This made possible the direct observation by a relatively insensitive physical method such as UV-visible absorption both of excited states (at least of the long-lived ones, which Lewis and Kasha had observed by more sensitive emission techniques; see below) and, most typically, of intermediates formed from them, in particular of radicals. For each flash, the change of absorbance at a fixed wavelength or the total spectrum at a fixed delay from the flash was registered. The method was versatile and could be used with both large and small specimens, in the gas or condensed phase. The time delay was introduced by inserting a rotating sector or electronically [14, 15].

A typical example was the study of the generation of the biatomic radical $ClO^{\bullet}$ by combination of atomic chlorine and oxygen (see Fig. 6.2) [16]. Notice that although in a 1947 Faraday Society meeting devoted to "The labile molecule" [17] there was almost no indication of pulse methods, progress was quite fast, and in 1954 a following Faraday meeting was organized on "The study of fast reactions" [18, 19] and was based on the new results on radicals derived from flash photolysis, pulse radiolysis, mass spectrometry, and other methods.

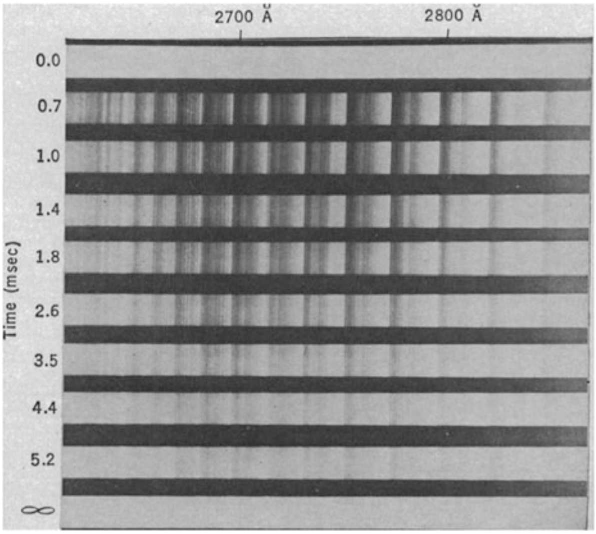


Fig. 6.2 Photographic plates showing a sequence of spectra of $ClO^{\bullet}$ after flash photolysis of a chlorine–oxygen mixture and the bimolecular decay of this species; reprinted by permission from [16]

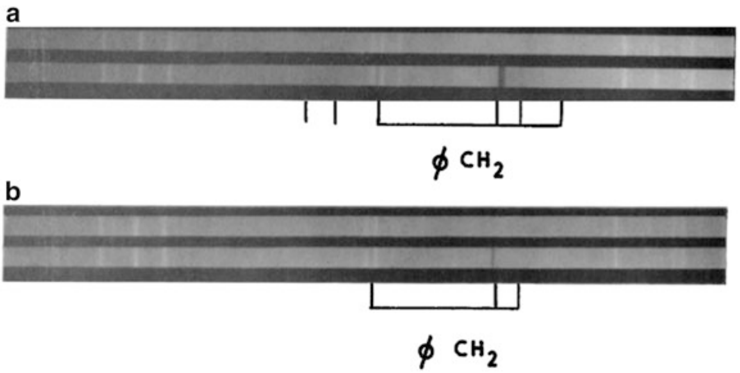


Fig. 6.3 Photographic plates of the original experiment by Porter for the identification of benzyl radical. Spectra detected before (*upper trace*) and during the photolysis of (**a**) benzyl chloride and (**b**) toluene, showing the appearance of the benzyl radical signals. Reprinted by permission from [19]

Likewise, organic radicals were detected, giving an unprecedented support to the understanding of the nature and reactivity of such intermediates. As an example, benzyl radicals, characterized by a strong absorption around 300 nm, were generated by homolytic fission of alkylbenzenes and benzyl halides (see Fig. 6.3). Thus, flashing of toluene vapor showed some distinct absorptions, in particular one around 305 nm, which were observed also from benzyl chloride and, with very little difference, from ethylbenzene and was thus attributed to the benzyl radical (see also the following section) [19]. The improvement of lamps for a short flash (2 μs in the spectra in Fig. 6.4) allowed a more detailed examination and the detection of further bands [20].

As mentioned, also long-lived aromatic triplets could be observed and their interaction could be studied by using flash lamps. In particular, the decay of triplet naphthalene and anthracene was observed and found to depend strongly from viscosity (Figs. 6.5 and 6.6). This fact was attributed to the deformation of the triplet with respect to the ground state [21]. Notice that the high energy of the flash generates a high local concentration of excited states, much higher than in preparative experiments. Thus, under these conditions, diffusion-controlled bimolecular triplet–triplet annihilation may be the predominant process, overcoming monomolecular decay [21]. Triplet–triplet annihilation (see Chap. 7) may in part lead to the singlet and "delayed" fluorescence (that is, the emission spectrum corresponding to the $S_1 \rightarrow S_0$ emission, but lifetime corresponding to that of T_1), a phenomenon well known from fluorescence studies [22].

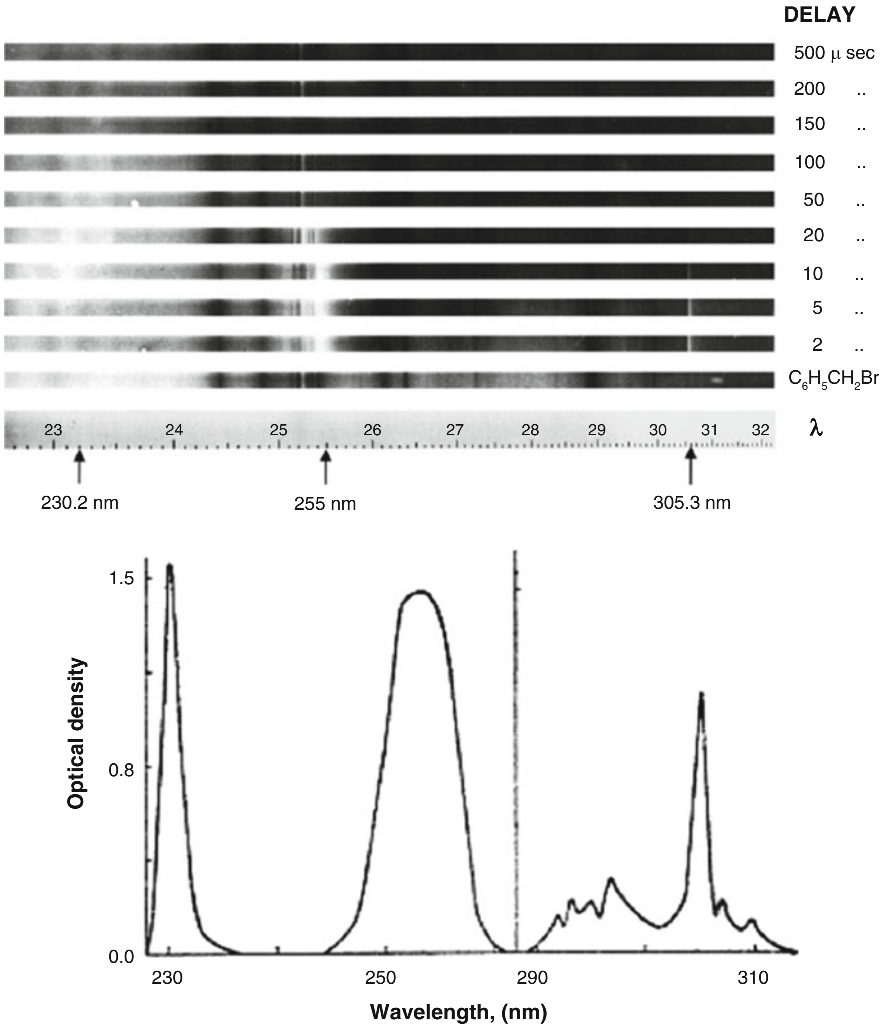


Fig. 6.4 Benzylic radicals generated by a much shorter flash duration than in Fig. 6.3a from benzyl bromide, photographic trace and diagram of the spectrum; by permission from [20]

Many radicals absorb in the visible and near UV region, and thus photographic detection is suitable. For those that do not, the development of appropriate lasers made it possible to observe high-resolution IR spectra within a short timescale for the study of radicals in the gas phase [23]. With the availability of relatively cheap

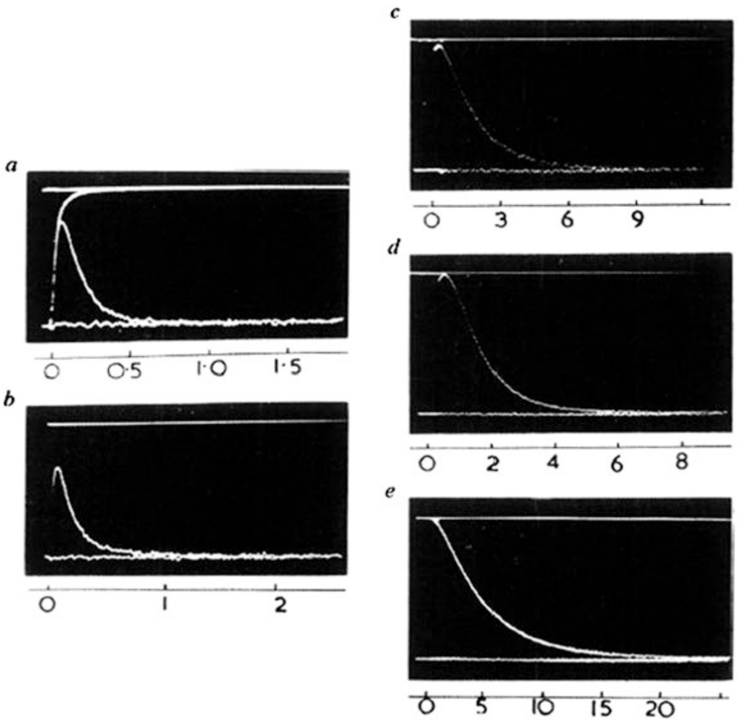


Fig. 6.5 Dependence of triplet lifetime on viscosity. Oscillographic records of the decay of triplet naphthalene in (**a**) *n*-hexane $\eta = 0.31$ cp, (**b**) water $\eta = 0.89$ cp, (**c**) ethylene glycol $\eta = 35.7$ cp, (**d**) paraffin $\eta = 33$ cp, (**e**) paraffin $\eta = 167$ cp. Time units, ms; cp, centipoise; by permission from [21]

and solid laser sources and the appropriate electronics for detection, resolution got down to a few nanoseconds with flash photolysis and then picoseconds and below with the pump-probe spectroscopy. With the last technique, the sample volume is repeatedly excited by a succession of short laser pulses. The detection system registers the combined accumulated signal at variable time delays between pump and probe, so that a kinetic profile can be obtained. In this way, it is possible to observe and characterize singlet and triplet states [15].

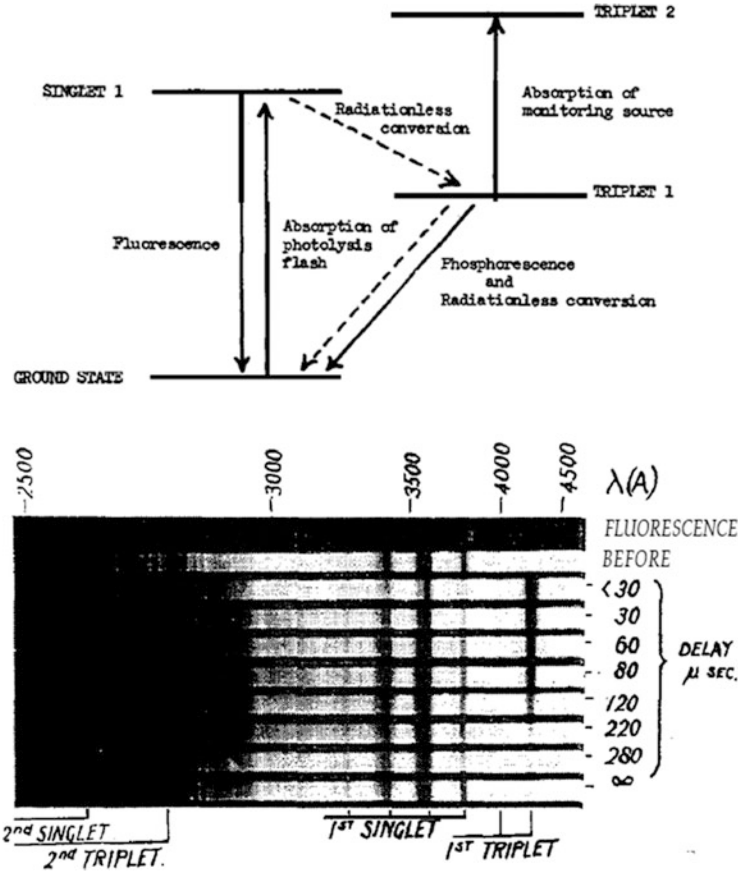
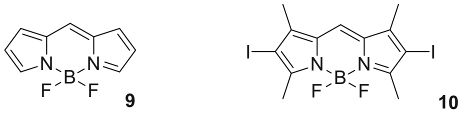


Fig. 6.6 Plates of the T_1–T_n absorption in aromatic molecules and state diagram. Reprinted with permission from [14]

6.2.2 Laser Flash Photolysis and Pump-Probe Spectroscopy

Let us consider an example. Time-resolved methods allow a detailed description of excited state and of their useful properties, e.g., as sensitizers. A popular class of oxygen sensitizers is that of boron dipyrromethene (**9**, BODIPY) and their derivatives, e.g., the diiodo derivative **10** in Scheme 6.4, in view of applications such as photodynamic therapy [24].

Scheme 6.4
Dipyrromethene sensitizers



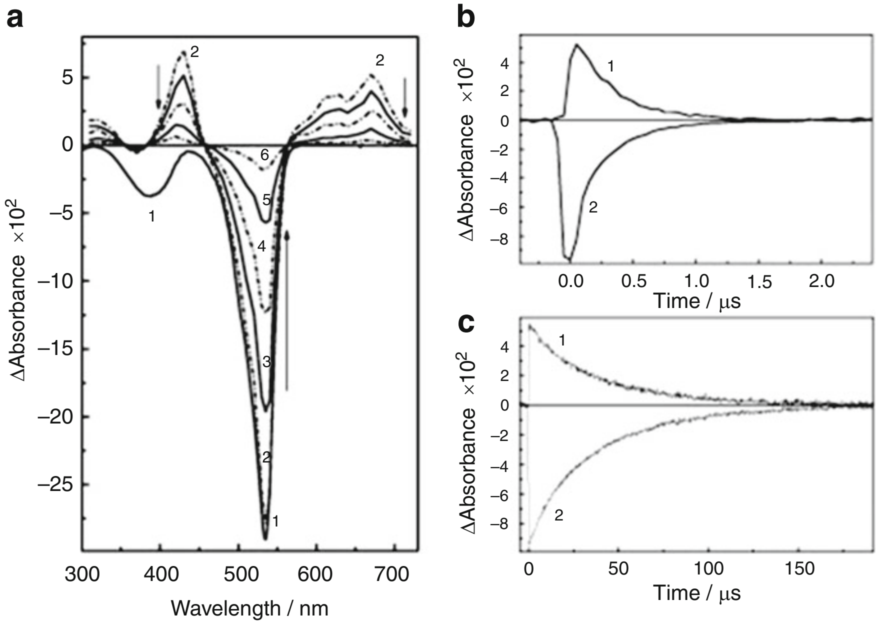


Fig. 6.7 Laser flash photolysis by a YAG/Nd pulsed laser (λ 532 nm, pulse duration ca 5 ns) on an argon-saturated solution caused the bleaching of ground state BODIPY (**9**, λ_{max} ca 530 nm), as shown in **a** by comparison with the inverted absorption spectrum. Two maxima at 430 and 670 nm characterize a transient absorption spectrum that is attributed to the lowest triplet state. This decays back to the ground state by T-T annihilation ($k_{T\text{-}T}$) or oxygen quenching (notice the strong quenching when comparing curves (**b**) and (**c**), lifetime in oxygen saturated solution, 300 ns). The intensity of the transient increases with increasing the intensity of the flash, until a top value is reached. This saturation values allows to determine quantitatively the molar absorptivity of the triplet. Reprinted with permission from [24]

Nanosecond flash photolysis and pump-probe experiments explore different time windows. The first one allows to detect the triplet state and its self-quenching in the absence of oxygen or by energy transfer to it when present (see Fig. 6.7). Femtosecond pump-probe experiments have contributed further mechanistic data detecting short-lived upper singlets in the initial time (see Fig. 6.8). Thus, the ground state bleaching is accompanied by the appearance of a transient at 420–480 nm. Kinetic curves representing the decay of the transient absorption in the whole wavelength range were satisfactory fitted by a three-exponential equation:

$$\Delta A(\lambda,t) = A_1(\lambda)\mathrm{e}^{1/\tau_1} + A_2(\lambda)\mathrm{e}^{1/\tau_2} + A_3(\lambda)\mathrm{e}^{1/\tau_3} + A_4 \tag{6.1}$$

The A_4 amplitude corresponds to T_1 state, invariant since its lifetime is much longer than the timescale femtosecond experiment. Adequate mathematical treatment leads to the full assignment of the transient spectra and of the rate of conversion, so that the complete state diagram is reconstructed (see Fig. 6.9).

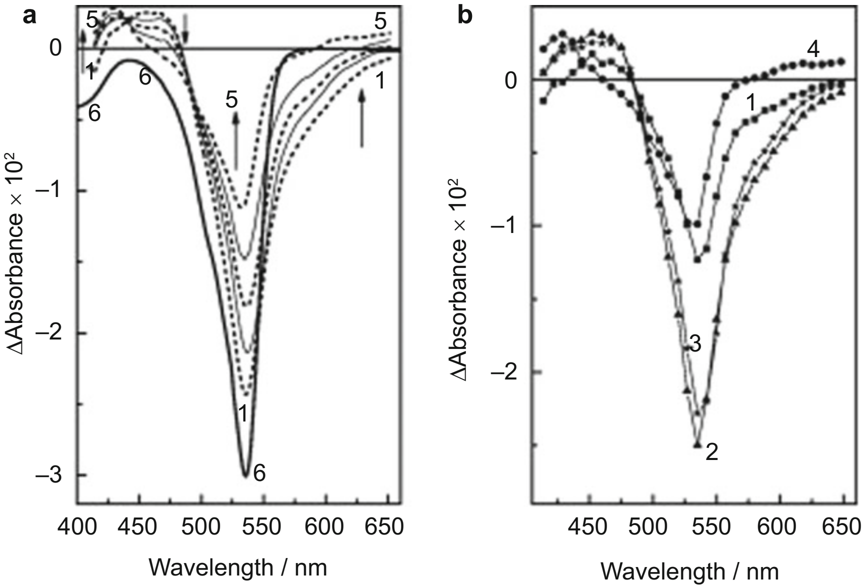


Fig. 6.8 Femtosecond pump-probe spectroscopy of diiodoBODIPY (**10**). (**a**) Inverted absorption spectrum (6) and transient absorption spectra at 0.5 (1), 20 (2), 50 (3), 110 (4), and 350 (5) ps delay between pump and probe pulses. (**b**) Differential absorption spectra of intermediate states obtained after modeling the experimental data by a three-exponential equation (see text) that is convoluted with the instrumental response function: (1) zero delay (sum of all amplitudes, S_2 state), (2) ultrafast relaxation of the S_2 state (sum of A_2, A_3, A_4 amplitudes), (3) thermalized S_1 state (sum of A_3 and A_4 amplitudes), (4) T_1 state (A_4 amplitude). Reprinted with permission from [24]

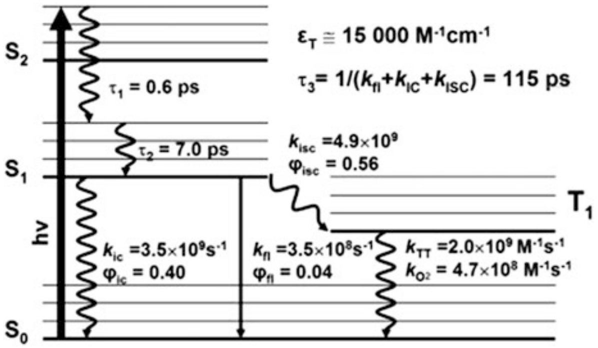
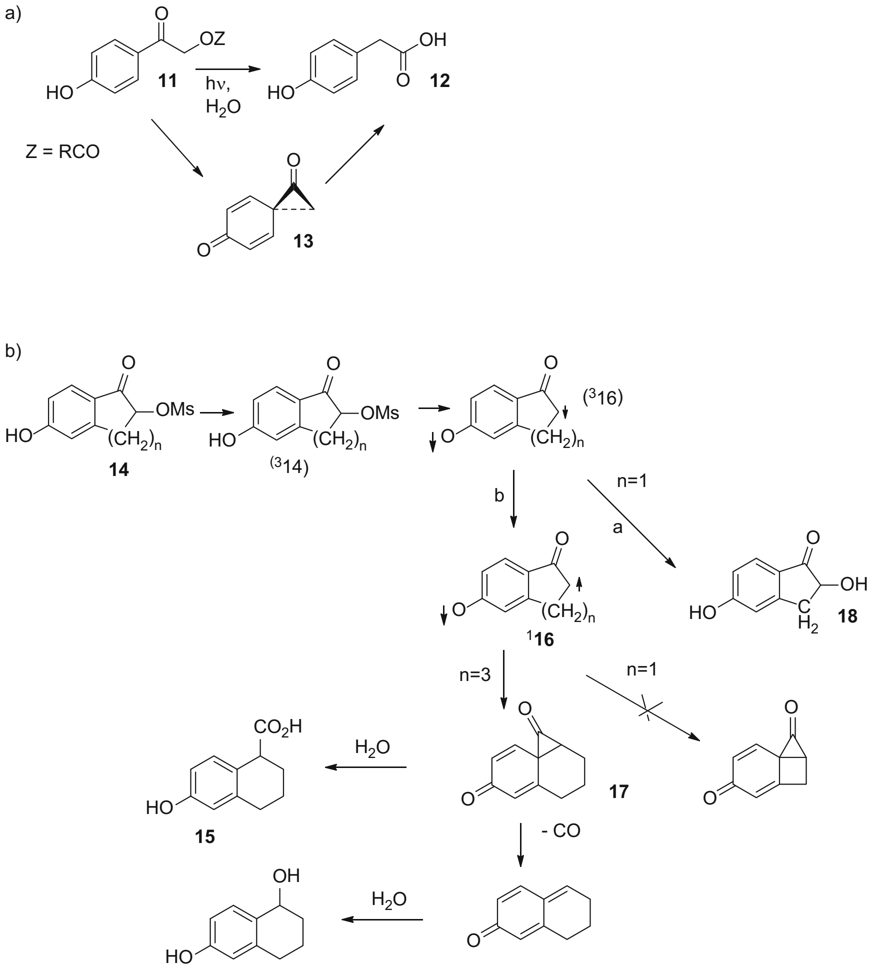


Fig. 6.9 Nanosecond laser flash photolysis (see Fig. 6.7) and femtosecond pump-probe experiments (see Fig. 6.8) allow to determine the spectra and the reaction rate of diiodoBODIPY (**10**) excited states and their reaction with oxygen. Reprinted with permission from [24]

p-Hydroxyphenacyl esters (**11**) are known to rearrange photochemically to *p*-hydroxyphenylacetic acids (**12**) via formation of spirocyclopropanone (**13**) and have found large use as photoremovable protecting groups (Scheme 6.5a). This mechanistically intriguing process has been investigated, inter alia by flash photolysis. The structurally analogous hydroxybenzocycloalcanones (**14**, $n = 1$–3) bearing a leaving group in α undergo the same reaction (photo-Favorskii rearrangement) to give a ring-restricted hydroxybenzocycloalkylcarboxylic acid (**15**, Scheme 6.5b). This has been rationalized by assuming the formation of a fused cyclopropanone (**17**). A laser flash photolysis/pump-probe study has revealed that triplet ketone ^{3}**14** decays similarly to esters **11** (1.5×10^{11} s^{-1} and 8.8×10^{9} s^{-1}, respectively, forming in both cases the triplet diradical (^{3}**16**) [25]; see Fig. 6.10).



Scheme 6.5 (**a**) Photochemical reactions of *p*-hydroxyphenacyl esters. (**b**) Photochemical reactions of some α mesityl ketones. The output depends on the ring size

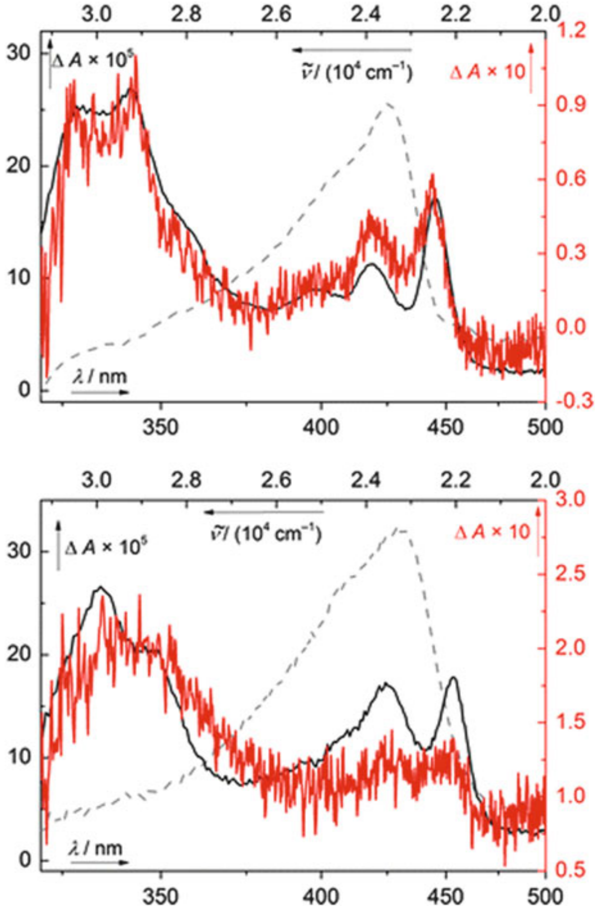
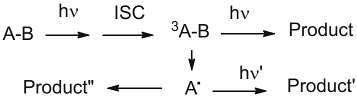


Fig. 6.10 Transient spectra of the triplet diradicals ^{3}**16** obtained by the global analysis of pump-probe data (in *black*; H_2O/CH_3CN (66:33, v/v), 3 M acetate buffer, pH = 3.6) and from nanosecond LFP (in *red*; H_2O/CH_3CN (99:1, v/v), 3 M acetate buffer, pH = 3.6; 1 ns after the laser pulse with 3 ns accumulation time). The *dashed gray* spectra (their intensity was reduced by a factor of 2.5) correspond to the triplet states of the reagent ^{3}**14** (*top*, $n = 1$; *bottom*, $n = 3$). Reprinted with permission from [25]

The key step is the elimination of the leaving group to afford a triplet biradical (^{3}**16**). Two competing pathways are observed. With a sufficiently large ring ($n \geq 3$), the Favorskii reaction takes place leading to a carboxylic acid and to an alcohol after intersystem crossing to the singlet diradical (^{1}**16**) (2.6×10^{8} s^{-1}), while with small rings this course is not accessible, because of the ring strain. Thus, when $n = 1$, the Favorskii path is completely skipped and the triplet intermediate (^{3}**16**) undergoes solvolysis to (**18**) (7.2×10^{7} s^{-1}) rather than intersystem crossing (*path b*). The work has general significance, also as a model of triplet oxyallyl diradical, an elusive species that has only recently been spectroscopically characterized and found to be energetically close to the singlet.

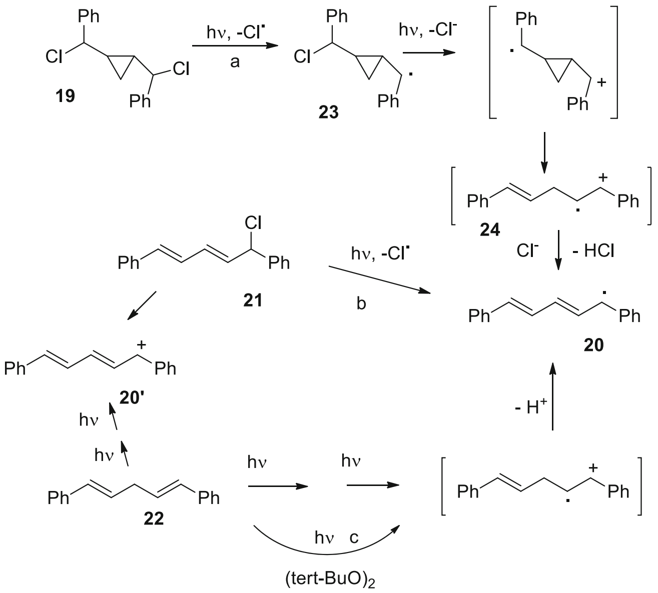
6.2.3 Two-Color Flash Photolysis

The high intensity of the laser beam introduces new reactions, not observed under conditions usual for preparative photochemistry (see Sect 6.2.1), such as triplet–triplet annihilation. Likewise, two photons may be absorbed and ionization may be observed from a higher excited state. However, the increased time resolution makes also possible to "manipulate" the intermediates. Thus, "two-color" flash photolysis makes use of a second laser pulse for inducing a reaction of a relatively long lived species, such as radicals and triplets (Scheme 6.6).



Scheme 6.6 An intermediate generated by flash photolysis is further excited by a second flash of a different color

Photochemical dechlorination of bis-(chlorobenzylcyclopropane) (**19**) mainly gives the stabilized radical (**20**, $\lambda_{\max}$ 380 nm, Scheme 6.7, path a) that is formed also by dechlorination of diphenyl chloropentadiene (**21**, path b) and by H abstraction from 1,4-diene (**22**, path c) by photochemically generated *t*butoxy radical (as well as by two-photon excitation of the diene). A parabolic dependence of the 380 nm signal on light intensity was evidenced, suggesting a multiphotonic process from compound **19**. The sequence of events was established by two-color flash photolysis. Thus, a solution of chloride **19** was flashed at 266 nm (sensitizing flash) to produce benzyl radical **23**. In turn, this could be irradiated by a second pulse at 308 nm (see Fig. 6.11). Under these conditions, an irreversible bleaching of the region at 290–350 nm was concomitant with formation of more benzyl radical. Thus, absorption of a second photon caused loss of chloride by intramolecular electron transfer and led to radical cation **24** by ring opening. In turn, hydrogen transfer from this species gave the pentadienyl radical **20**. Photoheterolysis of the diphenyl chloropentadiene **21** could also occur in MeCN as a competing pathway to homolysis and was revealed by two-photon, two-color experiments generating the cation (Fig. 6.12) [26].



Scheme 6.7 Two-photon chemistry of some benzyl derivatives

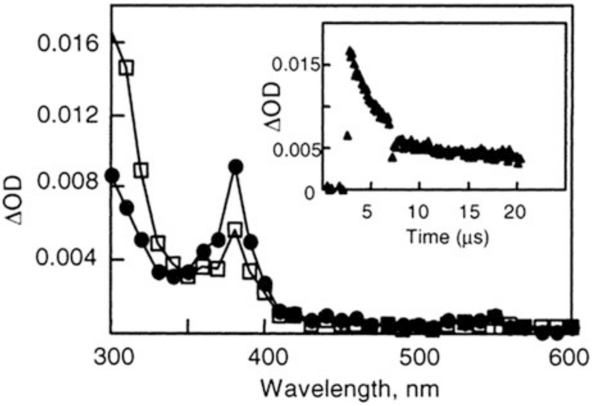


Fig. 6.11 Transient absorption spectra recorded following laser excitation of cyclopropane **19** (266 nm, *empty symbols*), and then by a second flash at a different wavelength (308 nm, 5 μs after the first laser pulse, *filled symbols*). The *inset* shows the kinetic trace at 290 nm, with bleaching of radical **23**. Reprinted with permission from [26]

6.2.4 Local Interactions

Flash photolysis is not only a way for understanding the mechanism of reactions, but also, once that the mechanism has been understood, or at least reasonably guessed, for using the photoactive species as a probe for understanding what

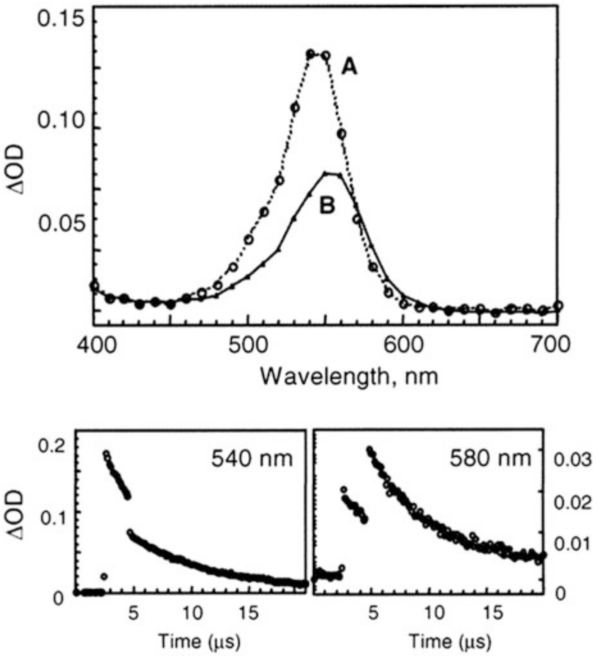
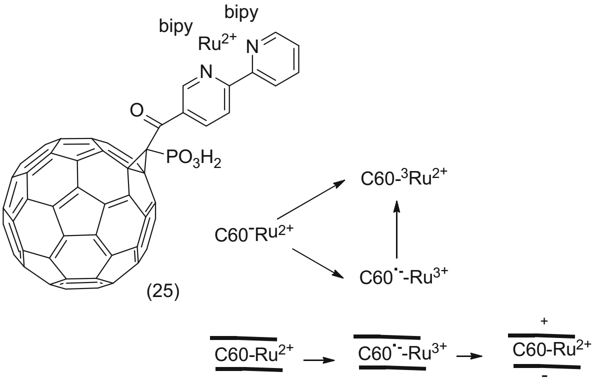


Fig. 6.12 *Top* (A) spectrum obtained by flash photolysis of (**19**) at 266 nm, 0.4 μs after the flash. (B) Spectrum obtained by two-laser, two-color excitation of diene **22** (first 266 nm, and then at 532 nm with a 2.56 μs delay). Kinetic profiles at 540 and 580 nm in the two photon experiment; notice the abrupt change in the absorbance of the intermediate generated by the synthetic pulse, all trans cation **20′**, due to *Z*/*E* isomerization. Reprinted with permission from [26]

happens in the environment. Indeed, this is an excellent method for the study of “local” interactions, by determining in which way the interaction between two moieties is affected. Thus, flash photolysis of dyad **25** (Scheme 6.8) at 532 nm led to a transient corresponding to the triplet localized on the metal (and quenched by oxygen), but a minor component resulted from the relatively slow collapse of the electron transfer pair (Fig. 6.13). This dyad was then fixed in two different ways onto a crystalline and an amorphous zircon-based matrix. The time-resolved diffuse reflectance of such opaque materials was completely different from that of the dyad in solution and showed a continuous emission over a large span, not quenched by oxygen (Fig. 6.14). This was rationalized as the indication that holes and electrons were formed on the inorganic material, as it happens on the surface of a semiconductor. This led to the proposal that the inorganic scaffolding acts as a semiconductor and harvests the holes and/or electrons produced by the active C_{60}-Ru^{2+} component and these materials were suitable for the use in solar cells [27].



Scheme 6.8 Photochemistry of dyad **25** in solution. Oxygen quenching and, for the minor part, electron transfer cause deactivation. When the dyad is fixed at a zircon surface, however, no oxygen quenching occurs and the process observed is rationalized as electron-hole transfer at the surface of the material, as it happens in excited semiconductors

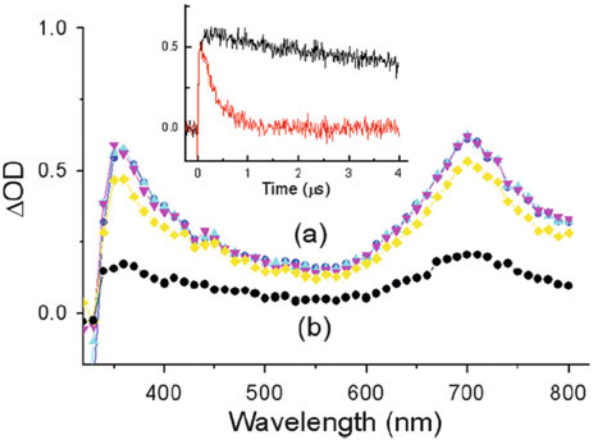


Fig. 6.13 Transient spectra recorded for dyad **25** in acetonitrile after 532 nm laser excitation of nitrogen purging (a, 0.5 and 1.5 μs) or oxygen purging (b, 1 μs). The *inset* shows the temporal decay of the signal monitored at 350 nm for the nitrogen (*black*) and oxygen (*red*) purged dyad **25** in solution. Reprinted with permission from [27]

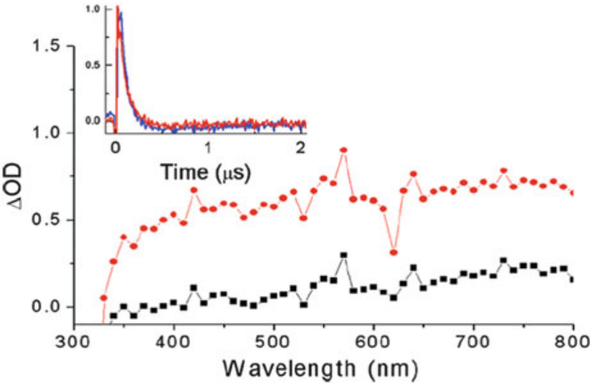


Fig. 6.14 Time-resolved diffuse reflectance spectra of dyad **25** when fixed on amorphous zircon-based matrix, 200 and 500 ns after the 532 nm laser flash. The *inset* shows the signal monitored at 500 nm for the resulting material under oxygen and nitrogen purging. Reprinted with permission from [27]

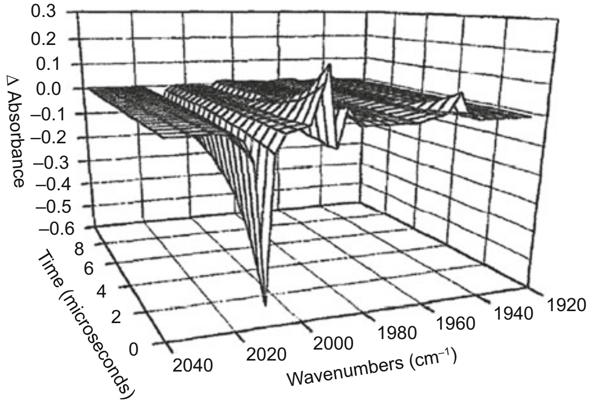
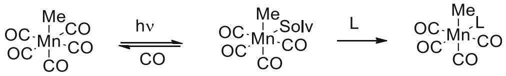


Fig. 6.15 Transient IR spectral changes following 308-nm laser flash photolysis of $Mn(CO)_5Me$ in cyclohexane at 295 K under 10 % CO (500-ns intervals). Reprinted with permission from [28]

6.2.5 *Flash Photolysis with Different Detection*

IR detection is less sensitive than UV-visible, but instrumentation has fast advanced [24]. The first application has been for the photochemistry of intensively absorbing intermediates, in the typical case coordinatively unsaturated species such as those formed of in the photochemistry of metallocarbonyls. This has allowed us to clarify the path toward selective substitution (Fig. 6.15 and Scheme 6.9) [28].



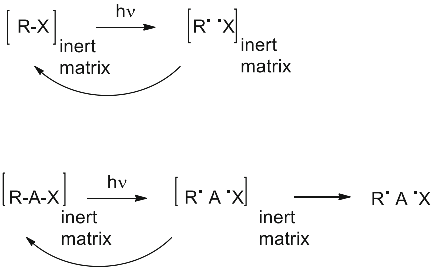
Scheme 6.9 Photolysis of a manganese carbonyl complex

Obviously, other spectroscopic time-resolved methods have been applied, although less general. Most often, EPR has been used for triplets and radicals (see for instance [29, 30]). Time-correlated single-photon counting, on the other hand, has proven to be a sensitive and informative method for mechanistic studies of singlet reactions [31, 32], besides than a technique useful for analytic applications, e.g. for determining the composition of mixtures of aromatics, when both lifetime and spectrum shape were required for obtaining a reasonable picture.

6.3 This Is How It Happens: Blocking the Intermediates

The other method is based on preventing the further reaction of the intermediate, so that it accumulates until a high enough concentration is reached to allow detection [33] (see Fig. 6.1). This method was devised independently by Pimentel and Porter in the early 1950s [34, 35]. Pimentel was investigating the mechanism of combustion and was baffled by the low concentration of the intermediates, which prevented spectroscopic detection. "*The intent of the method*", Pimentel commented "*is to trap active molecules in a solid matrix of inert materials, crystalline or glassy. If the temperature is sufficiently low, the matrix will inhibit diffusion of the trapped molecules, thus holding the active molecules effectively immobile in a non reactive environment.*" In this way, further reactions were prevented and a high enough concentration was reached for allowing detection by a normal instrument [35].

In a typical experiment, intermediates were produced in the gas phase and along with a flow of an inert gas were carried to a cold surface. Rapid solidification ensured that each host molecule would find itself confined in an isolated position and surrounded by a large excess of inert host molecules. In the sample obtained in this way, each substrate molecule was immobilized in a cavity surrounded by one or more layers of inert material and was thus "isolated" from the other substrate molecules in a "matrix" of the host gas, typically a rare gas at a few K (Scheme 6.10).



Scheme 6.10 Homolytic cleavage detected in an inert matrix. Recombination of radicals may occur, but is less likely if a double fragmentation occurs liberating a stable molecule (A). Compare Fig. 6.1

The term has been used extensively for any method where intermediates produced are prevented from diffusion by the rigid host molecules, such as glassy solvents obtained by fast freezing in liquid nitrogen of solvents that produces clear (and transparent in UV and visible range) glasses, such as ethanol, EPA, methyltetrahydrofuran, but also crystals, zeolites, polymers, boric acid glasses, or cryptands. These conditions have been largely used for UV-visible spectra and EPR spectra measurements. Rare gases are transparent over the IR region and thus a favorite choice since this region is usually richer of structural information. Intermediates

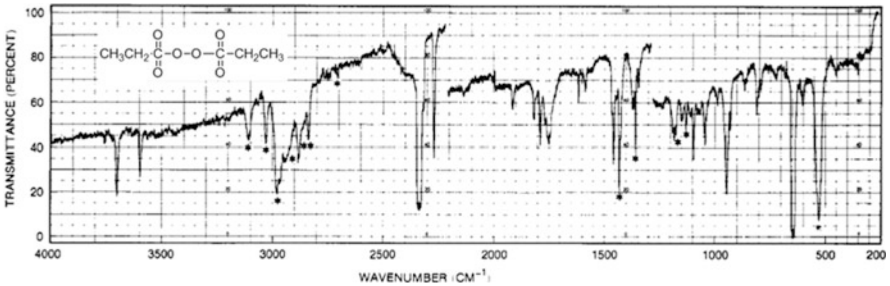
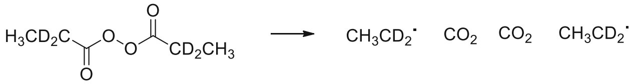


Fig. 6.16 IR spectrum of dipropionyl peroxide isolated in an argon matrix after 60 h irradiation with UV light with >20 nm. The bands different from those of the precursor are highlighted by an *asterisk*. Reprinted with permission from [37]

may be generated in situ by irradiation, a method that has shown to be reliable, provided that the possible interference with the matrix is taken into account. Thus, rare gases are transparent and the spectra registered at 10 K or below show a more detailed pattern, but are very poor heat sinks. This makes thermalization slow and the incipient intermediate may be formed with excess energy and further react. On the other hand, recombination of the fragments that can't escape from the cage may hide the occurring of a fragmentation reaction. As pointed out by Chapman, in these experiments "*kT is a nuisance, and must be taken as low as possible*" [36].

The convenient choice of the precursor may help to obtain the desired intermediate; thus, carbon-centered radicals are more efficiently obtained from iodides and nitroso derivatives, since fragments such as I or NO survive some time even when in cage with an organic radical. Likewise, double fragmentation causing elimination of a stable molecule, such as CO_2 or CO from acylperoxides or anhydrides, makes formation of radicals more effective. On the other hand, if the precursor is aggregated in the matrix, dimers may be formed. All of these factors may lead to a different course of the reaction with respect to solution. The ethyl radical has been obtained and characterized by irradiation of dipropionyl peroxide, thanks to the fact that interposed CO_2 molecules hindered fast recombination; see Scheme 6.11 and Fig. 6.16. Otherwise, the best solution is producing radicals externally at a high temperature, where they freely move, and trap them afterward [37].



Scheme 6.11 Generation of dideuteroethyl radicals from propionyl peroxide in matrix [37]

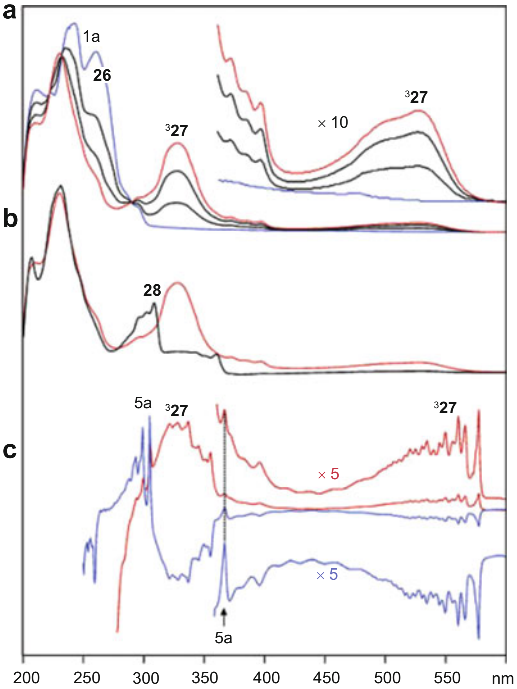


Fig. 6.17 (**a**) Stepwise 254-nm photolysis of azide **26** (*blue* spectrum) in EtOH at 90 K. The visible band of triplet nitrene ^{3}**27** (*red* spectrum) is enlarged for better visibility. (**b**) Photolysis of nitrene ^{3}**27** (*red* spectrum) at >450 nm. (**c**) Difference spectra showing the formation (by 254 nm photolysis of azide **26**, *red* spectrum) and the bleaching (by >515-nm irradiation, *blue* spectrum) of nitrene ^{3}**27** in an Ar matrix at 12 K. Reprinted with permission from [38]

An experiment in rare gas matrix at a temperature of a few K is by no means comparable to an experiment in a frozen solvent. Likewise, the IR spectrum is much richer of lines and thus gives much more structural information. This is apparent when the much better resolved spectrum of an intermediate, a nitrene, obtained by photolysis of azide **26** [38] in an argon matrix at 12 K is compared to that in ethanol at 90 K and the wealth of data that are obtained from the IR spectrum of this species is considered. Furthermore, it easy to check for their correspondence to the calculated spectrum. The secondary conversion of the first formed intermediate is also conveniently followed under these conditions (Figs. 6.17 and 6.18) (Scheme 6.12).

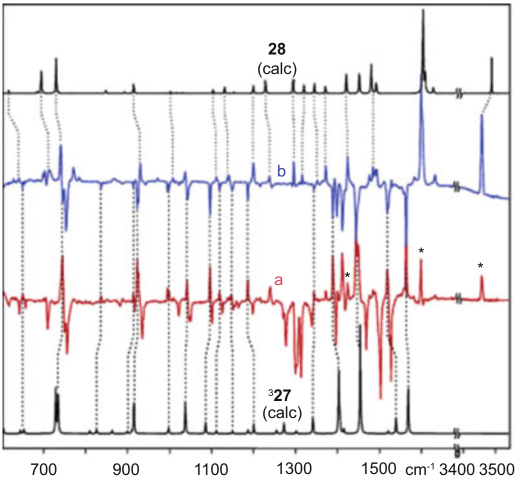
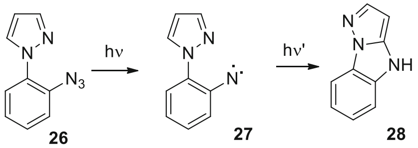
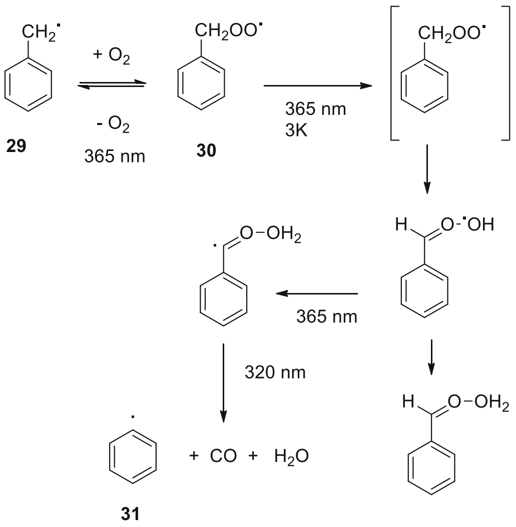


Fig. 6.18 IR difference spectra for (a) the formation of nitrene (^{3}**27**) by (254-nm photolysis of azide **26**, *red* spectrum) and (b) the >515-nm bleaching (*blue* spectrum) of nitrene ^{3}**27** by further irradiation in an Ar matrix at 12 K. The bands that increase in (a) and decrease in (b) (*dashed lines*) are correlated with those of the simulated spectrum of nitrene ^{3}**27** at the bottom (B3LYP/6-31G* calculation of most stable conformer). The bands that increase in spectrum (b) are correlated with those of the simulated spectrum of pyrazolobenzopyrazole **28** shown at the top (*dotted lines*). Reprinted with permission from [38]



Scheme 6.12 Photolysis of pyrazolylphenylazide **26** gives triplet nitrene ^{3}**27** that further rearranges to pyrazolobenzopyrazole **28**

Certainly, the knowledge of the chemistry of radicals involved in combustion has made a great advancement in this time and Pimentel idea that this method was useful for finding evidence about processes occurring under real-world conditions has been found correct. Thus, the benzyl radical **29** (see Sect. 6.3 for flash photolysis) has been characterized in great detail. This has been generated by flash vacuum pyrolysis of 1,2-diphenylethane at 620 °C. Trapping in argon containing 1 % oxygen at 25 K, where the matrix becomes softer and bimolecular reactions are possible, generated the benzylperoxy radical **30**. The matrix was then frozen at 3 K for registering the spectrum. Safe assignments of the latter radical, which is formed in two conformers, the main one with the peroxy group pointing toward—and the less abundant one far from—the aromatic ring, are based on the photolysis of both protio and deuterated bibenzyl by reaction with $^{16}O_2$ and $^{18}O_2$. The changes occurring on isotopic substitution were as expected. The conformers interconvert even at 3 K (see Scheme 6.13, Fig. 6.19).



Scheme 6.13 Reaction of benzyl radical (**29**) with oxygen in matrix

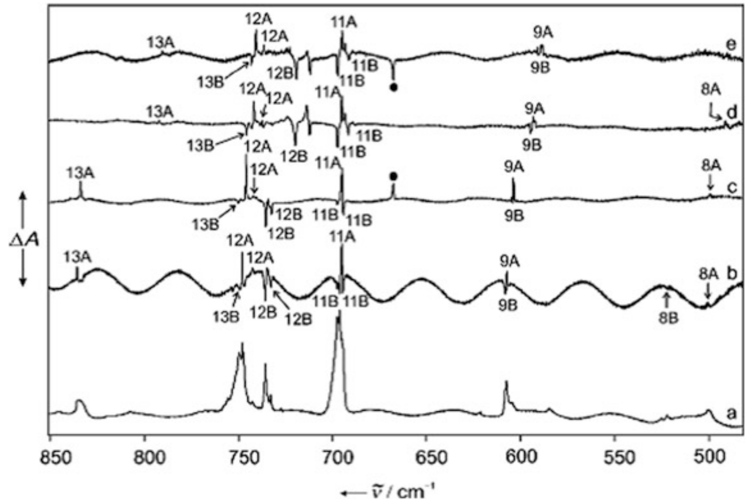


Fig. 6.19 (**a**) Part of the IR spectrum obtained after flash vacuum pyrolysis of bibenzyl and topoisomers at 620 °C, followed by cooling the products in argon at 25 K. The spectrum was recorded after cooling to 3 K and shows bands assigned to benzylperoxy radical $PhCH_2OO\cdot$. (**b**–**e**) Difference IR spectra of the four topoisomers of the radical showing changes induced by cooling the matrix from 25 to 3 K. The first spectrum was taken immediately. After cooling at 3 K, the second one was registered approximately after 15 min. The bands pointing downward are of decreasing intensity, and those upward increasing at 3 K: (**b**) $h_2{}^{16}O_2$; (**c**) $h_2{}^{18}O_2$; (**d**) $d_2{}^{16}O_2$; (**e**) $d_2{}^{18}O_2$. Bands labeled A are assigned to the main conformer, B to the minor one. Reprinted with permission from [39]

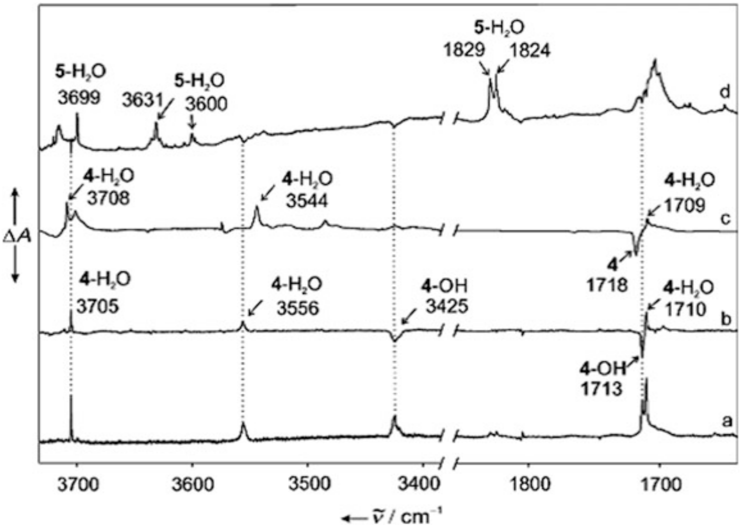


Fig. 6.20 Difference IR spectra in the O–H and C=O stretching regions showing the photochemistry of benzylperoxy radical matrix isolated in argon. Bands pointing upward appeared and bands pointing downward disappeared during the irradiation. (**a**) 10 min irradiation at 365 nm at 3 K. (**b**) Same matrix as in (**a**) warmed at 25 K. (**c**) Reference spectrum of benzaldehyde, matrix isolated in 1 % H_2O-doped argon. The difference spectra, taken at 3 K and after warming at 30 K, show the formation of the 4-H_2O complex. (**d**) Same matrix as (**b**) after additional 10 min irradiation at 320 nm [39]

The photochemistry of the thus formed benzylperoxy radical was then studied in the matrix. Irradiation at 365 nm caused a formal 1,3 hydrogen migration followed by cleavage of the peroxyl bond and prolonged irradiation finally yielded phenyl radical **31**, CO, and water. This result shows that the benzyl radical is transformed via a series of exothermic steps into even more reactive radicals, such as OH and phenyl radicals [39] (see Scheme 6.13, Fig. 6.20).

Notice further that in situ generation of the intermediates is limited to compounds sufficiently volatile (though special techniques are available for nonvolatile compounds). In alternative, products can be generated externally in the gas phase, provided that, as mentioned, they live long enough to survive the transfer. This is typically applied with metals that are trapped by complexing agents.

$$\text{Metal atom} + \mathrm{A(H_2O, N_2, CO_2\ldots)} \rightarrow \text{M-A} \tag{6.2}$$

Summing up in a sentence, matrix isolation gives more structure information based on spectroscopic identification of products, but under conditions that are very

Table 6.1 Pros and cons of matrix isolation and flash photolysis, summarized by Dunkin [40, 41]

Matrix isolation	Flash photolysis
Solid-phase reactions only, but the precursors must be volatile	Reactions in gas, liquid, or solid phases
Reactive species stabilized in the abnormal conditions of a matrix cage	Reactive species observed in the normal conditions of a reaction medium
Reactive species long-lived, often indefinitely	Reactive species transient, and lifetimes can be measured
Spectra recorded normally, and in favorable cases, different types of spectra can be recorded from the same matrix	Spectra usually recorded at one wavelength per flash; multiple flashes are needed
Many types of spectroscopy applicable including far-, mid-, and near-IR absorption, Raman, UV-visible absorption, ESR, and various types of emission spectroscopy	Detection of transient species by UV-visible or IR absorption, but only part of the IR region is accessible at present
Reactive species can be generated by a range of methods including photolysis, vacuum pyrolysis, microwave discharge, and chemical reactions	Reactive species generated by photolysis

far from the usual room temperature solution adopted for preparative photochemistry, to which flash photolysis gets closer (once that differences due to the high concentration of excited states are taken into account), but with less structure information (Table 6.1).

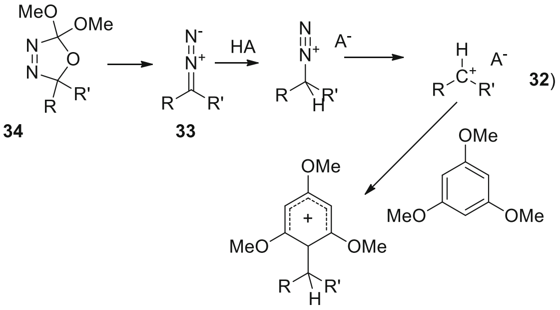
As discussed by Bally [33], matrix photochemistry has obtained excellent results, provided that back reaction is not overwhelming. This is a problem with radicals, much less for carbenes and nitrenes when formed by elimination reactions from diazo compounds and respectively azides. In the latter case, N_2 is eliminated with no significant alteration of the matrix. There are exceptions, however, as is the case of parent carbene, the identification of which has long been hindered by the efficient recombination occurring, and finally demonstrated by ^{14}N–^{15}N exchange [42].

6.4 Anything You Can Do, Photochemistry Can Do Better: Generating Intermediates

Over the years, photochemistry has given to chemistry in general an inestimable help, by offering direct, spectroscopic information about the structure of intermediates on which almost every chemical reaction is based, and that under controlled, “cold” conditions. Most often, these species can only be investigated indirectly under thermal conditions (unless under harsh conditions, such as a high temperature, as in flash vacuum pyrolysis, or by the action of a strong chemical, such as magic acid). On the contrary, when starting from the high-energy position of electronically excited states these species are smoothly formed and evidence about their structure is obtained through their spectra. In this way, it becomes possible to have a direct portrait of intermediates, not of a trapping product, contrary to what generally happens when these are thermally generated, and structures that had been previously only a hypothesis come before our eyes as actual species.

6.4.1 Carbocations

Even with non-absorbing intermediates, photochemistry is the best method. Thus, alkyl carbocations **32** can be generated photochemically, e.g., via diazonium salts **33** (in turn photochemically generated by photolysis of oxadiazoline **34** in the presence of a proton source [43]) These are trapped by π-nucleophiles (Scheme 6.14 and Fig. 6.21).



Scheme 6.14 Revealing aliphatic cations through their adducts onto 1,3,5-trimethoxybenzene

Aliphatic carbocations are conveniently examined in this way: more stabilized ones, such as benzyl radicals, can be accumulated and have been characterized as reference electrophiles, but also intrinsically unstable species such as phenyl cations (**35**) are generated photochemically and characterized [44]. Indeed the phenyl cation and some of its substituted derivatives have been characterized by both matrix and flash photolysis methods. These species are strong electrophiles

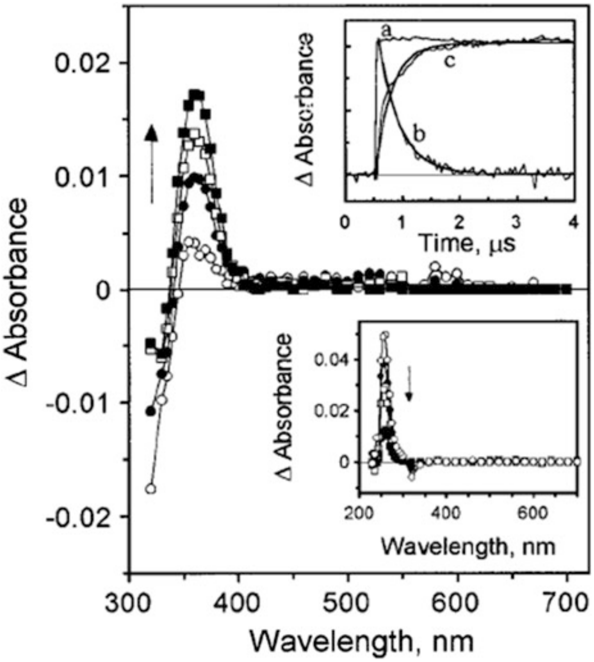


Fig. 6.21 Time-resolved UV-visible spectra of 1-cyclobutyl-2,4,6-trimethoxybenzenium ion obtained after 308-nm laser flash photolysis of oxadiazoline (**34**, R, R′ = $(CH_2)_3$) in hexafluoroisopropanol containing 1.34 M trimethoxybenzene and 0.002 M **34** at 22 °C. The data were collected at intervals of 260 ns (*open circles*), 620 ns (*filled circles*), 720 μs (*open squares*), and 2.3 μs (*filled squares*) after the laser pulse. The *lower inset* shows the time-resolved UV-visible spectra obtained after 308-nm laser flash photolysis of the same oxazoline in hexafluoroisopropanol containing 0.002 M TFA at 22 °C with the data collected at the same time intervals. *Upper inset* shows the time-resolved UV-visible absorption traces (overlayed and normalized) observed at 250 nm (a, stable intermediate; b, decay) and 355 (growth) wavelengths following 308-nm laser flash of (a) the oxazoline in hexafluoroisopropanol, (b) in the presence of 0.002 M trifluoroacetic acid, and (c) in the presence of both 1.34 M trimethoxybenzene and 0.002 M trifluoroacetic acid [43]

and react both in matrix and in solution, e.g., with nitrogen to give phenyldiazonium cations or with CO or nitrogen to give acyl and respectively diazonium cations in matrix (Fig. 6.22, Scheme 6.15) [45, 46] or with π-nucleophiles in solution to give phenonium cations (**36**) and various phenylated products (Fig. 6.23; Scheme 6.15) [47].

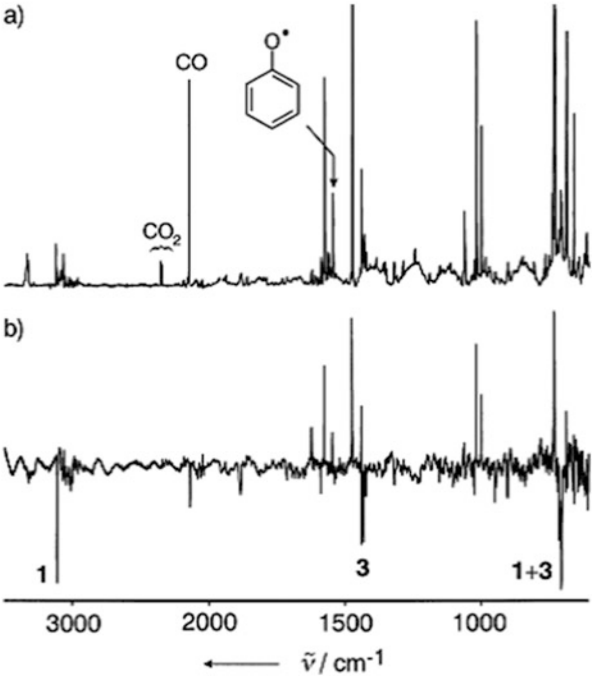
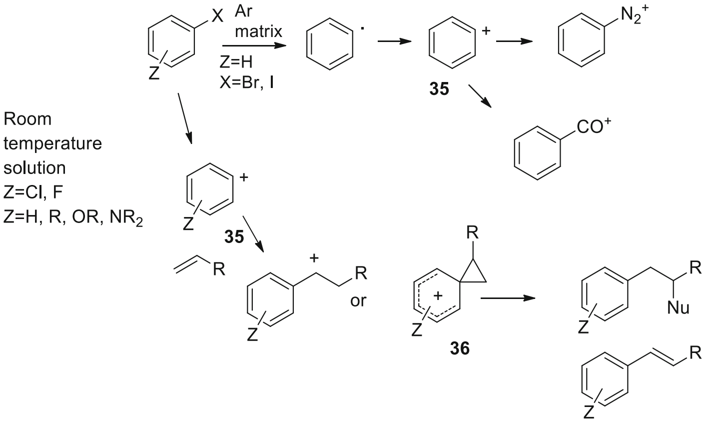


Fig. 6.22 IR detection of phenyl cation. (**a**) IR spectrum of iodobenzene after argon resonance irradiation; (**b**) difference spectrum of the same matrix showing the bleaching of phenyl radical and cation. The bands pointing downwards disappear during irradiation with $\lambda > 400$ nm, whereas absorptions of iodobenzene and phenoxyl radical increase in intensity. See [45, 46]



Scheme 6.15 Chemistry of photogenerated phenyl cations in matrix (*top*) and in solution (*bottom*) [45–47]

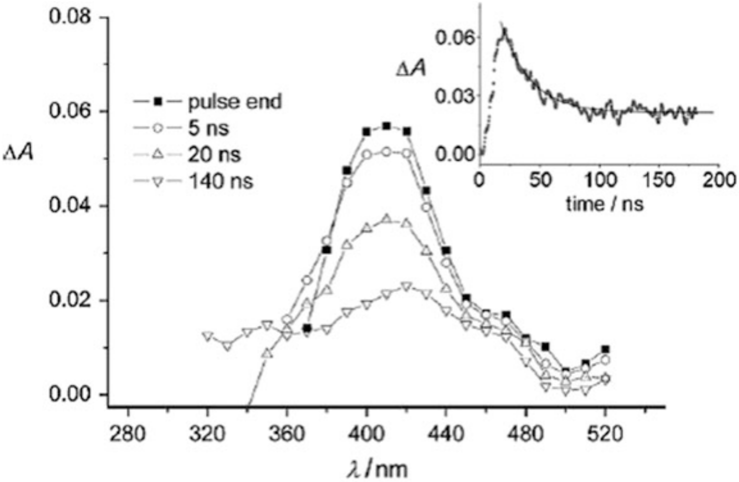
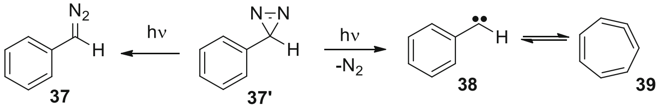


Fig. 6.23 Difference absorption spectra of a solution of 4-chloroanisole (1.3×10^{-3} M) in argon-saturated trifluoroethanol at various delays after a 266-nm laser pulse (4.0 mJ per pulse). *Inset*: zero time at pulse onset. Reprinted with permission from [47]

6.4.2 *Carbenes*

Among the most investigated examples are carbenes and nitrenes [48–50]. The photodecomposition of diazo compounds and of diazirines has been largely used for the generation of carbenes and of products arising from them, often with preparatively useful yields (Scheme 6.16, Fig. 6.24). Besides carbenes, the method can be extended to the synthesis of compounds containing a chain of *unsubstituted* carbon atoms, most often generated by different techniques, more akin to those used in mass spectroscopy, but then codeposited in a rare gas matrix for spectroscopic characterization [51]. Compounds with a sequence of five unsubstituted carbons (**40**) are best envisaged as dialkynyl carbenes having a triplet ground state and have been prepared by decomposition of a diazodiyne (Fig. 6.25). In accord with the above structure, theses species react with oxygen at the central position [52, 53].



Scheme 6.16 (Photo)decomposition of phenyldiazomethane (**37**) and phenyl diazirine (**37′**) yields phenylcarbene (**39**) that is in equilibrium with cycloheptatetraene (**38**) [50]

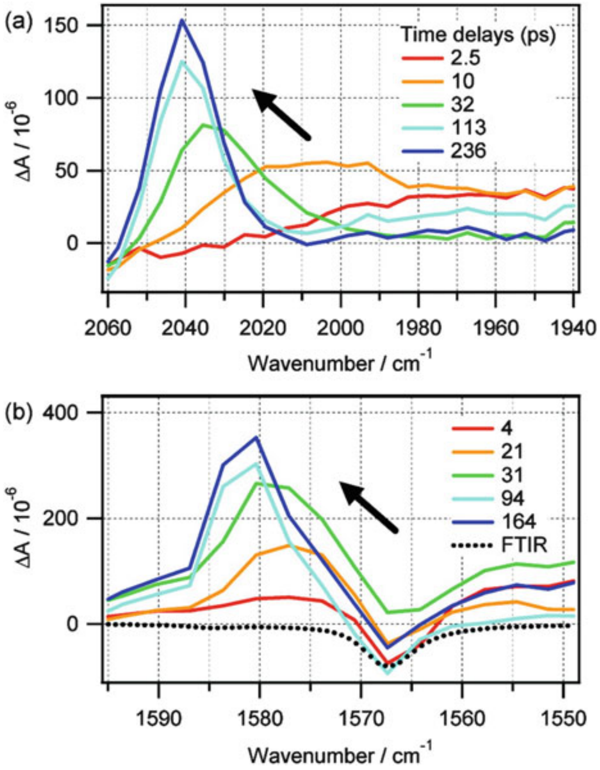


Fig. 6.24 Transient IR spectra of chlorophenyldiazirine in chloroform at selected time delays from the flash. (**a**) In the region of the diazo band (2060–1940 cm^{-1}) and (**b**) in the region of the carbene band (1600–1550 cm^{-1}). Reprinted with permission from [48–50]

6.4.3 Nitrenes

In contrast to aryl carbenes that give a good yield of trapping products, the photodecomposition of aryl azides generally yields poor amount of *characterizable* organic compounds and thus the use of nitrene in synthesis has progressed slower than that of carbenes. Mechanistic studies showed, however, that this is due to the fact that the first generated intermediate undergoes an electrophilic intramolecular

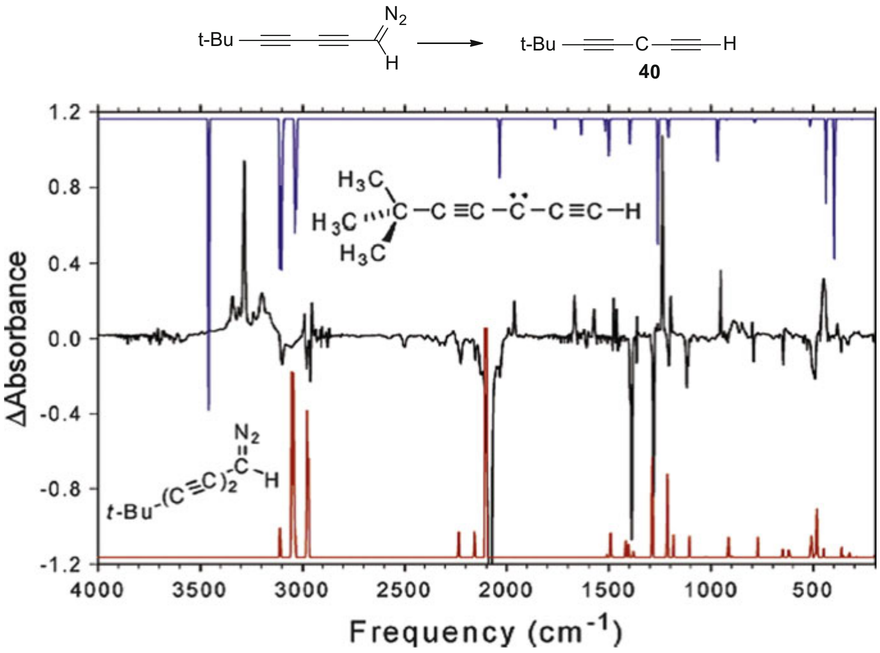
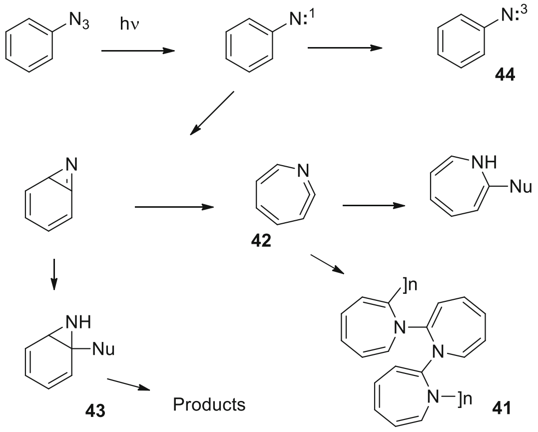


Fig. 6.25 *Top*: Computed IR spectrum of triplet t-BuC$_5$H (**40**) (1a) (B3LYP/cc-pVTZ). *Middle*: IR subtraction spectrum showing the disappearance of a diazodiyne compound and the growth of triplet t-BuC$_5$H **40** upon irradiation ($\lambda > 497$ nm, 13.5 h, N$_2$, 10 K). *Bottom*: Computed IR spectrum of the diazo compound (B3) (BLYP/6-31G*). The computed intensity of the diazo stretching vibration (2103 cm^{-1}) has been truncated in order to depict the vibrations with lower intensity. Reprinted with permission from [52]

rearrangement to give a dehydroazepine (**42**), whether or not via a benzoazirine (**43**, generally more stable with azides of polycyclic aromatics, rather than with phenyl azides), whereas triplet nitrenes are essentially unreactive (**44**, “lazy triplet,” Scheme 6.17). These further electrophilic intermediates react with nucleophiles at a different rate depending on medium and structure. When no trap is present, phenylazide and simple derivatives give what has long been considered an intractable tar, but a more thorough examination has shown to be an electron-conducting polymer (**41**), still not a typical organic target, but of some interest of its own. Recognizing the nature of the intermediates and their chemistry helps of course in devising new molecules that have a more selective behavior, e.g., electron-withdrawing substituted phenylazides exhibit increased electrophilic attack onto a variety of nucleophiles, useful, if not in organic synthesis, in a variety of surface treatments, etc. Finding an accord between preparative studies and flash or matrix experiments has required a long work.



Scheme 6.17 Intermediates and end products formed by photolysis of phenylazide

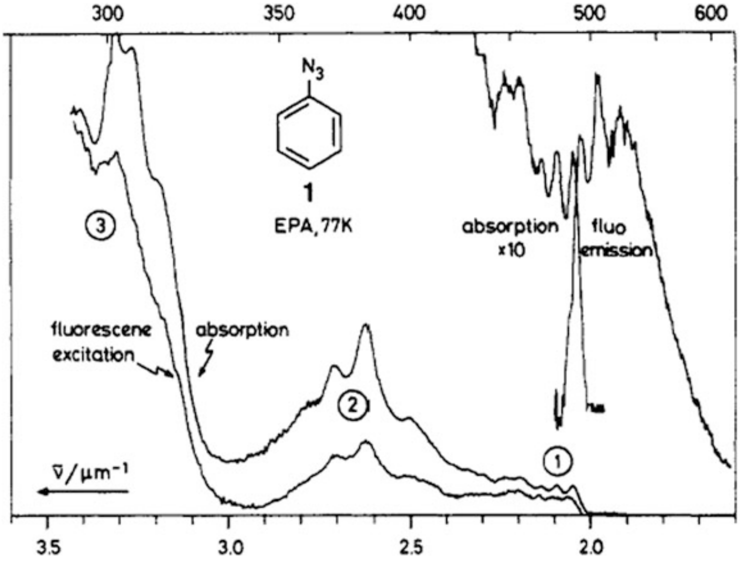


Fig. 6.26 Absorption, fluorescence excitation, and fluorescence emission spectra of triplet nitrene obtained by 334-nm photolysis of phenylazide in EPA solution at 77 K [54]

As discussed in Sect. 6.2, matrix photogeneration offers an excellent way for characterizing highly unstable intermediates. UV spectroscopy is highly sensitive and certainly useful for determining the role of intermediates, but IR spectra are much richer of information (and less affected by small amounts of impurities, while contaminants with a high ε might give a wrong impression in UV). Irradiation in a rigid medium formed by rapid cooling of a solution was a convenient choice. Thus, irradiation of phenylazide in EPA at 77 K led to the formation of an absorption in the visible, with a weak band around 470 nm and further bands at 400 and 320 that could be attributed to triplet nitrene (Fig. 6.26). A weak emission at ca. 500 was

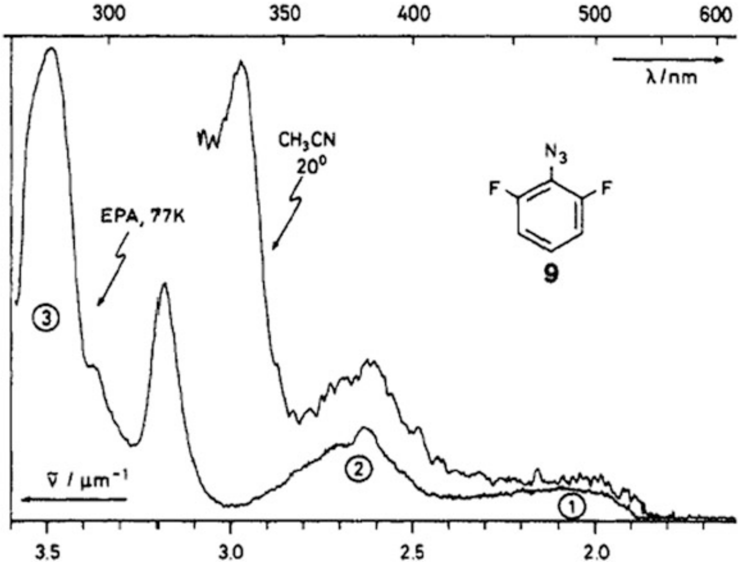


Fig. 6.27 *Lower curve*: absorption spectrum of the nitrene produced by 254 nm photolysis of 2,6-difluorophenylazide in EPA solution at 77 K. *Upper curve*: transient absorption spectrum observed 50 ns after 308-nm laser flash photolysis of the azide in aerated acetonitrile at ambient temperature [55]

assigned to the T_1–T_0 nitrene emission and the good match between both fluorescence excitation and absorption spectrum and the transient observed by flash photolysis at room temperature strengthened the proposal that a single species was responsible for all of the bands (which is not always the case for nitrenes) [54]. Similar spectra were obtained from most azides studied (Figs. 6.26, 6.27, and 6.28) [55]. Secondary photochemistry could be observed by further irradiation in matrix.

Matrix generation has allowed us to study dinitrenes. Conjugated derivatives are strongly ferromagnetic in nature. However, interaction is reduced when nonconjugated, and such intermediates are only weakly antiferromagnetic [56].

6.4.4 Aromatic Biradicals: Didehydrobenzenes and Didehydrotoluenes

A smooth entry to ortho-benzyne is irradiation of phthaloyl peroxide [57]. As early reported, in appropriate solvents many reactions characteristic of this species (cycloaddition, ene reaction) have been detected (see Scheme 6.18, Fig. 6.29) [58].

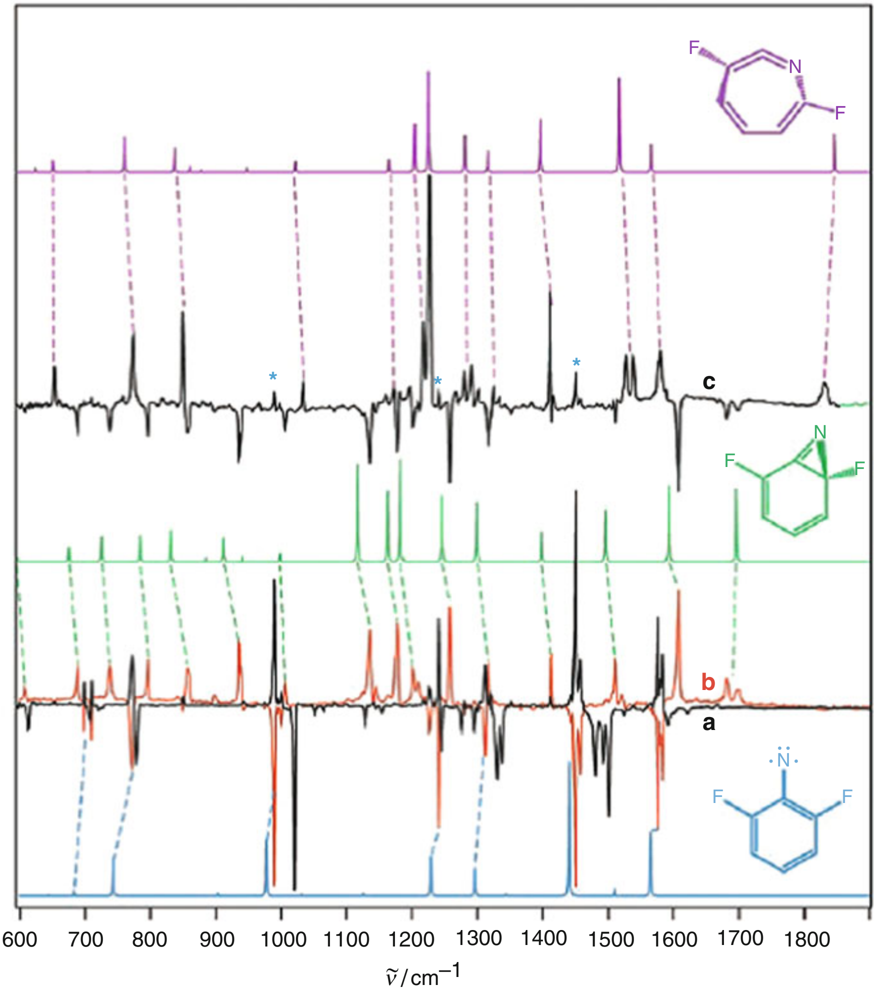
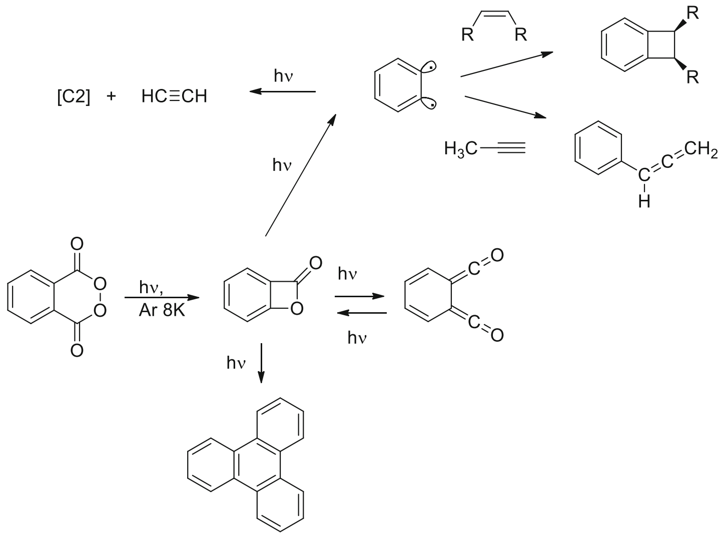


Fig. 6.28 IR difference spectra for (**a**) photolysis of 2,6-difluorophenylazide in an Ar matrix at 14 K and 254 nm, (**b**) subsequent irradiation at 485–515 nm (Ar-ion laser in multimode), and (**c**) irradiation at 313 nm (medium-pressure Hg/Xe lamp, interference filter).The *colored traces* represent the IR spectra calculated by the B3LYP/6-31G* method for didehydroazepine (*blue*), azirine (*green*), and triplet nitrene (*purple*).The *asterisks* in spectrum **c** indicate the major peaks of the dehydroazepine, which also forms on the photolysis of the azirine at 313 nm [55]



Scheme 6.18 Generation and chemistry of *o*-benzyne

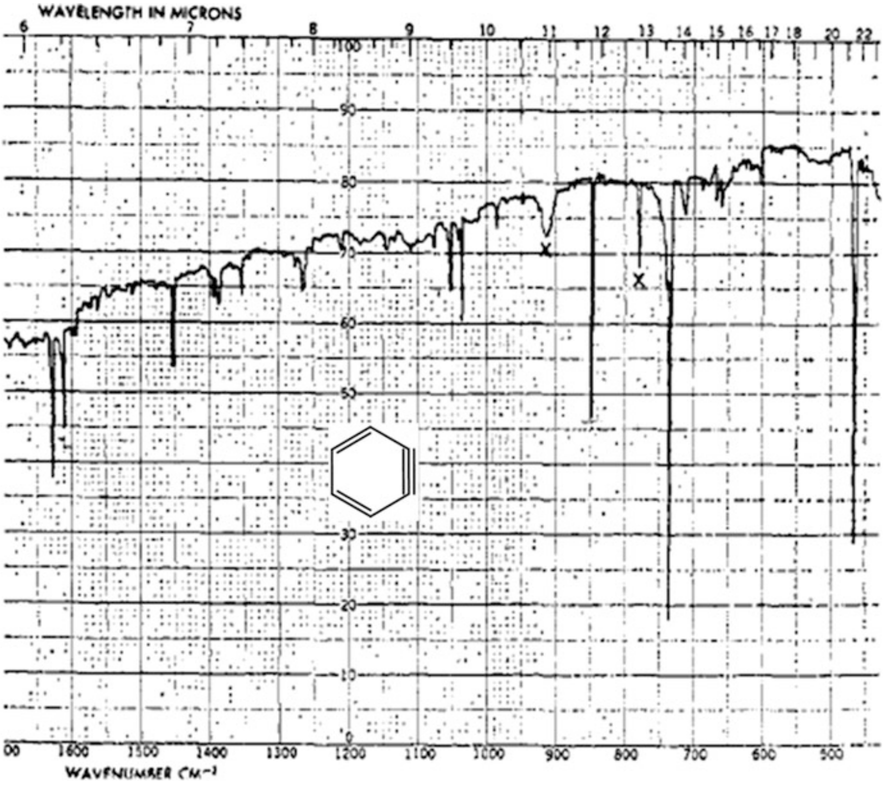


Fig. 6.29 IR spectrum of benzyne (matrix isolated in argon at 8 K) prepared by irradiation of phthaloyl peroxide. Bands at 1627, 1607, 1451, 1053, 1038, 49, 736, and 469 cm^{-1} are definitely benzyne bands. The bands marked with an x are definitely not benzyne bands [57]

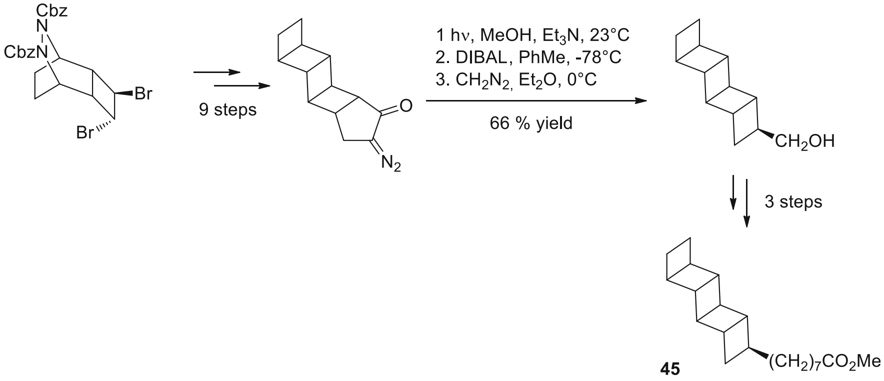
Dehydrotoluenes have likewise been obtained by double photochemical elimination from chlorobenzylsilanes and chlorophenylacetic acids [59, 60].

6.5 Anything You Can Do Photochemistry Can Do Better: Making (Strained) Molecules

As mentioned above, photochemistry by definition offers a favorite entry to intermediates when the thermal process confronts a high-energy barrier or involves an intrinsically slow process. Therefore, photochemistry appears to have a key role in synthesis for making possible "*a thermally unachievable, energetically uphill reaction*" (in the words by Noyori [61]), as well as for giving access to intermediates with a different multiplicity with respect to the reagent. In fact, the enormous amount of energy involved in photochemical reactions is generally not incorporated in the products, or only partially so. Among photochemical reactions, only those leading to severely strained structures would be markedly endothermic in the ground state. But in this field, photochemistry is an inexhaustible source of strained molecules, in particular of both homo- and hetero-small ring compounds. Starting from the 1960s and 1970s, photochemical syntheses that lead to three- or four-membered rings via 2+2 cycloaddition, ring restriction by the Wolff rearrangement, (oxa, aza) di-π-methane rearrangement, electrocyclic rearrangement, reactions via carbenes and nitrenes, and many others have been largely exploited for this aim.

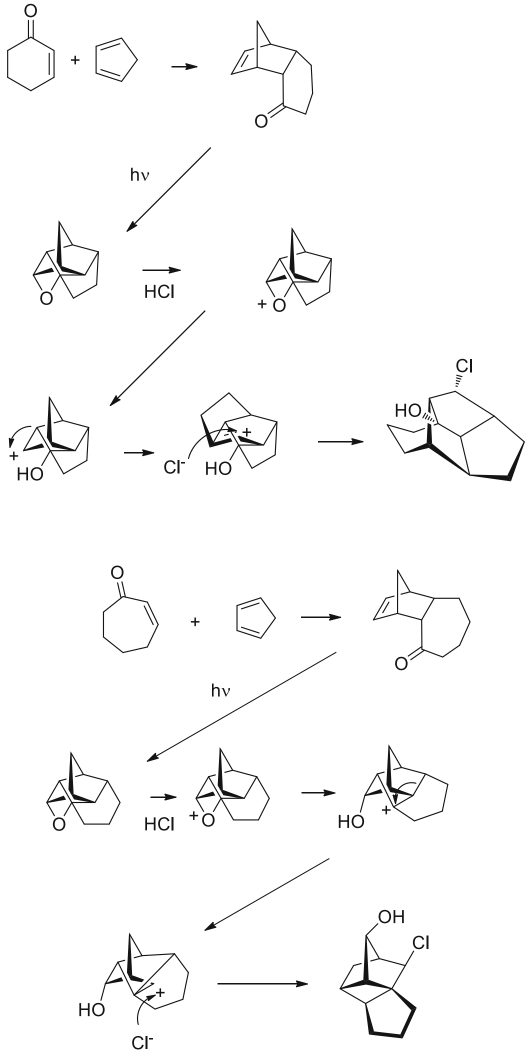
In many cases synthesis of new highly symmetric structures is justified by a sense of pleasure in creating a nice object as well as by the wish of accumulating high amount of energy (for example, for fuel of extra features), but small rings are often present among natural compounds and their synthesis is quite often a valuable source for the better characterization of products present in nature in too low an amount for complete characterization. As an example, in the anaerobic microbe *Candidatus Brocardia annamoxidans* the main lipid component of the dense membrane is a highly unusual C_{20} fatty acid, known as pentacycloanammoxic acid (**45**) [62].

This has been synthesized starting from the 2+2 cycloadduct between cyclopentenone and cyclobutene by introducing the diazo function and applying the Wolff rearrangement for building a tricyclic alkene. A further photochemical cycloaddition with a cyclopentenone derivative, followed by a new introduction of the diazo function, photo-Wolff rearrangement, and reduction of the acidic function for enabling insertion of the chain lead to the acid, after this succession of (five!) photochemical reactions (Scheme 6.19).



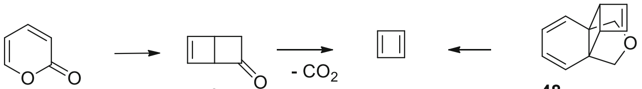
Scheme 6.19 Synthesis of pentacycloanammoxic acid ester **45**

In many cases such strained structures are smoothly opened to form further interesting compounds. An example is the intramolecular Paternò–Büchi reaction of Diels–Alder cycloadducts between enones and dienes. Upon acid treatment, oxetanes open up to chloroalcohols, but the intermediate cation generally rearranges before addition of chloride. The actual process occurring depends on the bridges length, as shown below for the case of the rearranged products formed from two oxetanes differing by one carbon in a bridge, and thus in the forced pyramidalization of the cationic center (Scheme 6.20) [63].



Scheme 6.20 Synthesis of chloroalcohols by ionic opening polycyclic oxetanes prepared by Paternò–Büchi cycloaddition [63]

The anti-aromaticity of cyclobutadiene (**46**) has made this molecule a topic of choice in research by matrix isolation, where it occupies an important chapter. It was initially obtained by matrix photodecomposition of α-pyrone by a prolonged irradiation at 20.4 K in argon matrix via a series of intermediates (Scheme 6.21). The peaks marked in the unexpectedly simple spectrum obtained were attributed to such species (Fig. 6.30). To finally establish the structure of this molecule, rectangular or square, many further experiments were required, in particular the generation from a different precursor and testing the effect of specific deuteration in the spectrum [8].



47 **46** **48**

Scheme 6.21 Generation of cyclobutadiene **46** from bicyclo[2.2.0]cyclohexenone **47** and from tetracyclic ether **48** [8]

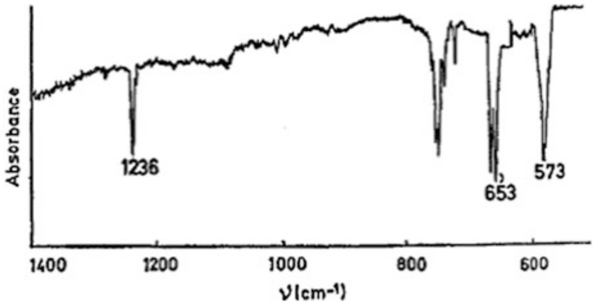
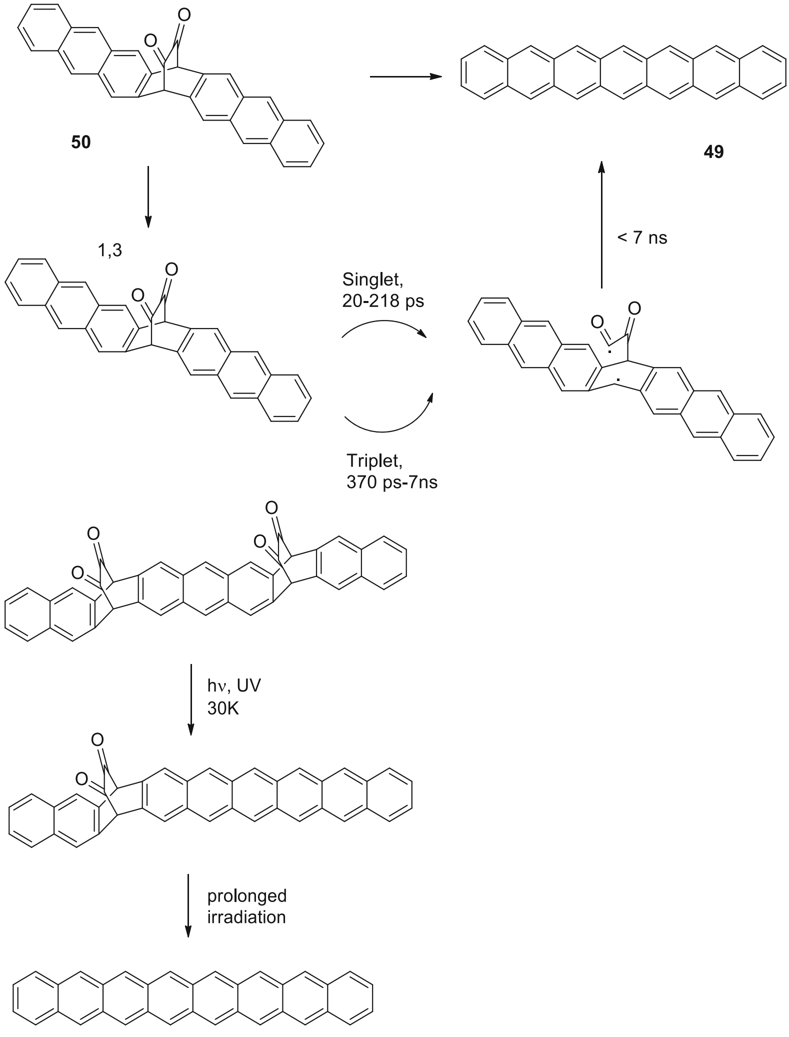


Fig. 6.30 IR spectrum of richest portion of photolyzed compound after 75 h of irradiation of a sample of α-pyrone in an argon matrix. Reprinted with permission from [8]

The interest for poly(acenes) is growing because of the interesting properties of these materials as low-temperature photoconductive materials. However, their stability is limited, particularly from hexacene onward. Double elimination from the corresponding diketone has been proved to offer a valuable access. In the case of heptacene **49**, the reaction takes place from precursor **50** via both the singlet and the triplet manifold and is complete within 7 ns [64]. This approach has been extended to octacene and nonacene from the doubly bridged precursors (Scheme 6.22). Long wavelength irradiation causes partial decarbonylation, but prolonged irradiation in the UV eliminates also the second bridge [64].



Scheme 6.22 Photochemical synthesis of heptacene and octacene

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Chapter 7
Of Excited States Again

7.1 Expanding the State Diagram

The generalizations about photochemical reactions emerged in the 1950s are perhaps too narrow. The key photochemical steps, as shown in Sect. 7.3, involve absorption of one photon (according to the Stark–Einstein law, k_a 10^{15}–10^{16} s^{-1}), internal conversion, and/or intersystem crossing down to the lowest excited singlet or the lowest triplet (Kasha–Vavilov rule, k_{ic} or k_{isc} up to 10^{11} s^{-1}) and emission or photochemical reaction from thermalized S_1 (k_f, $k_r(S)$ often around 10^8–10^9 s^{-1}) and T_1 states (k_p, $k_r(T)$ often around 10^6 s^{-1} or slower). Deviations from such simple behavior, e.g., fluorescence from an upper singlet in the case of azulene or thioketones, were well explained by the fact that in such cases the energy gap between S_2 and S_1 was as large as that between S_1 and S_0, justifying that k_f from S_2 competed with k_{isc}. Advancement in experiments and in theory has led to a better understanding of the conversion between electronic states, whether these are two states of the same chemical species, or something that can be called a reagent and a chemical product, and how fast this may happen. As for the last term, the photochemical literature of the last decades abounds of newly coined terms containing the prefix ultra, or super, or multi. This is no manifestation of the vanity of the authors, but rather the expression of genuine technical advancements that demonstrate that the photochemical paradigms emerged in the 1950s are oversimplifications. Instrumental advancements achieve a better description of excited states and their evolutions and many limitations that had seemed to be inherent to the systems studied can actually be overcome under suitable conditions, thus opening new fields of application. Each of the paradigms of Chap. 3 must therefore be reconsidered and nonlinear processes must be taken into account (Scheme 7.1).

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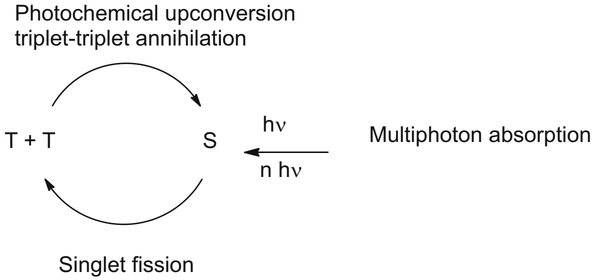
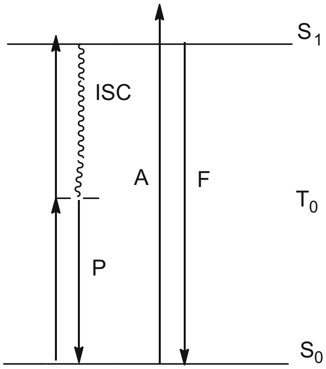


Scheme 7.1 Nonlinear processes. Two-(or multi-)photon absorption may occur under appropriate conditions (and exploit also low-energy photons. Singlet fission may lead to two triplet states (and thus to more photochemical acts). Two triplets may be annihilated and form a singlet of higher energy (photochemical upconversion). These phenomena must be taken into account because they lead to important applications

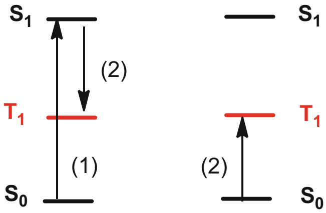
It has been long known that some photochemical processes require consideration of interactions between excited states, such as delayed fluorescence. These were clearly distinguished in the work by Lewis, Kasha, and Parker [1].

- E-type delayed fluorescence. As defined by the IUPAC Gold book [2], this is the process “in which the first excited singlet state becomes populated by a thermally activated radiationless transition from the first excited triplet state. Since in this case the populations of the singlet and triplet states are in thermal equilibrium, the lifetimes of delayed fluorescence and the concomitant phosphorescence are equal.” This process takes its name from eosin and is typically observed with dyes, where the S_1–T_1 gap is small.
- P-type delayed fluorescence: “The process in which the first excited singlet state is populated by interaction of two molecules in the triplet state (triplet–triplet annihilation), thus producing one molecule in the excited singlet state. In this biphotonic process the lifetime of delayed fluorescence is half the value of the concomitant phosphorescence.” This takes its name from pyrene and is observed from most aromatic molecules, where S_1 and T_1 are too far for thermal activation of the latter.
- Recombination fluorescence: The first excited singlet state becomes populated by recombination of radical ions and electrons or by recombination of radical ions of opposite charge (Scheme 7.2).



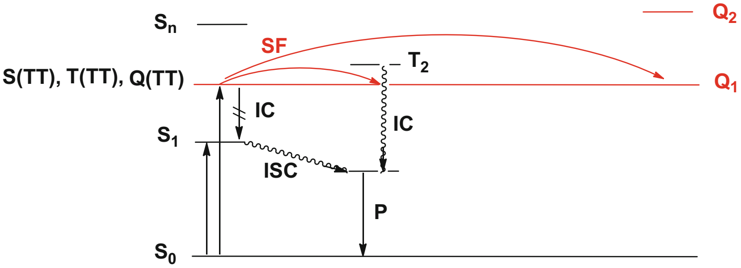
Scheme 7.2 Fluorescence (F) and phosphorescence (P). "Normal" fluorescence (F) arises from S_1 (independently from which singlet has been initially reached, and thus its shape is not affected by the energy of the wavelength used, provided that this has been absorbed. This is the Vavilov rule, rationalized by Kasha as due to the fact that internal conversion among states of the same multiplicity is always the fastest process, see Chap. 3). Delayed fluorescence may involve triple–triplet annihilation, in which self-quenching of the triplet leads back to the singlet S_1, with the usual fluorescence spectrum but the triplet lifetime

As shown when discussing the state diagram in Chap. 3, in a molecule containing a single chromophore, access to the triplet manifold by absorbance is not viable either by direct absorption (*forbidden absorption*), or indirectly from the singlet manifold (intersystem crossing), since spin prohibition extends also to horizontal transitions. However, the systems considered in practice do not contain a single molecule, or it may be that the molecule considered contains two or more chromophores. In such all-important cases, a different path has to be considered and involves the interaction between an organic chromophore in an excited singlet state and a neighboring one (either of the same or a different kind) in the ground state, whereupon both of them are converted into triplet excited states (Scheme 7.1). In such Singlet Fission, the two triplets are generated coupled in a singlet state and the overall path is spin allowed. This transition can be very fast (down to the ps timescale or even below), competing with vibrational relaxation and easily overcoming direct fluorescence. Actually, cases of triplet quantum yield up to 2 have been reported for solid samples or aggregates. More precisely, the three sublevels of each triplet state result in singlet ^{1}(TT), triplet ^{3}(TT), and quintet ^{5}(TT) states, not exactly degenerate. As pointed out by Michl [3], singlet fission has the potential for converting singlets into both triplets and quintets efficiently, thus *expanding* the Jablonski diagram as shown in red in Scheme 7.3. Generalizations about favorable structural features are available. Thus, two-photon absorption is observed in donor–acceptor systems and depends on the polarizability of the molecule, the length of the π-conjugated system, the strength of the donating/accepting groups, and the way in which the systems are connected, with a preference for more complex system over simpler analogues. A high fluorescence quantum yield is generally related to the rigidity of the structure and requires avoiding heavy atoms and substituents such as the nitro group that favor ISC to the triplet (and often photochemical reactions).

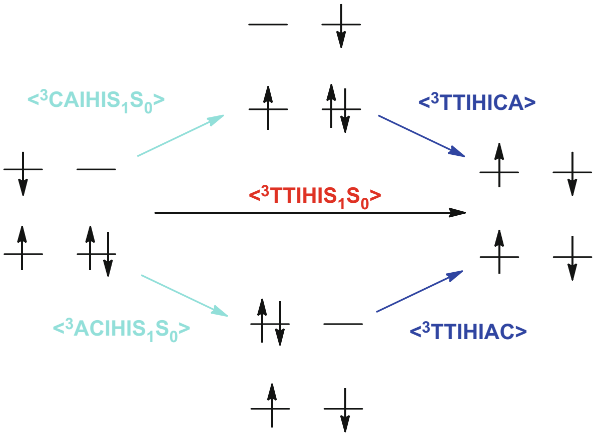


Scheme 7.3 Singlet fission: (1) the chromophore on the left undergoes initial excitation to S_1. (2) The excited chromophore shares its energy with the chromophore on the right, creating a T_1 from each of the initial states. Reprinted with permission from [3]

The mechanism involved is represented in Scheme 7.4, where both direct process and singlet fission mediated by charge transfer states are presented. The conditions that have to be met for occurring of this phenomenon, which can be considered a sort of internal conversion, are stringent, but it has now been observed in several cases, and appropriate theories that account quantitatively for both singlet fission and the reverse phenomenon, triplet–triplet annihilation, and their role in solids have been put forward [3]. With aromatics, where the singlet–triplet gap is large, the phenomenon is often significant, although the emission may be weak and not easily detected. In particular, molecules, such as tetracene, where the energy of S_1 is almost exactly twice as much as that of T_1 have been extensively studied, both on the crystals and on phenylene-linked dimers as covalently blocked models. In crystals, direct evidence for the fission of initial singlet state into a superposition of triplet pair states has been reported. The beat frequencies depend on crystal orientation with respect to the magnetic field, consistent with theoretical predictions. The long-time behavior of the fluorescence decay reflects association and separation of triplet pairs and relaxation into different spin states. Similar phenomena have been found also with rubrene [4–6]. Most interestingly, singlet fission was observed on ultrathin single crystals, where the expected quantum beats in the delayed fluorescence arising from recombination of spin-coherent triplet pairs were observed. This indicated that singlet fission proceeds through a direct single-step process within 200 ps at room temperature and gives a pair of unperturbed triplets that have negligible interaction with each other [7]. Theory is not simple, and is being still developed, but important advancements have been made and it is now possible to predict which chemical structures are likely to undergo this phenomenon. The relevant models are indicated in Scheme 7.5, where different mechanisms for singlet fission are recognized, viz., direct population of S_1 (red arrow and matrix element) and charge transfer-mediated mechanism (via S_2, cyan arrows and matrix elements followed by blue arrows and matrix elements).



Scheme 7.4 Singlet fission (SF). Expanded Jablonski diagram with the singlet fission shown in *red*. Also indicated, *F* fluorescence, *IC* internal conversion, *ISC* intersystem crossing, *P* phosphorescence. Reprinted with permission from [3]



Scheme 7.5 Mechanism of direct singlet fission (*red*) and charge transfer-mediated singlet fission (*blue*). Reprinted with permission from [3]

Further related processes occur in inorganic materials (quantum cutting) and in quantum dots [8, 9].

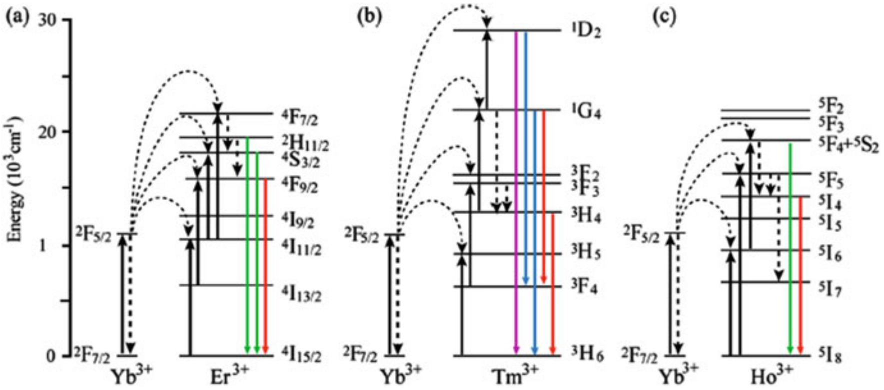
7.2 Upconversion

In the contrary process, two triplet states may give a singlet of high energy (triplet–triplet annihilation, TTA). Fluorescence from the thus formed singlet occurs at an energy higher than that of the exciting light [10]. In a typical scheme, a light absorbing sensitizer and an annihilator transparent to the excitation wavelength produce an anti-Stokes emission [Eq. (7.1)]

$$2\ \text{Sensitizer (Triplet)} \rightarrow \text{Annihilator (singlet excited)} \rightarrow \text{Fluorescence} \quad (7.1)$$

The annihilator should fluoresce efficiently, have a triplet energy above that of the sensitizer, but below a half of that of its own singlet, have a long triplet lifetime, and obviously be photostable. Sensitizers should have a large intersystem crossing efficiency and a slow phosphorescence emission. The singlet–triplet gap should be not too large and comparable to the singlet triplet gap of the annihilator. Annihilators are typically aromatic hydrocarbons (anthracene, tetracene, perylene, pyrene, and their simple derivatives and heteroanalogues). Most largely employed sensitizers are heavy metal complexes with porphyrin or phthalocyanines and many other ligands, but also aromatics, generally heavy-atom substituted for increasing ISC, fullerene–chromophore dyads, as well as nanoparticles, nanocapsules, dendrimers, and on the other hand simple molecules such as biacetyl. The change in the color of emission due to the appearance of triplet–triplet annihilation is in many cases visible by naked eye in a dark room by using a laser pointer. An experiment for undergraduate has been reported, where the benchmark orange fluorescence of ruthenium tris(bipyridyl) is quenched and is substituted by the blue fluorescence of diphenylanthracene [11].

Besides triplet–triplet annihilation, a further process for achieving upconversion luminescence emission under continuous wave low-energy irradiation is based on the use of lanthanide ions, most often erbium, holmium, and thulium (III) cations. In particular, a large variety of phosphors based on an inorganic host doped by lanthanide cations have been developed. The abundance of available states in these cations opens a large variety of paths for upconversion. As an example (Scheme 7.6), upconversion nanoparticles codoped with ytterbium and erbium cations exhibit a green emission due to the transitions from $^2H_{11/2}$ and respectively $^4S_{11/2}$ excited states to the ground state $^4I_{15/2}$ as well as a red emission from the $^4F_{9/2}$ state [10].



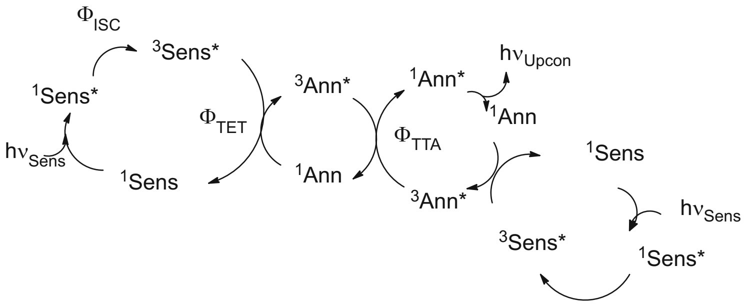
Scheme 7.6 Upconversion mechanism of nanoparticles codoped with (**a**) Yb^{3+} and Er^{3+}, (**b**) Yb^{3+} and Tm^{3+}, or (**c**) Yb^{3+} and Ho^{3+}. Reprinted with permission from [10]

In a summary of the state of the art in the field, Schmidt and Castellano [12] listed the most important advances:

- The observation of photoinduced upconversion using noncoherent photons in solution and in soft polymer matrices;

- The demonstration of linear incident power dependence for upconversion process using both coherent and noncoherent light sources;
- The expansion of the acceptor/annihilator genre beyond aromatic hydrocarbons;
- The development of near-IR-to-visible light conversion compositions;
- The illustration of upconversion quantum efficiencies greatly exceeding the putative TTA spin statistical limit of 11.1 % (due to competing quintet and triplet formation).

In Scheme 7.7, the sensitizer (Sens) absorbs a photon and the singlet intersystem crosses to the triplet, which in turn sensitizes the annihilator (Ann). This is a long-lived species and interaction of two such intermediates leads to the singlet sensitizer, which emits at a shorter wavelength than that of Ann. Castellano observed that the practically obtainable yield depends on a number of factors: the ISC yield, Φ_{ISC}, the triplet energy transfer yield, Φ_{TET}, the TTA yield, Φ_{TTA}, and the fluorescence quantum yield of the emitter in the upconversion environment, Φ_F. Two photons must be absorbed and thus the upconversion yield, Φ_{UP}, is expressed by [Eq. (7.2)]



Scheme 7.7 Light is absorbed by a sensitizer (Sens). Triplet energy transfer (TET) and triplet–triplet annihilation (TTA) in a molecule that acts as annihilator brings to singlet excited sensitizer

$$\Phi_{UP} = (\Phi_{ISC}\Phi_{TET}\Phi_{TTA}\Phi_F)/2 \qquad (7.2)$$

Of this quantities, Φ_{ISC} can be brought near to unit by inserting heavy atoms. Energy transfer to Ann is a bimolecular process, governed by diffusion and the rate of competing reactions; in practice the lifetime of triplet Sens must be >10 μs for having an efficient sensitization. Furthermore, an appropriate pair of molecules must be chosen so that neither the triplet nor the quintet of the ^{3}Ann–^{3}Ann pair reaction is significant, and only the channel to the singlet is open. This depends on the energy position of excited states, singlet S_1 and triplets. As an example, conversion to the singlet is selective with perylene, not with 2-chlorobisphenylanthracene. Considering these and other factors, a kinetic analysis demonstrates that at a sufficient high concentration of Sens and Ann in solution, an upconversion quantum yield of several percents can be reached. Indeed, there seem to be no reason why the value Φ_{UP} 0.5 should not be reached. Furthermore, advancement is expected also in the solid phase [12].

7.3 Multiphotonic Processes

Multiphotonic processes and multiple excitations

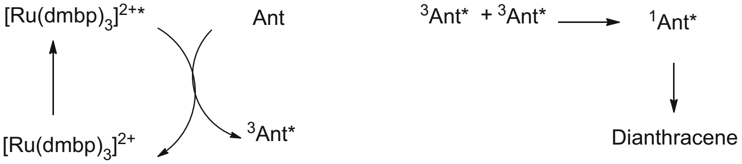
That the simultaneous absorption of two (or more) photons [Eq. (7.3)] to generate an excited state is possible was predicted theoretically by Maria Göppert Meyer [13] in 1931 (the unit of cross section has been named in her honor, $1\ \mathrm{GM} = \delta = 1 \times 10^{-50}\ \mathrm{cm}^4\ \mathrm{s\ photon}^{-1}$), although the likelihood of such phenomenon is quite poor, and its occurrence was demonstrated much later, when high-intensity lasers became available.

$$2 \text{ or more photons} \rightarrow \text{excited singlet} \rightarrow \text{anti-Stokes fluorescence} \tag{7.3}$$

The selection rules for two-photon transitions are different and many dyes that have a large coefficient for one-photon absorption exhibit two-photon cross sections in the order of at most a few GM [14]. Correspondingly, a two-photon emission (excited state → two photons) is observed as a weak emission, since only the total energy is conserved, not the energy of each individual photon. Thus, emission is a weak continuum of interest more of astrophysicists than of chemistry practitioners, but advancement in the field has been remarkable [15].

Recent research has made available generalizations about structural features favorable for a multiphoton process. Thus, two-photon absorption is observed in donor–acceptor systems and depends on the polarizability of the molecule, the length of the π conjugated system, the strength of the donating/accepting groups, and the way in which the systems are connected, with a preference for more complex system over simpler analogues. Multiphotonic excitation thus is possible, although this is orders of magnitude less effective than normal linear absorption. However, the simultaneous absorption of two or more low-energy photons in place of a high-energy one gives important advantages to this alternative. First, in these processes an enhanced spatial resolution is achieved, because the rate of absorption depends on the square of the light's intensity and thus the effect decreases very sharply from the center of the beam to its periphery. Second, excitation is made by using low-energy photons and it is easier to avoid absorption by the medium. These properties make two-photon excitation the elective method for applications that require to minimize absorption by the medium and precise detail with three-dimensional spatial control, such as optical imaging, where a deeper penetration allows to obtain high contrast three-dimensional images. Notice also that this phenomenon is not limited to photophysics and reactions have been found in some cases. Thus, anthracene (Ant in Scheme 7.8) has been found to give the [4+4] dimer when irradiated (visible light) in the presence of ruthenium (II) tris (4,4′ dimethyl-2,2′-bipyridine) cations (see

Scheme 7.8). This distinctive singlet reaction is thus achieved by exploiting low-energy photons via the triplet [16].



Scheme 7.8 Sensitization of anthracene by Ru(dmbp)$_3$. Triplet–triplet annihilation generates singlet anthracene that dimerizes

7.4 Quantum Yield of Excited States Larger than One

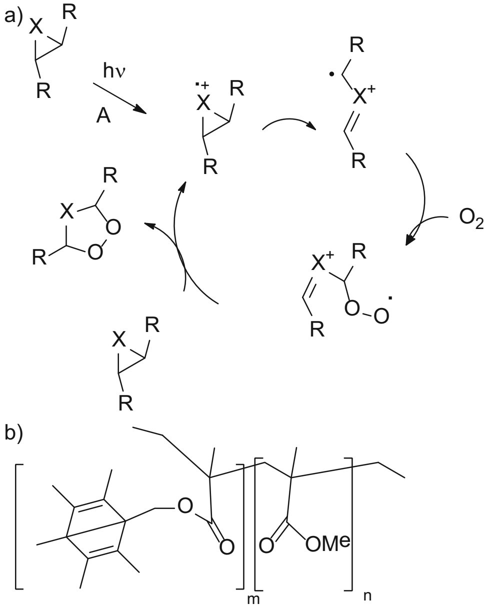
As discussed in Sect. 7.3, the Einstein equivalence law predicts a unitary quantum yield when correctly applied, that is it states that the absorption of one photon leads to one excited state. The quantum yield of a *product*, however, may be any number. This is often important when photochemistry is used for reproducing a text or image, and thus sensitivity is the issue. Very large quantum yields are measured for chain processes, silver halide photography, photopolymerization, and photo-acid (or -base) generators in photolithograpy and in other cases. However, it may also happen that the quantum yield of *excited states* is larger than 1. This happens typically for low-lying excited states with high-energy sensitizer, since energy transfer takes place more than once before the ground state is reached. Typical is the case of quenching of a molecule M by molecular oxygen when both S_1–T_1 and T_1–S_0 gaps in that molecule are larger than the small gap between $^1O_2$ and $^3O_2$ [Eqs. (7.4), (7.5)]

$$^1M^* + {}^3O2 \rightarrow {}^3M{*}^1O2 \tag{7.4}$$

$$^3M^* + {}^3O2 \rightarrow {}^1M + {}^1O2 \tag{7.5}$$

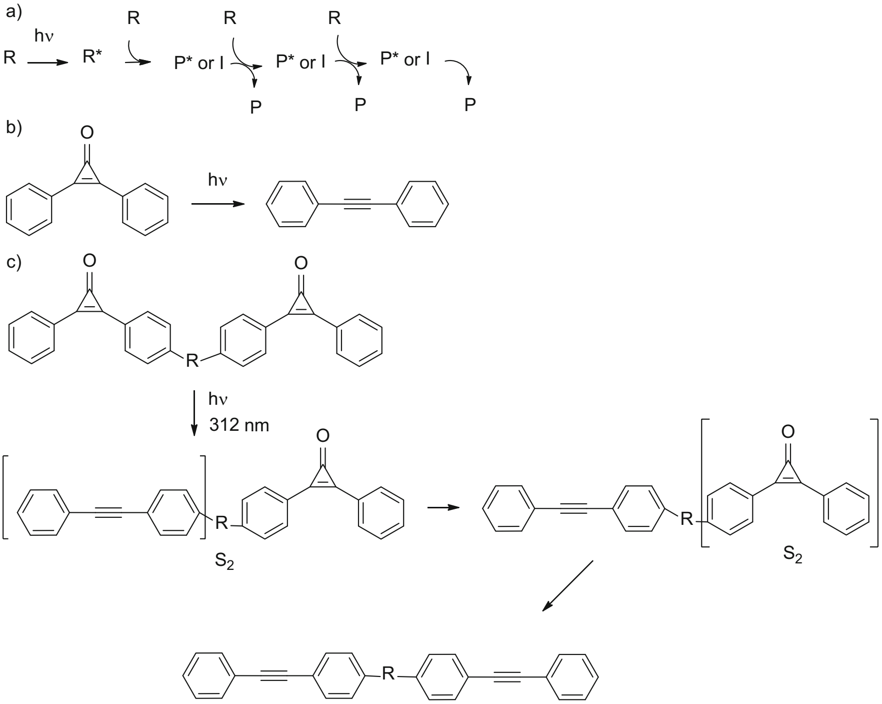
In this case, the overall quantum yield of singlet oxygen is the sum of that produced in Eqs. (7.1) and (7.2) (in the latter case with the statistical correction of 1/9) and may be larger than one [17].

Another category is that of radical and radical ion chain processes that may be involved in reactions of mechanistic and applicative interest. The oxygenation of tetrasubstituted alkenes and three-membered (hetero)cycles occurs in many cases via photoinduced electron transfer generating a radical cation (Scheme 7.9a). A chain process may take place in every case where the product is more easily oxidized than the reagent. Indeed, this principle has been applied in polymers and "quantum amplified isomerization" via a radical cation chain. These processes has been found to occur with moderate efficiency in the presence of electron-poor molecules, such as dicyanoanthracene and *N*-methylquinolinium hexafluorophosphate, both when the donor had been incorporated in the chain and when it was codissolved. Thus, incorporating easily oxidizable moieties, such as hexamethyl Dewar benzene in methyl methacrylate, and preparing the corresponding copolymer gave films that were then rearranged to hexamethylphenyl ester via a radical chain mechanism (Scheme 7.9b) [18].



Scheme 7.9 (**a**) Photoinduced electron transfer generates a radical cation. This initiates a radical cation chain. (**b**) A Dewar benzene containing polymer

Recently, solid phase studies have extended the potential of the method. As an example, diphenylcyclopropenone undergoes adiabatic dissociation along the S_2 surface, expelling CO and forming diphenylacetylene (Scheme 7.10b). Independently from which is the exact mechanism, the reaction in the crystal phase resulted to be favorable to energy transfer to a closely lying molecule of the ketone. Thus, Garcia-Garibay proposed that the excited product or a high-energy intermediate would transfer energy to the neighbor molecule, and this would react in the same way, until in the *n*th step the ground state product would be formed (Scheme 7.10a).



Scheme 7.10 (**a**) A quantum chain mechanism via radical cation. Immediately when formed an activated product (P*) or an intermediate transfer energy to another molecule causing a second reaction. (**b**) Elimination of CO from cyclopropenone. (**c**) Decarbonylation in S_2 is followed by energy transfer and a second decarbonylation

The scheme was further supported by studies on dimeric diphenylcyclopropenones. Excitation at 365 nm, where S_1 was reached, caused decarbonylation. Irradiation at 312 nm, however, causes decomposition with a quantum yield of 2.7. In this case, adiabatic reaction via S_2 occurs and (Dexter) energy transfer to the other function initiates a quantum chain (Scheme 7.10c) [19, 20].

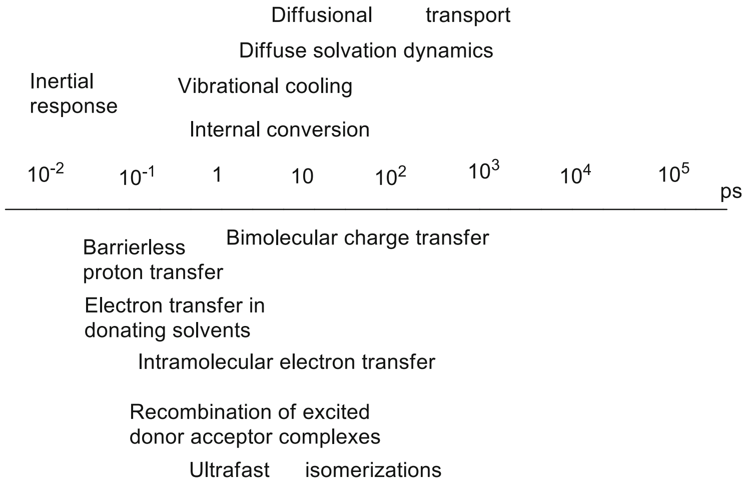
7.5 Ultrafast Processes

Ultrafast phenomena have been reported in an increasing number in recent years, due to the availability of highly sensitive instruments that achieve fs resolution. Such processes are often revealed by the dependence of the reaction quantum yield on the irradiation wavelength and thus by the initial generation of higher singlets. As an example, in terthiophene, the triplet is arrived in two ways. The additional channel for ISC starts from an unrelaxed twisted terthiophene molecule and takes place via nonplanar, twisted singlet and triplet states. The two states in this case have almost equal energy and a very strong spin–orbit coupling factor, which causes the observed fast triplet generation.

The Frank–Condon principle states that excitation does not alter the configuration of the molecule and thus the nuclear degrees of freedom of both the solute and the solvent remain in the configuration appropriate for the solute ground state even after excitation. The large amount of energy accumulated in an excited state is dissipated in essentially two ways. Thus, the relaxation processes of the nuclear degrees of freedom may be much faster of the photochemical or photophysical reaction considered, so that the only reacting or emitting states are in fact S_1 and T_1 as stated in the Kasha and Vavilov rules. On the other hand, the reagent may begin to move along the reaction coordinates before the nuclear coordinates have reached the equilibrium configuration of the excited state and also higher states may be involved in the chemical process. As it has been remarked by Vauthey, in the first time after excitation, the chromophore and its first solvation cell undergo the so-called inertial response, which leads to a coherent wave packet dynamics in the excited state potential manifold, which is of quasi-reversible character. "The coupling to fluctuating intra- and intermolecular modes leads to subsequent dephasing and transforms the initial coherent dynamics into kinetics of diffusional character" [21]. This may lead to ultrafast transitions. The timescale of relaxation and reaction are no more well separated and relaxation processes may actually affect the mode of reaction. A conical intersection may be located in the vicinity of a Frank–Condon state and an ultrafast processes may allow (or hinder) access to it. Thus, the course of the reaction may depend on temperature and on solute–solvent interaction and one may think of a fine-tuning of photochemical reactions by this way, although theoretical and experimental advancements are required before actual application. What is apparent is that internal conversion is a complex phenomenon, strictly intertwined with chemical reaction. The almost unavoidable excess vibrational energy with which the excited state is formed is initially mainly distributed in the high-frequency vibration modes, but fast intramolecular redistribution populates the low-frequency modes and eventually leads to a thermally equilibrated distribution in those modes. Intermolecular vibrational relaxation with coupling of vibrational modes of the excited molecule and the solvent occurs more slowly, but also, as suggested by recent investigations, in parallel. The understanding of the dynamics of solvation after the abrupt change in the structure caused by excitation is not yet completely satisfactory and probably advancement will result from the availability of new instruments [22].

7.6 Reactions via Upper States

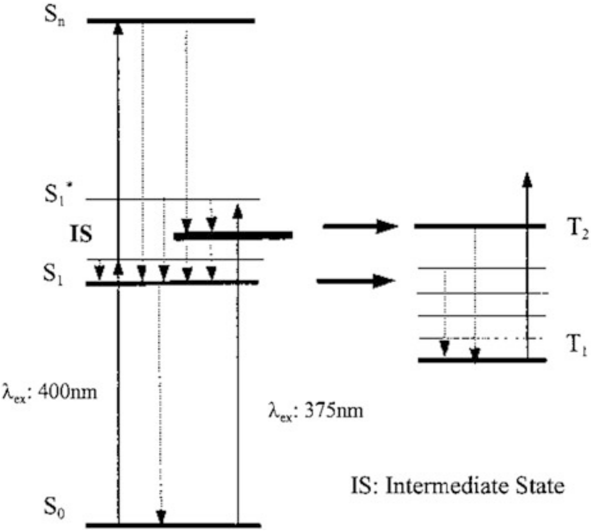
An increasing number of processes occurring at a faster than diffusion rate are being revealed, while advanced experimental methods become available. Advanced studies have afforded a much greater detail of the time evolution of electron transfer and proton transfer processes, but also some isomerization reactions occur at a rate in the ps range (see Scheme 7.11). The most studied case is the conversion of 11-cis retinal to al trans retinal that is the basis of vision and occurs on the subpicosecond timescale. Modern theory envisages this process as requiring not only a twist around the C=C double bond but also a distortion along at least another coordinate [23, 24].



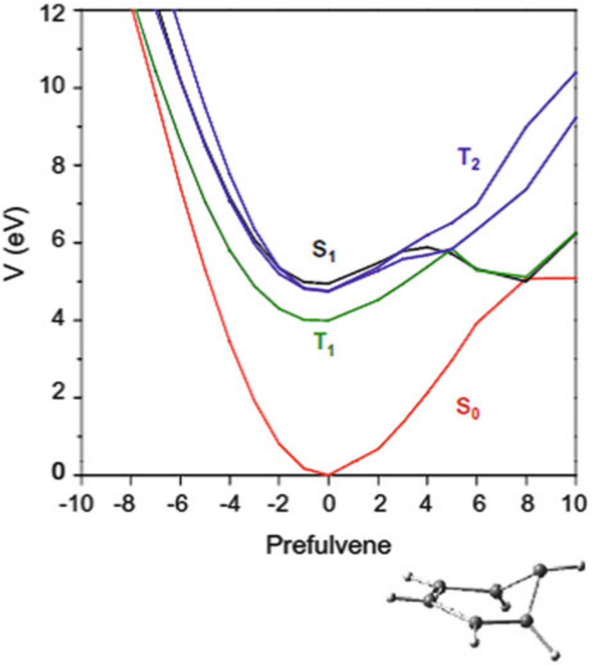
Scheme 7.11 Rate constants for fast photochemical processes

Intersystem crossing likewise may follow more complicated mechanisms. Generalizations such as that expressed by the El Sayed rules prohibiting S–T transition when both states were nπ* or ππ* have been reexamined, evidencing a new path for the $S_1(n\pi^*) \rightarrow T_1(n\pi^*)$ transition [25]. In nitroaromatics, intersystem crossing occurs within 100 fs following the path $S_1(\pi\pi^*) \rightarrow T_3(n\pi^*) \rightarrow T_1(\pi\pi^*)$, apparently due to large spin–orbit coupling involving a quasi-isoenergetic vibrational excited state in the triplet manifold. In 1-nitronaphthalene both the lowest excited singlet and T_1 have a ππ* character both in polar and in apolar solvents. This corresponds to the HOMO–LUMO transition, with π orbitals localized mainly on the ring carbons and on the nitro group, respectively. T_2 is again a ππ* state, but T_3 has a contribution both from a π type and from a n_O orbital and lies just below S_1, viz., 0.18 eV in cyclohexane, where it decays within 100 fs, and a mere 0.02 eV in acetonitrile and methanol, where the decay is still faster, making this aromatic the compound with the fastest multiplicity change as yet measured for an organic molecule [26]. In the case of terthiophene, it has been shown that there exists a non-spectroscopic intermediate state that allows ISC to T_1 within 2 ps, much faster than ISC from S_1. This has been proposed to involve a planarization of excited twisted conformers (Scheme 7.12) [27].

Scheme 7.12 Schematic energy diagram for terthiophene. Reprinted with permission from [27]



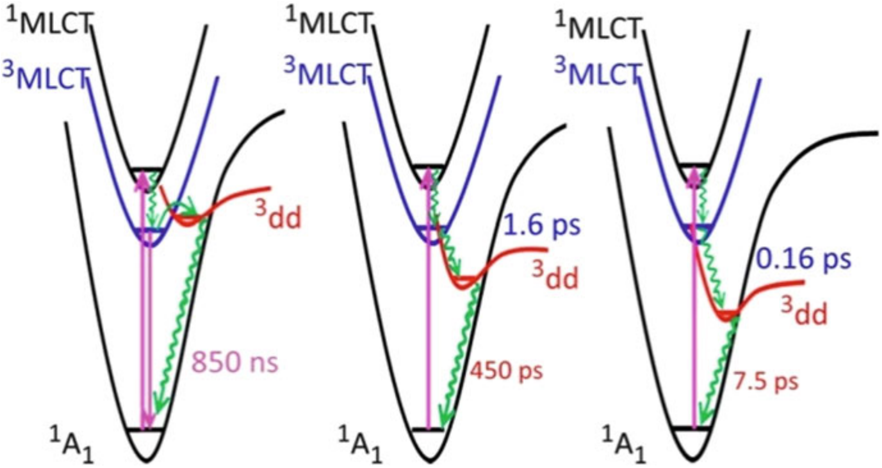
Considering the simplest aromatic molecule, benzene, a phenomenon known since 1966 is that the fluorescence quantum yield (channel 1) is 0.2 when the excitation energy is slightly above that of the lowest singlet state ($^1B_{2u}$), the competing path being in this case intersystem crossing (channel 2). However, when excess excitation energy reaches 3000 cm^{-1}, the yield of fluorescence drops abruptly due to the opening of a further path (channel 3) on the nature of which much effort has been devoted. It appears that this channel involves IC to the ground state via a "prefulvene" conical intersection that occurs at a strongly distorted geometry, where one of the carbon atoms is strongly displaced out of the molecular plane and gets close to the two neighboring carbons. At this geometry both ultrafast internal conversion and ultrafast intersystem crossing to a triplet state occur (Scheme 7.13) [28, 29].



Scheme 7.13 Cut through of the potential energy surfaces of benzene along the “prefulvene” mode—a vector from the Franck–Condon point to the S_1/S_0 conical intersection—calculated using the MOLPRO program at the CASPT2 level with a (6,6) CAS space and a Roos ANO basis set truncated to 6-31G-quality: S_1 (*black*), S_0 (*red*), T_1 (*green*), and T_2 (*blue*). Reprinted with permission from [28, 29]

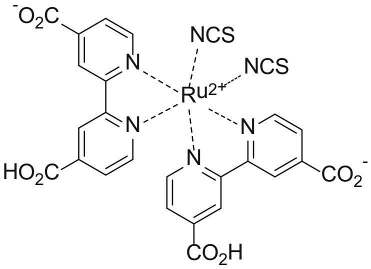
Prefulvene-like minimum energy conical intersections have been found also in other aromatic derivatives, e.g., in aniline, where, as in general happens with strongly donating substituents, the relaxation to the ground state is faster, τ 80 ps, and the fluorescence is much weaker. The amino group carrying carbon atom is distorted out of plane in the conical intersection connecting the ππ* S_1 to the ground state [30].

The situation is more complex in transition metal complexes, where transitions of different type are involved. The popularity of Ru(bipy)$_3$ as energy and electron transfer sensitizer is based on its inefficient photosubstitution that arises from the fact that the lowest state is a strongly emitting triplet of MLCT character (formed by very fast ISC from the corresponding singlet, lifetime 50 fs). However, introducing a methyl group on the bipyridine ligand (in position 6) lowers the energy of the ligand field state and internal conversion from the ^{3}MLCT is now possible (Scheme 7.14). Thus, emission is internally quenched. The introduction of a second methyl group further increases IC. ISC then from ^{3}dd to the singlet ground state depends on vibronic coupling [31].

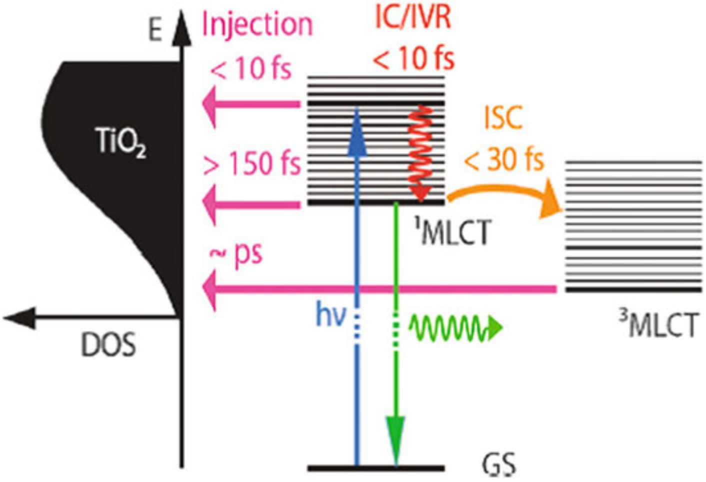


Scheme 7.14 Schematic representation of the potential energy surfaces of the ground and of the relevant excited states of ruthenium tris-bipyridine, as well as of the 6-methylpyridine and of the 4,4′,6,6′-tetramethylpyridine analogues. Radiative and non-radiative processes are indicated by smooth and wavy lines, respectively. Reprinted with permission from [17]

Particularly interesting, in view of the application to solar cells, is the competition between inter- and intramolecular processes. Thus, the dye RuN719 has been found to fluoresce with a very short lifetime in solution (<30 fs), non-changing when absorbed on substrates, whether electron injection occurred (titania) or it didn’t (alumina). It was thus concluded that intramolecular energy redistribution occurred within 10 fs (Scheme 7.15). Thus, injection likewise had to occur on the <10 fs timescale and involved non-thermalized states of the dye. Ultrafast processes are of great significance for dye-sensitized solar cells [32].



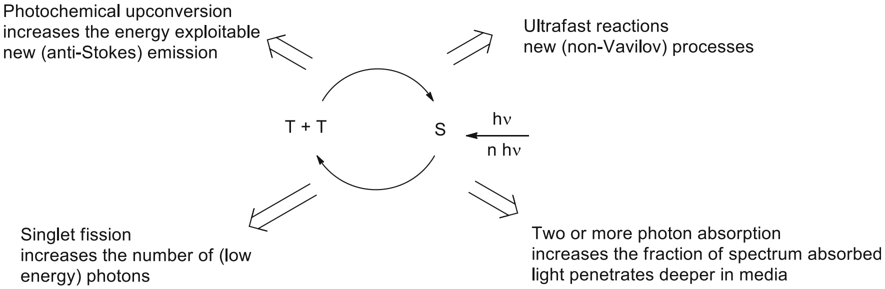
RuN719



Scheme 7.15 Schematic representation of the photophysical processes occurring in the dye RuN719 adsorbed on TiO_2. Note the dramatic dependence of the electron injection rate on the relative position of the dye excited state with respect to the density of states (DOS) of the conduction band of TiO_2. Reprinted with permission from [31]

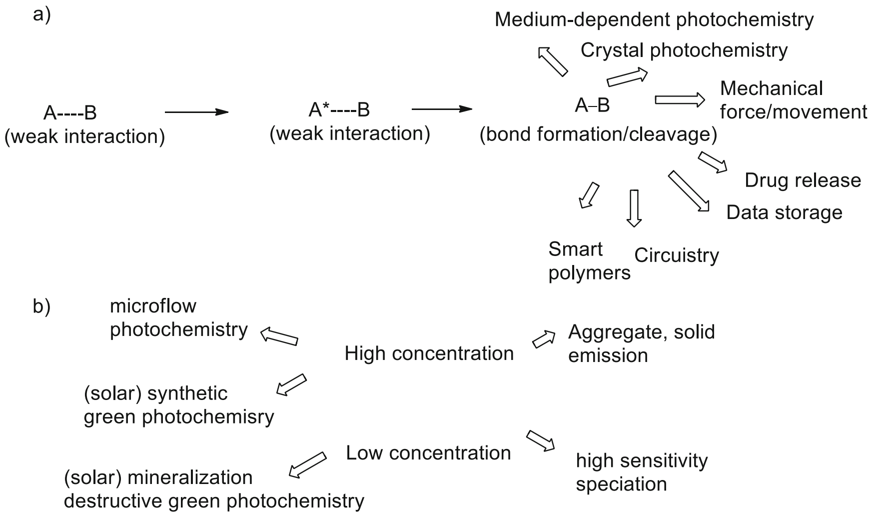
7.7 The Future of Photochemistry

It is probably a vain exercise to try to precisely sketch which will be the development of photochemistry, as well as any scientific discipline. Studying the history of this, and any other, part of science evidences how discontinuous this has been, and how the actual development depends from the contribution of every single scientist as well as on the developing of new techniques or instruments, and further on whether practical applications become available or social changes intervene, all factors that affect whether a scientific project will pursued in depth or on the contrary abandoned. In the case of photochemistry, an initial outburst around 1910 was followed by the definition of the paradigms of this science around 1950. At the beginning of the twenty-first century, the impression is that of a rapid centripetal motion [33]. As summarily sketched above, photochemistry is literally exploding out of the limits it was confined in, and profound developments affect the basic tenets of this discipline showing the potential for a wealth of applications. Certainly, nonlinear phenomena have shifted from a rare curiosity to a significant part of "everyday" photochemistry and have permeated the core of this science, the excited state (Jablonski) diagram and the rate constants of the processes they originate, as shown in Scheme 7.16, increasing the possibility of tuning the light–matter interaction towards different targets.



Scheme 7.16 Generation and behavior of excited states may involve more paths than initially thought and introduces new possibilities of tuning the reactions occurring

From the more technical point of view, some directions that appear to be important for the development of photochemistry in the near future are schematized in Scheme 7.17. A key property of photochemistry involves exploiting the high energy of the photon for making covalent bonds of molecules conserving the conformation they adopt spontaneously or by effect of the environment, exploiting weak interactions for generating high selectivities (medium-dependent photochemistry, crystal photochemistry). Photochemistry causes in-depth changes of molecular structure. The geometric change caused at the molecular level may be relatively modest, but it can originate a much larger effect. Micro/macroscopic switches, electronic components at molecular level, data storage, and smart polymers are typical applications, see Scheme 7.17a. On the other hand, photochemistry is expected to develop rapidly on the two extremes of concentration regime. At the low extreme, new effective signal emitters are developed for the speciation of ions or the specific identification and measurement of molecules, while destructive photocatalysis proves effective for the mineralization of persistent pollutants. At the high concentration extreme enhancement of emission in aggregates or in the solid state is developing, while preparative photochemistry finds a way more palatable for industrial chemistry through a thorough consideration of the practical aspects in batch and in microflow processes (Scheme 7.17b).



Scheme 7.17 Effect of the environment (**a**) and of concentration on photophysical/photochemical properties of molecules (**b**)

Some aspects of photochemistry that may lead to important advancements are briefly sketched in the following chapters, each of which centers on a specific application, although single molecules often find use in several fields.

Photochemical synthesis (Chap. 8)
Drug/medicinal photochemistry (Chap. 9)
Solar energy conversion (Chap. 10)
Photoactivated actuators (Chap. 11)
Green photochemistry (Chap. 12)

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Chapter 8
Photochemical and Photocatalyzed Synthesis

8.1 Application in Synthesis: Synthetic Sequences

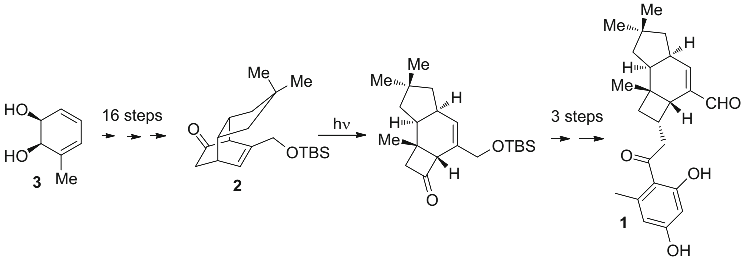
Many characteristics of photochemistry seem ideal for synthesis, in particular the large value of the energy involved, of the same order of bond dissociation energies and the mild conditions exhibited despite the relative tolerance to varying conditions, such as pressure, temperature, viscosity, and proticity of the solvent. These characteristics offer flexibility to fine-tuning of a reaction by manipulating conditions (that are benign, since no waste is generated and often the amount of energy used can be minimized, a fact that is becoming more and more important). Excited state reactions are really different from the thermal ones, and further one may (in principle) exploit a further variation by choosing the multiplicity of the path followed. These facts much widen the available palette of methods synthesis practitioners can use.

Despite these positive characteristics, the role of photochemistry in synthesis is not growing at the rate it may, but the knowledge about the potential of this discipline is getting diffused, at least for some classes of reactions. Formation of four-membered rings by either cycloaddition or cyclization as well as the ene and cycloaddition reactions with singlet oxygen are examples of transformations where the photochemical option comes, or should come, first. But many other reactions, not necessarily those that are most studied by photochemistry "professionals," are welcome for synthesis. At any rate, one may consider that a large choice of photochemical reactions is now available to synthesis practitioners, and it is not rare that these are included as a step of a complex synthetic sequence with the same reliability as better known thermal alternatives. Thus, the key points are, first, that new reactions are to be introduced in particular in the case of photochemistry, because excited states have been less extensively explored than ground states, as confirmed by the continuous flow of fully new processes appearing in the recent literature and, second, that nowadays, a large choice of new photochemical reactions is available, which are well known and can be chosen with confidence during the retrosynthetic project.

A. Albini, *Photochemistry*, DOI 10.1007/978-3-662-47977-3_8

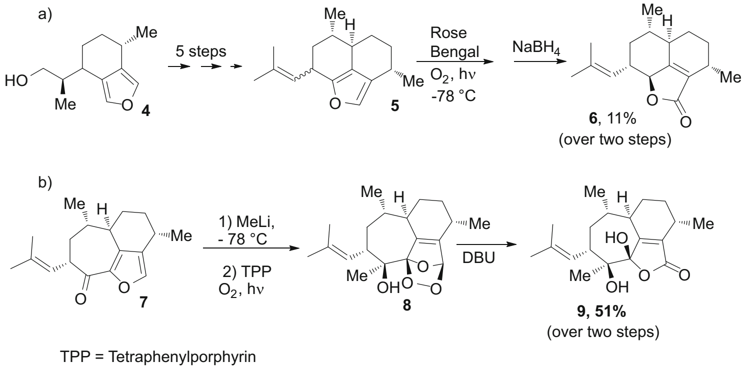
8.1.1 Photochemical Steps in Synthetic Planning

A few examples of photochemical key steps in complex synthetic sequences are reported below. Protoilludane aryl ester (+)-armillarivin (**1**) has been prepared through a 21-step sequence, one of the key features of which was building a four-membered ring through a photochemical 1,3-acyl shift on precursor **2**, itself elaborated from a Diels–Alder adduct onto diol **3**, in turn obtained from the whole-cell biotransformation of toluene (Scheme 8.1). This nice combination of enzyme-catalyzed reaction and photochemical reaction appears to fulfill the wish Paternò had expressed more than 100 years ago as the key issue for developing the future synthetic chemistry [1].



Scheme 8.1 Photochemical step in the synthesis of (+)-armillarivin

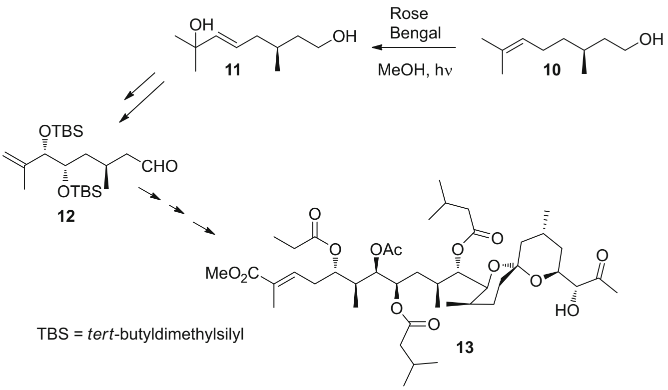
Oxygenation reactions have often been found useful in synthetic planning. As an example, the furan derivative **4** was prepared in gram quantities and used for the preparation of marine metabolites such as amphilectolide **6**. Elaboration of **4** gave **6** in five steps, but attempted conversion of the furan **5** into the butenolide **6** via photooxygenation (RB sensitizer, −78 °C, immediate reduction by sodium borohydride) gave a complex mixture, from which **6** was isolated in the modest 11 % yield (Scheme 8.2a).



Scheme 8.2 Application of singlet oxygen in synthesis

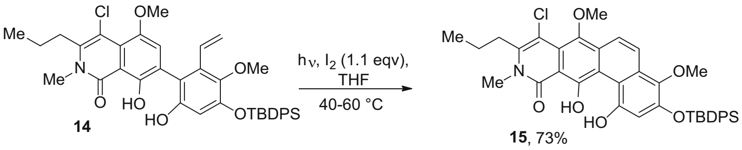
However, the synthesis of structurally related sandresolide B (**9**) from furan **7** was much more successful. Thus, after methylation of the carbonyl function, photosensitized oxygenation, in this case with tetraphenylporphyrin (TPP) as sensitizer and treatment with DBU of the *endo*peroxide **8** that caused a Kornblum–DeLaMare rearrangement (cleavage of an endoperoxide to give a ketone and an alcohol), gave the desired **9** in 51 % over the two steps (Scheme 8.2b) [2].

The reliability of the ene reaction with singlet oxygen is attested by the fact that this has been chosen as the first step for the conversion of *S*-citronellol **10** into one of the four fragments (**12**) from which the complex structure **13**, which has been proposed for the synthesis of the HIV-active didemnaketal A, has been assembled (Scheme 8.3) [3].



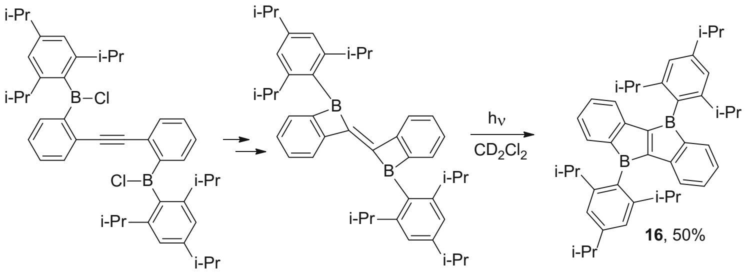
Scheme 8.3 Application of singlet oxygen in synthesis

The photoelectrocyclization of stilbene derivatives under oxidative conditions (air or iodine generally used as oxidants) has been largely exploited for the synthesis of various natural product systems. As an example, the benzophenanthridine ring of kibdelone **15** was best prepared from the stilbene derivative **14** by irradiation in the presence of 1.1 equivalent iodine and excess THF as a trap for the cogenerated HI that would otherwise cause extensive degradation of the products (Scheme 8.4) [4].



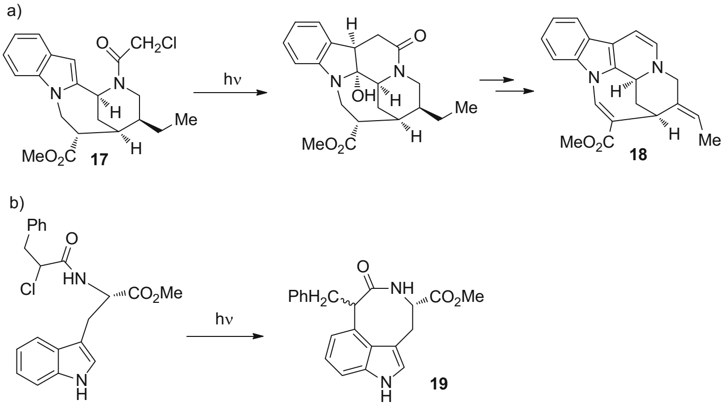
Scheme 8.4 Application of an electrocyclization in synthesis

Electrocyclic reactions are a powerful synthetic method, largely applied to heteroatom containing compounds, as an example for the synthesis of ladder borane **16** (Scheme 8.5). These conjugated materials have very interesting properties, such as efficient luminescence and high carrier mobility [5].



Scheme 8.5 Synthesis of ladder borane by electrocyclization

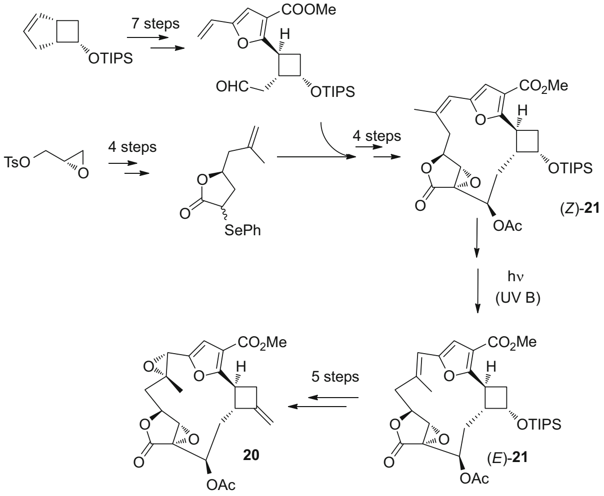
Chloroacetamides of aminoalkyl derivatives of electron-rich aromatics **17**, such as phenols, anisoles, or electron-rich heterocycles, easily dechlorinate and offer a useful entry to new medium-sized heterocycles (e.g., apogeissoschizine **18**), according to Scheme 8.6a [6]. This is another example of the photochemical access to complex structures, that has been conveniently extended to macrocycle **19** (Scheme 8.6b), as well as to the reaction of *N*-alkylphthalimides [6].



Scheme 8.6 Synthetic applications of photoinduced charge transfer chloroacetamide fragmentation

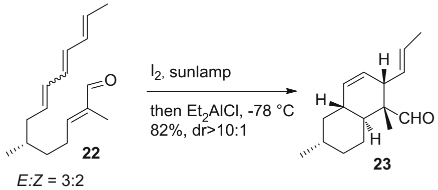
One of the most typical photochemical reactions, C=C double bond isomerization, may have a synthetic value. Thus, the highly oxygenated cembrane 17-deoxyprovidencin **20** has been built by joining two separately prepared building blocks and further elaboration of the macrocycle **21** via a *Z*-selective ring closing metathesis. The *Z* C=C bond isomerizes by irradiation with Pyrex-filtered light that causes a clean conversion (notice that UV B is not absorbed by the highly strained and conformationally restricted *E* isomer, while shorter wavelengths are absorbed and only an inseparable mixture is formed when using quartz filter due to consecutive reactions). A few further steps lead to the desired natural compound (Scheme 8.7) [7].

Scheme 8.7
E/Z isomerization in a macrocycle



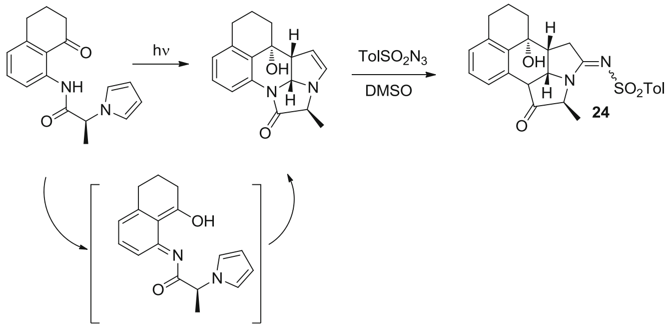
Reaching the desired configuration is possible also under radical conditions by visible-light irradiation in the presence of iodine, as shown in one of the first steps of the synthesis of fusarisetin A (**23**), where the *E*/*Z* mixture of **22** obtained by a Wittig reaction was brought to the desired isomer (Scheme 8.8) [8].

Scheme 8.8
E/Z Isomerization



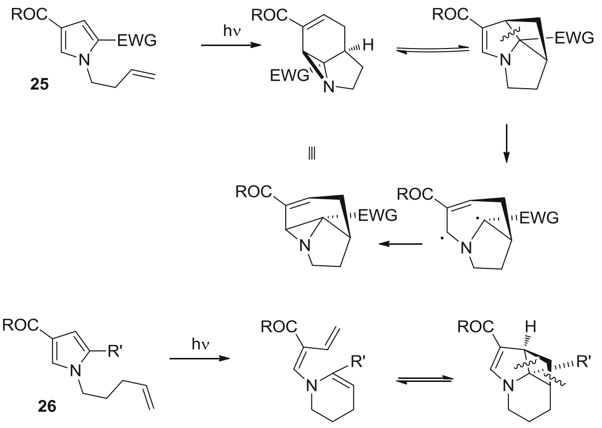
8.1.2 *Old and New Strategies in Synthesis*

The point has been made that successful drug candidates contain a large number of sp^3 carbons with respect to sp^2 carbons, a characteristics that is not easily introduced in practice, especially when stereochemistry is considered. However, Kutateladze pointed out that in this sense photochemistry is situated in a favorite position, since catalytic sp^2–sp^2 carbon coupling and electrophilic substitution are well-developed methods that allow building of polysubstituted aromatic molecules, which in turn easily form complexes in a predetermined arrangement (Scheme 8.9). Aromatics absorb light and give rise to new systems characterized by a higher number of saturations and a strict control of stereochemistry. An example is the intramolecular 4+2 cycloaddition via the photogenerated xylylene to form fused heterocycle **24** [9].



Scheme 8.9 4+2 cycloaddition

This principle has been largely employed by Wender [10] with carbocycles. Examples in heterocycle chemistry are the [4+2] intramolecular cycloaddition of photochemically generated bis-methylenecyclohexadienes onto pyrroles or, with the same heterocyclic ring, the [2+2] cycloaddition in alkenylpyrroles **25** and **26**. The following course of the reaction depends on the chain length. A metathesis reaction takes place when starting from pentenylpyrroles through homolytic fragmentation (the cleavage occurring is marked) to give a more stabilized radical (Scheme 8.10). Mixtures are formed, but the preferred path is largely determined by the chosen wavelength. Once again a heteroaromatic system is transformed photochemically (compare Chap. 2) into a rigid, much more saturated structure with full control of steric arrangement [11].

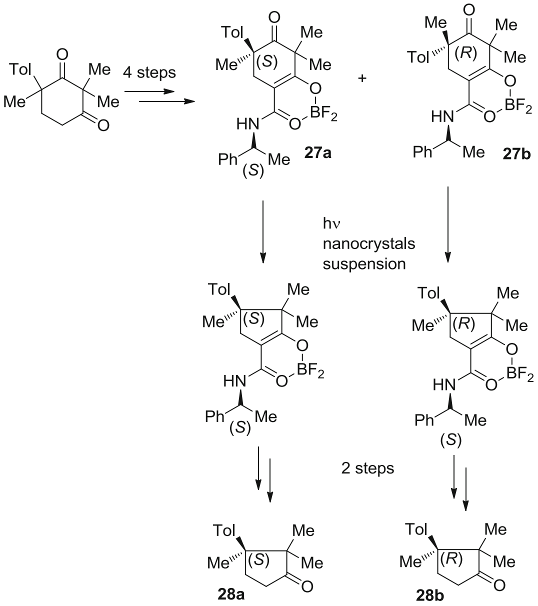


Scheme 8.10 Photochemistry of some pyrroles

8.1.3 Synthesis via Chiral Auxiliary

As in thermal chemistry, the formation and separation of diastereoisomers via chiral auxiliaries are excellent paths toward enantiomeric synthesis. The decarbonylation of 2,2,6,6-tetralkylcyclohexanones offers an expeditious access to cyclopentanes possessing two adjacent stereogenic centers, and irradiation in crystals leads often to better yields than in solution. A related decarbonylation of 1,3-cyclohexandione isomers **27a** and **27b** (Scheme 8.11) has been used for the synthesis of (*R*)-cuparenones and (*S*)-cuparenones (**28a** and **28b**, respectively). The racemic ketones were obtained by solid-state irradiation. These were separated by C-alkylation of the diketone with cyanoformate, and treatment with $BF_3 \cdot OEt_2$ and then with (*S*)-methylbenzylamine gave the mixture of the diastereoisomeric dioxaborinanes that were separated by chromatography. The desired compound was obtained by elimination of the boron substituent. However, the pure (*S*) enantiomer did not crystallize under various conditions. Despite this limitation, both isomers of cuparenone were obtained by irradiation of a suspension of nanocrystals obtained by adding an acetone solution of each of the dioxaborinanes to water containing cetyltrimethylammonium bromide. The reaction was successful and caused 100 % stereoselective ring restriction with 80 % yield of each isomer [12].

Scheme 8.11 Stereoselective ring restriction



8.2 Asymmetric (Photochemical) Synthesis

Within synthesis, one of the key issues of modern synthetic methods is asymmetric synthesis. Asymmetric photochemistry, or more precisely photochirogenesis, a term proposed by Inoue for stressing the fact that chirality is generated in the photochemical step, has an enormous role to play in various aspects, although intensive research in the last decades has evidenced more the limitations than the opportunities inherent in the method. However, recent work seems to suggest that the heavy delay with respect to thermal chemistry in this field may be reduced.

8.2.1 Absolute Asymmetric Synthesis

Absolute asymmetric synthesis that is preparing a chiral compound in the absence of any chiral compound is possible by introducing the chiral message in light itself. Circularly polarized light (CPL) is easily produced and is a true chiral entity, so that its use may lead to chiral from achiral compounds in different ways, that is, by preferential photochemical destruction of one of the enantiomers in a racemate, by enriching photochemically interconverted enantiomers in one of the isomers, and by the enantioselective photochemical formation of an optically active compound from a prochiral precursor. The enantiomeric excess (ee) obtained depends on the different absorptivities of the isomers at the irradiation wavelength. Since this is quite low, the degree of inducible optical activity is also quite low. A long studied example involves the oxidative cyclization of stilbenes to form helicenes, but the ee obtained has rarely exceeded 0.5 % [13]. This is a tool reserved to photochemistry and typically applied to inherently chiral compounds such as helicenes through a stilbene-phenanthrene cyclization.

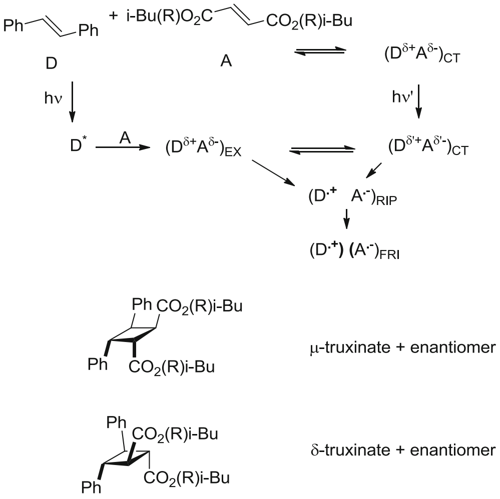
Another possible absolute synthesis is the irradiation in the solid state of an achiral compound that crystallizes in a chiral space group. This method has been demonstrated to be viable in a few cases and is an example of selectivity in solid-state photoreactions, due to the fact that bonds are broken and built in a strictly limited spatial environment. Unfortunately, however, very few compounds present these characteristics [14].

The study of CPL is progressing and the optimal conditions and the range of application are being clarified. As an example, amorphous films of racemic alanine have been irradiated by CPL, and it has been found that the photochemical decomposition occurring can be predicted on the basis of the helicity of the sample and depends on the wavelength used. Enantiomeric excess up to 4.2 % has been obtained. This is highly important for understanding the long debated role of CPL in the origin of homochirality on Earth, but remains too low to make one think that the method will attain a preparative significance (see, for instance, [15–18]).

8.2.2 Chirality Transfer

Any other approach is based, as in thermal chemistry, on the complexation with a chiral catalyst. Any interaction may be useful. Typically, aromatic molecules form both ground state complexes (that have a ground state spectrum of their own) and complexes formed by the excited state (Scheme 8.12). In principle, these are different species with a different structure and may give a different product distribution. By irradiating stilbene in the presence of a fumarate, mixed dimers were formed. When using a *chiral* fumarate, such as (*R*) i-butyl fumarate, pairs of enantiomeric cyclobutanes were formed. Both the μ/δ-truxinate ratio and the diastereomeric excess obtained were recognizably different when the system was irradiated in the CT band ($h\nu' = 365$ nm) rather than in the separated chromophore ($h\nu = 313$ nm). Temperature and pressure changes had a variable effect. Thus, weak interactions may have a role, and different situations (the excimer vs the excited donor–acceptor complex) gave (slightly) different results [19].

Scheme 8.12 Reactions of chiral fumarates with stilbene

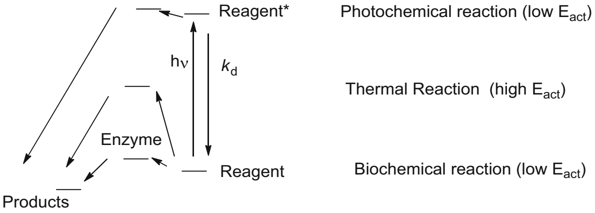


Calculations evidenced that the degree of charge transfer was fairly small, merely amounting to 2.0 and 2.5 % for the si, re-complex and re, si-complex, respectively.

Such cases are mechanistically interesting, but less so preparatively, since it is unlikely that a sufficiently strong interaction develops for obtaining a large ee in such complexes. Perhaps paradoxically, in the fast development of recent years asymmetric photochemistry profits of the enormous advancement of catalysis by metal complexes and organocatalysis. To this, photochemistry adds the knowledge of (and the trust in) photoinduced electron transfer that has been developed in the meantime. In such "supramolecular photochirogenesis," chirality is present in a ground state complex. Different from the case of weak complexes above, in the interactions in the ground state, the key factors are the relatively strong, long-lasting, noncovalent (or covalent, but in fast equilibrium under the conditions used) interactions between the host and the guest. The supramolecular confinement upon complexation and subsequent photoreaction is expected to synergistically increase the efficiency and selectivity of chirality transfer after excitation state. Crucially, the interaction between chiral catalyst and guest has to be maintained after excitation, so that diastereoisomeric transition states are reached, and through them, enantiomeric products are obtained [20–22].

The problem obviously is to avoid background nonselective reaction. As mentioned, the very nature of excited states, characterized by high energy and short lifetime, becomes a stumbling block here, because stereoselectivity requires a strict contact between the two species, in order that the achiral molecule takes the appropriate shape. In this sense, photochemistry is the exact contrary of biochemistry. In both fields, reactions can be highly selective as far as the product formed, because in both cases, only low-energy paths are accessible (from the excited and respectively the ground state; see Scheme 8.13), but *stereo*selection requires more time (there is no hope of building a long-lived complex in the excited state, comparable to those that enzymes build in the ground state) and thus the key intermediate has to be there *before* irradiation.

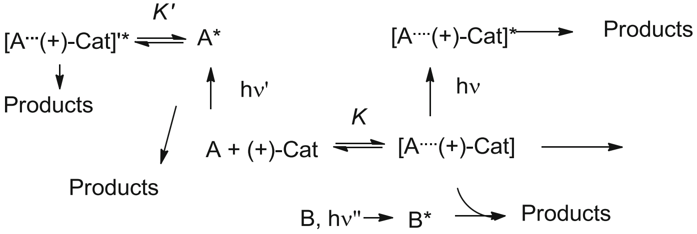
Scheme 8.13 Ground and excited states complexes



8.3 Catalysis

8.3.1 Organocatalysis

The ways in which a chiral entity (+)-Cat, used in a substoichiometric quantity, may induce an enantioselective reaction of achiral A involve the excitation of a ground state complex or its reaction with an excited state, as summarized in Scheme 8.14.



Scheme 8.14 Enantioselective reactions via complexes

As hinted above, it is generally difficult that the tridimensional arrangement required for making a reaction path preferred develops in the short time available before the excited state A* decays, and it is more likely either that a ground state complex is excited and reacts or that a different excited state B* independently reacts with the complex.

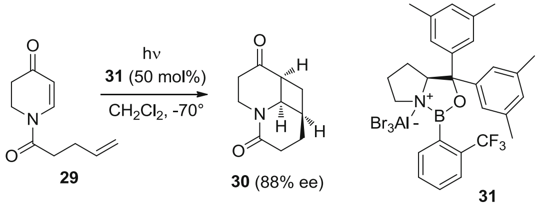
The role of electron donor–acceptor (EDA) complexes is well known from thermal chemistry, and their structure is easily tailored to photochemical approach to a specific target. Apart from the usual choice of a low temperature and the appropriate solvent, further important approaches for increasing the selectivity are available. Not all of the mechanisms invoked for such processes, sometimes quite involved and not rarely using more than one photocatalyst or cocatalyst for one-pot processes, have received a strong support as yet, but probably this is not that important. As soon as the topic grows, it will become stronger [23].

8.3.2 Catalysis: Only the Complexed Reagent Is Activated

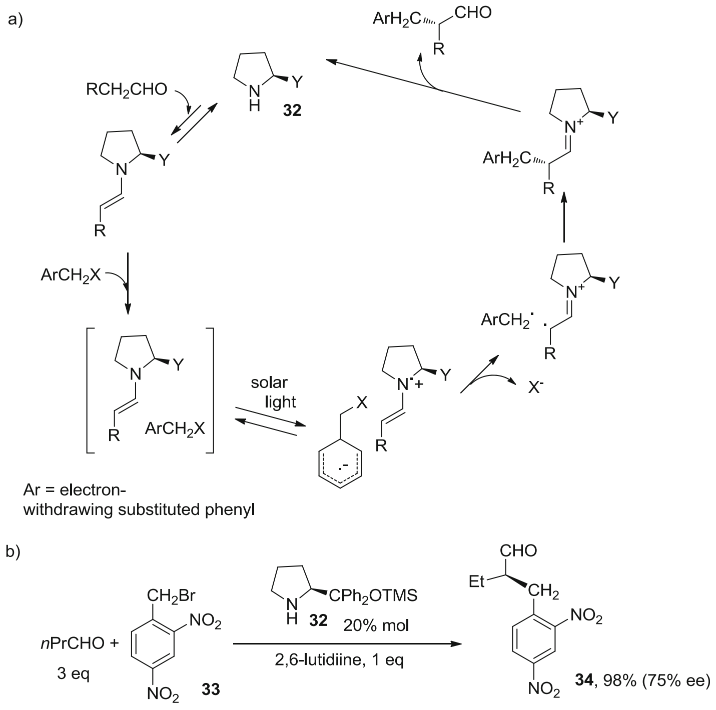
The main mechanisms are illustrated with reference to Scheme 8.14. By having *hν* as different as possible from (and longer than) *hν′*, it is possible to irradiate selectively only the complexed form.

Thus, the tetrahydropyridine **29** forms a complex with Lewis acids, characterized by an unusually large Stokes shift (over 50 nm). This involves the strong band attributed to the ππ* transition (from 291 to 343 nm with boron trichloride), not of the weak band (probably an nπ* transition, at ca. 360 nm). Thus, selective excitation is possible by irradiation at 366 in the presence of a chiral Lewis acid (**31**) at −70 °C, giving the desired cycloadduct **30** with a remarkable ee (see Scheme 8.15) [24].

Scheme 8.15 Selective excitration of a ground state complex



Likewise, Melchiorre reported that chiral amines **32**, so often used in thermal organocatalysis, find use also in photochemistry and form *colored* EDA complexes with electron-withdrawing substituted benzyl halides (**33**), and irradiation leads to electron transfer and benzylation of aldehydes (an example in Scheme 8.16 for the synthesis of **34**) [25, 26].



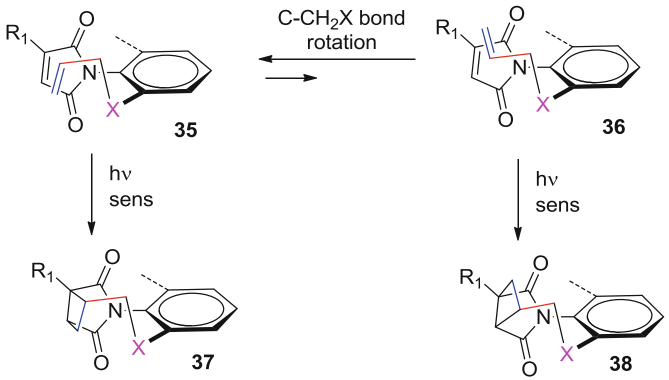
Scheme 8.16 Benzylation of aldehydes

Organocatalysis offers highly reactive intermediates. As an example, α-amination of aldehydes has been obtained via addition to the enamine of an aminoalkyl radical, produced by the photoinduced electron transfer that in turn completes the synthesis [27].

8.3.3 Catalysis: Atropisomerism

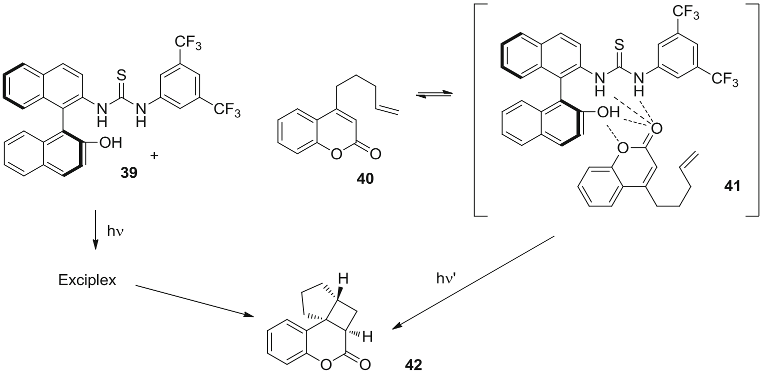
A particular case in this category is that of atropisomeric compounds (those where chirality originates from a barrier to rotation over a single bond). In a thermal reaction, racemization occurs unless the temperature is sufficiently low. The peculiar temperature independence of photochemical reactions allows to transform axis chirality into point chirality with no loss.

The two atropisomers **35** and **36** are different conformations with different physicochemical characteristics and can be specifically irradiated/sensitized for selective reactions (see, for instance, [28–32]) to form differently substituted cyclobutanes **37** and **38** (Scheme 8.17).



Scheme 8.17 Atropisomeric compounds

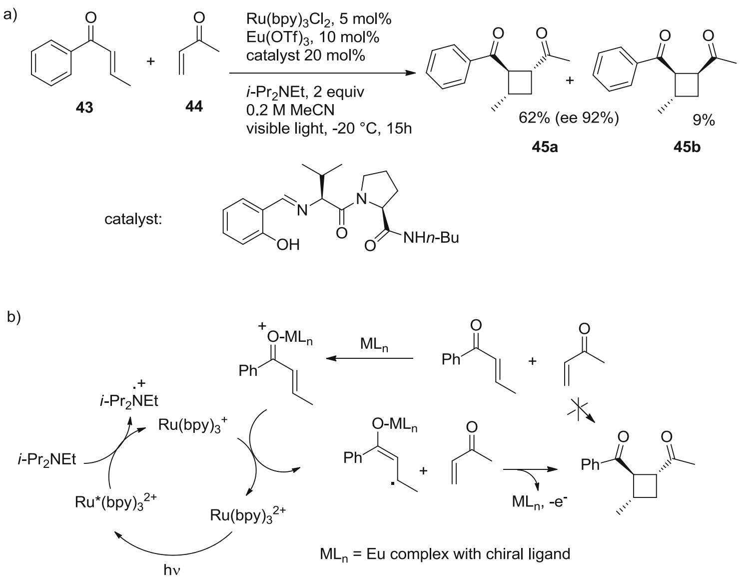
Alternatively, selective sensitization can be obtained. Very promising results have been obtained in the selective 2+2 photocycloaddition of alkenylcumarine **40** occurring in the presence of the thiourea **39** [33] to give cycloadduct **42** via formation of complex **41** (Scheme 8.18).



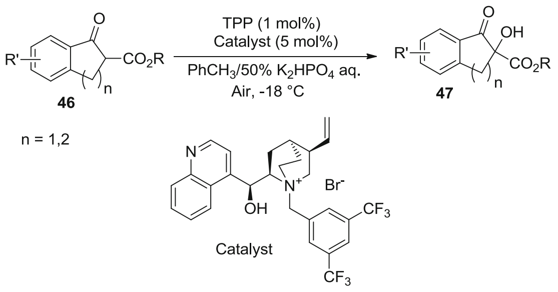
Scheme 8.18 Selective 2+2 photocycloaddition

8.3.4 Catalysis: Only *the Complexed Form Is Reactive*

As an example, Yoon [34] has studied the inter- and intramolecular 2+2 cycloaddition of unsaturated ketones (an example in Scheme 8.19). A chiral version of the reaction cannot be obtained by simply adding a chiral catalyst, because electronic excitation promotes the addition of the aromatic ketone also when not complexed, as indeed it is often the case with this kind of reactions. However, he was successful when he used two catalysts, viz., a visible-absorbing transition metal photocatalyst and a stereocontrolling Lewis acid cocatalyst. Under these conditions, the excited molecule could react only with a molecule complexed with a chiral ligand (Scheme 8.20).



Scheme 8.19 Photocatalyzed 2+2 cycloaddition (**a**) Synthesis and (**b**) mechanism for the photocatalyzed synthesis of cyclobutane **45a**

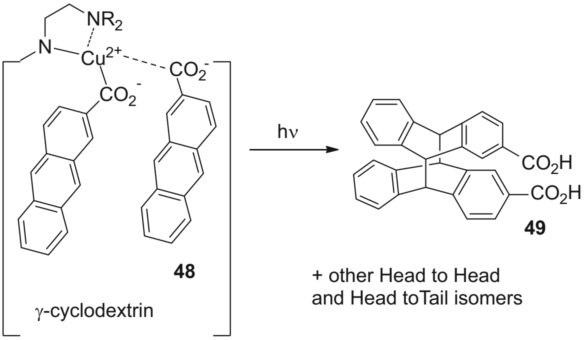


Scheme 8.20 Phase transfer catalysis in an oxygenation reaction

In the case above, the photocatalyst operates via a redox step. Alternatively it could chemically react, as is the case for the hydroxylation of β-keto esters **46** that occurs with a significant enantioselectivity and has been obtained in the presence of a quinine-derived phase-transfer catalyst at −13 °C via singlet oxygen (TPP as the sensitizer). This is an example of B* in Scheme 8.14, for the synthesis of **47** [34].

8.3.5 By Using a Strong Chiral Complex in a Way to Limit Reversibility, Even When Hindered

Large molecule, such as cyclodextrins, may be useful, as it has been demonstrated in the case below with the use of γ-cyclodextrin bearing amino groups in the presence of copper ions (see in Scheme 8.19, for the selective cycloaddition of anthranoic acid **48**) or in the complex with human serum albumin [35] (Scheme 8.21).



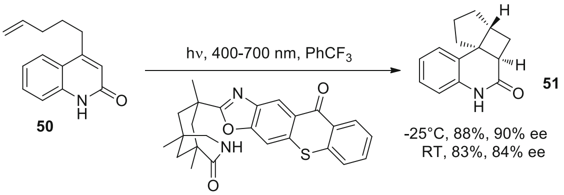
Scheme 8.21 Selective cycloaddition of anthranoic acid salts

Likewise, the reaction occurs with a large enantiomeric excess when the acid is bound to a chiral site in human serum albumin. Studies by fluorescence anisotropy revealed that under these conditions, rotational mobility is restricted, so that one of the prochiral faces is protected by the protein. These studies may be the starting point for the rational design of supramolecular photochirogenic systems [36, 37].

Another promising approach is fixing the reagent in a sterically controlled way. An example is the use of a chiral metal-organic framework (MOF), which has been obtained through the cooperative combination of triphenylamine photocatalysis (as a donor) and proline-based asymmetric organocatalysis within a single MOF. In this way, the α-alkylation of aldehydes has been achieved with a good ee [38].

8.3.6 *Polyfunctional Catalysis*

In another approach, the catalyst performs different functions. As an example, different functions are combined in the catalyst, thus having a chiral catalyst covalently bound to a light-absorbing sensitizer [39, 40]. Derivatives of Kemp acids have proven to be excellent complexing agents, and when a sensitizer moiety is incorporated, the cycloaddition occurs with excellent stereoselectivity at −25 °C, which does not diminish much by shifting to room temperature. These characteristics make the reaction suitable for the application of solar light (Scheme 8.22).

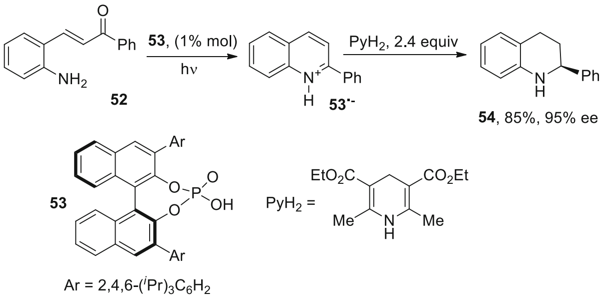


Scheme 8.22 A Kemp acid derivative functions both as photosensitizer (through the thioxanthone moiety) and as complexing agent

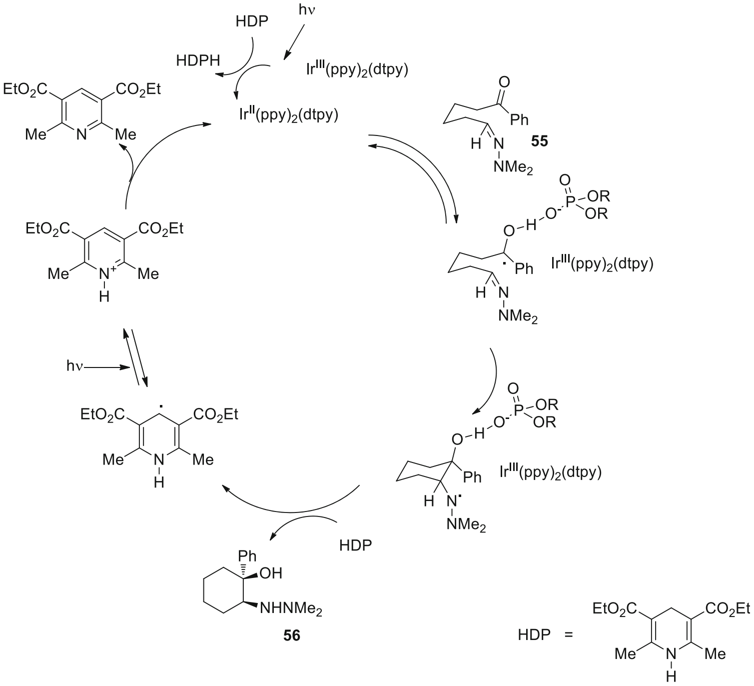
8.3.7 By Resorting to an Intrinsically Fast Reaction, Such as Proton Transfer

Cyclization of a chalcone **52** to tetrahydroquinoline **54** in the presence of a BINOL donor (**53**) leads to an ion pair that is reduced by excess Hantzsch ester. The reaction is highly effective under flow conditions (Scheme 8.23) [41].

Scheme 8.23 Stereoselective photochemical synthesis of 2-substituted tetrahydroquinoline



Another choice is intramolecular biradical closure, as illustrated in Scheme 8.24. Here reduction of the starting ketone **55** by photogenerated Ir^{2+} complex is

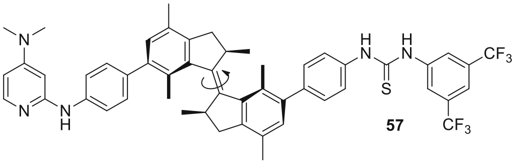


Scheme 8.24 Photoinduced electron transfer from ketone 56 to the iridium complex occurs concertedly with protonation by the chiral phosphate. In the process, the ketyl radical becomes significantly more basic than phosphoric acid, and rapid radical cyclization from the neutral ketyl as an H-bonded adduct to the chiral phosphate occurs. Asymmetric induction results, due to the rapid radical cyclization. Hantsch dihydropyridine esters provide the required proton and hydrogen atoms

endoergonic unless it is accompanied by protonation and subsequent ring closure. Hydrogen atom extraction from a Hantzsch ester then leads to an azapinacole **56** with regeneration of the other components [42].

The integration of moieties that cooperate as organocatalysts, such as dimethylaminopyridine Bronsted base and thiourea hydrogen-bonding donor, gives a molecule that promotes Michael addition in a way that depends on the configuration (**57** in Scheme 8.25). Under irradiation a 360° unidirectional rotary cycle occurs resulting in a different catalytic action. During one 360° photochemically induced rotation, the action changes leading either to racemic (*R*,*S*) or preferentially to *R* or *S* enantiomer of the chiral adducts. Thus, light acts as an external signal that controls the chiral space in which a catalytic reaction takes place [43].

Scheme 8.25 Photochemically induced rotation around the double bond controls the chiral space

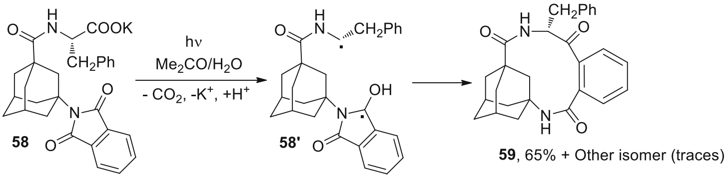


57

8.3.8 *Catalysis: Chiral Memory*

Related to the reactions discussed above are reactions exhibiting chiral memory, that is, start from a chiral molecule and give a chiral product via a reactive intermediate, which does not bear the same stereogenic center as the reactants and products.

As an example, the phthalimido derivative **58** undergoes decarboxylation upon acetone sensitization, but diradical **58′** has axial symmetry and is bulky and hindered due to the rigid adamantane moiety. As a result, coupling occurs conserving the stereochemistry, and thus ring enlargement brings to optically active ketone **59**, with only traces of the other stereoisomer (Scheme 8.26) [44].

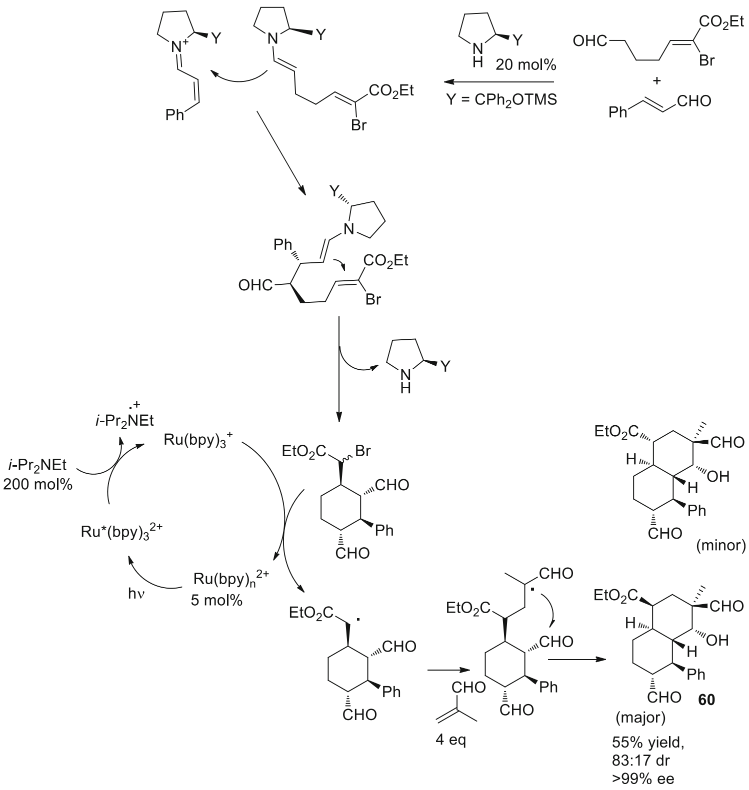


Scheme 8.26 An example of chyral memory in synthesis

In a similar way, large ee have been reported for photoreactions of chiral molecules, but here photochemistry is not different from thermal chemistry [45].

8.3.9 One-Pot Catalytic Procedure

In an interesting example, two unsaturated aldehydes form each the corresponding enamine in the presence of a proline-derived catalyst. A first iminium–enamine Michael addition is followed by a second addition onto the unsaturated ester function present in one of the initial reagents. Photoinduced electron transfer and debromination give a radical that adds onto methacrylic aldehyde and cyclize to a highly functionalized decaline **60** (see Scheme 8.27) [46].



Scheme 8.27 One pot photochemical synthesis of a highly functionalized decaline

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Chapter 9
Medicinal and Diagnostic Applications

Many advancements of photochemistry, and of chemistry in general, have been obtained for answering the demand of more efficient means of diagnosis and healing by medicine and pharmacology. A quick overview of the expected advancements in photochemistry and photophysics of molecules and materials can be presented by adopting this perspective, although in some of the systems presented, different targets are more important.

9.1 Where and When

9.1.1 Photochemical Drug Release

Light can be delivered where and when desired. Thus, photochemical reaction can be used for the local delivery of a drug and/or its activation where and when it is needed and in the correct amount. A straightforward example is that of CO, well known for its toxic properties but that in trace amount has a healing effect on wounds and protective effect against ischemia. CO generation from metal carbonyls has been shown to have a pharmacological significance [1]. The basic idea is generating a pharmaceutical active molecule in situ or having some photoactivatable drug carrier that is cleaved and releases its load of active molecules where desired. The mode of irradiation adopted obviously depends on whether an organ, a cell, or a subcellular feature is the target. Exposure to solar light has a long tradition for causing a general benefit (as well as inducing very dangerous skin tumors when a sensible limit of exposure is overcome). In Chap. 4, it is mentioned that irradiation was early found effective against some form of skin cancer. The tumors were painted with a solution of a dye and the patient had to remain exposed to solar light.

A. Albini, *Photochemistry*, DOI 10.1007/978-3-662-47977-3_9

This was the basis of photodynamic therapy, involving the activation of molecular oxygen by a sensitizer to form singlet oxygen or other active species. The method has largely progressed, and a number of dyes have been approved for the clinical use (Photofrin, actually a mixture of different dyes, was the first one in 1990); others followed, and all of them are either porphyrins, or their biological precursors, such as benzoporphyrin derivative monoacid ring A (BPD-MA), *meta*-tetra(hydroxyphenyl)chlorin (*m*-THPC), *N*-aspartyl chlorin e6 (NPe6), or precursors of endogenous protoporphyrin IX (PpIX), viz., 1,5-aminolevulinic acid (ALA), methyl aminolevulinate (MAL), and hexaminolevulinate (HAL) (for some reviews on PDT photosensitizers, see [2–5]). The point of application is no more restricted to the skin, although this remains an important field, due to the simplicity and inexpensiveness of the treatment, but also internal tumors can be treated. In this case, the important difference is that the dye is preferably localized in the tumor cells, so that the selectivity due to localization of irradiation adds to that due to the choice of light wavelength. Irradiation is carried out through an optical fiber for small areas and through various instruments able to diffuse light homogeneously for large surfaces, e.g., bladder [6–8]. The ultimate application of the local control has been achieved by building a photochemical lancet, where a photochemical reaction set free the sensitizing dye under a flux of light and oxygen, thus creating the optimal conditions for singlet oxygen generation in the point of choice (Fig. 9.1) and minimizing broad damage to the tissues [9, 10].

9.1.2 Applications with UV Light

The whole body of molecular photochemistry can in principle be used when UVA light is adopted (UV B is erythematogeneous) and thus for external treatment. The field that has expanded more rapidly is photochemotherapy (PUVA) mostly based on the use of psoralens or related heterocycles and solar or artificial light against a variety of skin disorders. In long-term treatments, however, there is the risk of premature skin aging and formation of squamous carcinoma cells. Therefore, advanced studies address the issue of safe treatment, e.g., by digitalization of the method [11–13].

A number of further UV-based therapies have been tested, or at least a proof of concept has been reported. An improved local stent therapy was proposed for the palliative treatment of intestinal tumors by UV light, where polymer filaments were modified with drug-loaded polymer microgels. Laser irradiation caused the release of the active substance [14]. The potent cytotoxic agent 5-fluorouracil has been generated in situ by retrocycloaddition of the non-cytotoxic dimer contained in a microgel. The dimer was in turn prepared by benzophenone sensitization. Apart from cancer treatment, new perspectives are opened in various aspects of medicine, including antibiotics, although for the moment mainly limited to in vitro therapies [15].

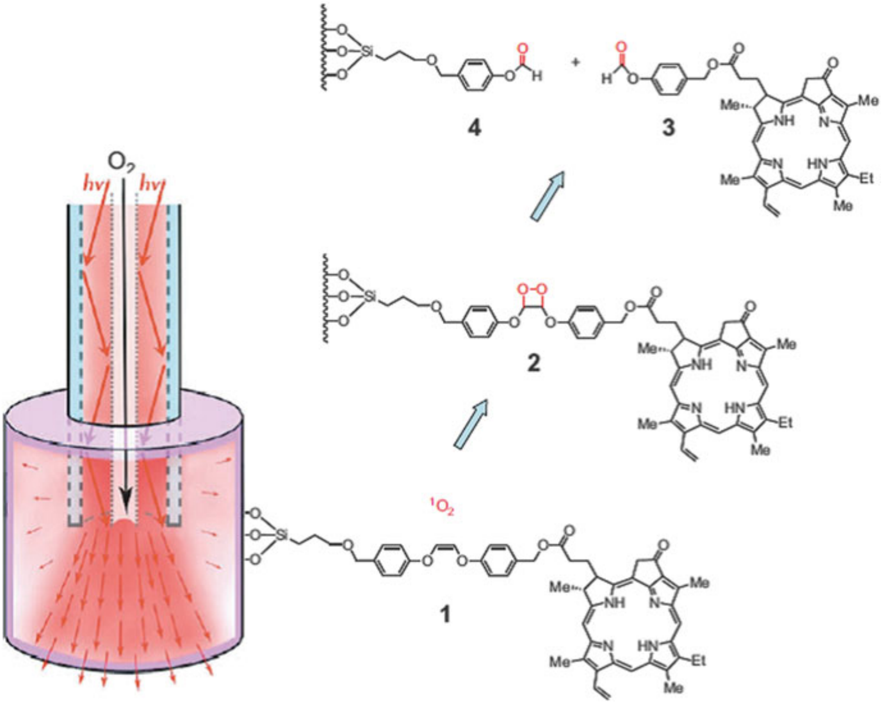
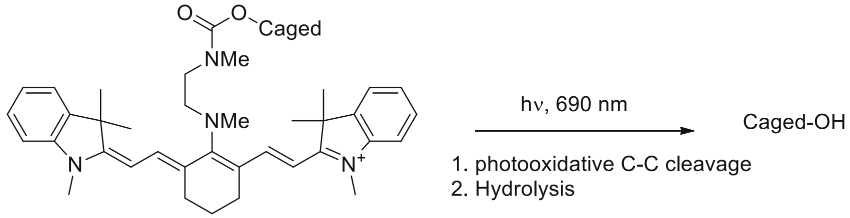


Fig. 9.1 Fiber tip attached and photocleavable pheophorbide sensitizer system. The 5 × 8-mm^2 probe tip is made of porous glass with a *cylindrical shape* and has a hole extending lengthwise 4 mm. The center of the fiber is a gas flow tube that was coupled to a compressed oxygen gas tank. The glass tip is capable of cleaving sensitizer **3** free via the scission of a dioxetane intermediate **2**. Reprinted with permission from [9, 10]

9.1.3 Application with Near IR

The skin is most transparent to light with λ ca. 870 nm that penetrates down to the hypodermis, while it is fully opaque to $\lambda < 300$ nm, and >1060 nm and visible light between 600 and 900 nm penetrates the dermis to a various degree [16], thus it is desirable that sensitizers absorbing in that range are developed. Although porphyrins are largely the most used dye in photodynamic therapy, completely different systems are continuously reported as photolabile groups, mostly having again an oxidation as chemical step. In particular, a choice of NIR activated groups for liberating drugs where desired in an organ or a cell, with the maximal spatial and temporal control, is available. As an example, readily synthesized C_4'-dialkylamine-substituted heptamethine cyanines have demonstrated to be convenient chaperons able to liberate the drug *Caged*-OH (in the test either nitrophenolate, detected by absorbance, or cumarines, detected by fluorescence at 450 nm) upon low-energy irradiation at 690 nm. The reaction involves oxidative degradation of the dienamine moiety in

4 followed by intramolecular cyclization of the ethylenediamine liberated. The process is compatible with biological conditions (Scheme 9.1) [17].



Scheme 9.1 An oxygen-labile protecting group

9.1.4 Nanoparticles

Most (suggested) applications are based on the well-known fact that tumor cells differ from the normal ones due to the enhanced permeability and retention effect with liposomes and nanoparticles. Thus, liposomes cross the blood vessel and either accumulate in the tumor area through a passive effect (passive targeting) or are taken up by the cells (active targeting in Fig. 9.2). If at this point the membrane is destroyed, the drug contained in the liposome is liberated in the vicinity of, or within, tumor cells. For this job, a number of liposomes have been elaborated by inserting photoactivatable groups in the phosphatides. Actually the idea does not work as expected in vivo, since liposomes are preferentially captured by the reticuloendothelial system. This limitation can be overcome by inserting polymers (PEG) or by polymerization of a vinylbenzoyl moiety through a radical mechanism. Phototriggerable liposome drug delivery platforms have been explored since decades and offer versatile and tunable systems where the desired conditions (wavelength, intensity, time of irradiation) can be chosen, provided that the lipid molecules retain their liposome-forming property and that the photochemical trigger is efficient also in some depth in the tissue. Various compounds have been studied, such as plasmalogen, a natural compound that contains a vinyl ether moiety sensitive to activated oxygen, polymerization, isomerization of an azo moiety, and polymerization of alkenes and alkynes (polymerization destroys the possibility of forming liposomes) [18]. Various photoactivated phospholipids were considered (see Scheme 9.2). Thus, nanocapsules and vesicles suitable for transporting and releasing drugs were obtained from lipid-based hollow spherical nanocapsules prepared from phospholipids bearing 3,5-divinylbenzoyl groups by radical polymerization (also UV assisted) and cross-linking.

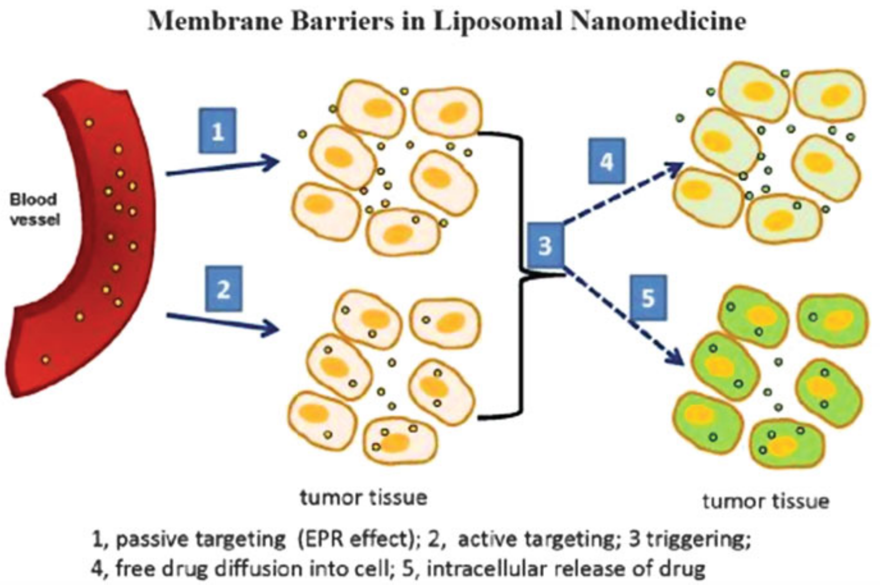
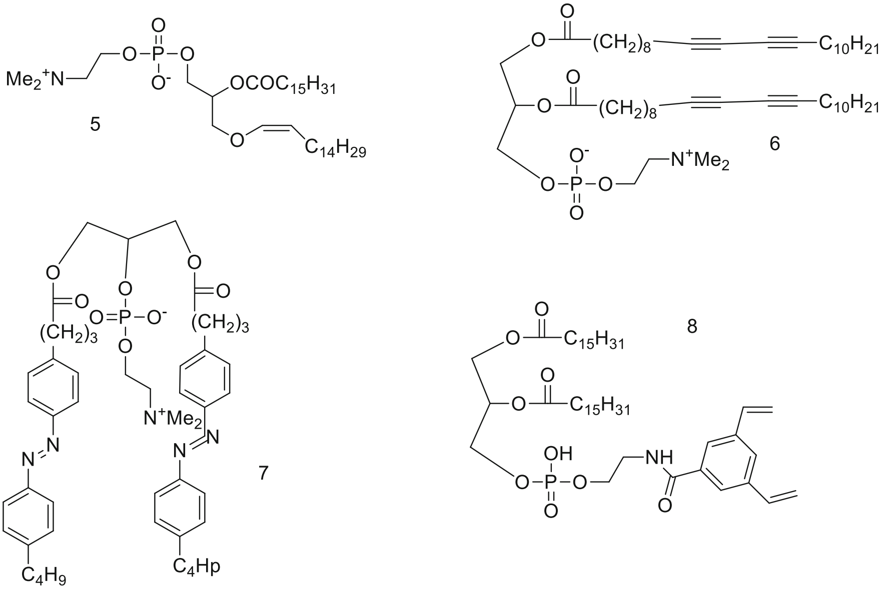


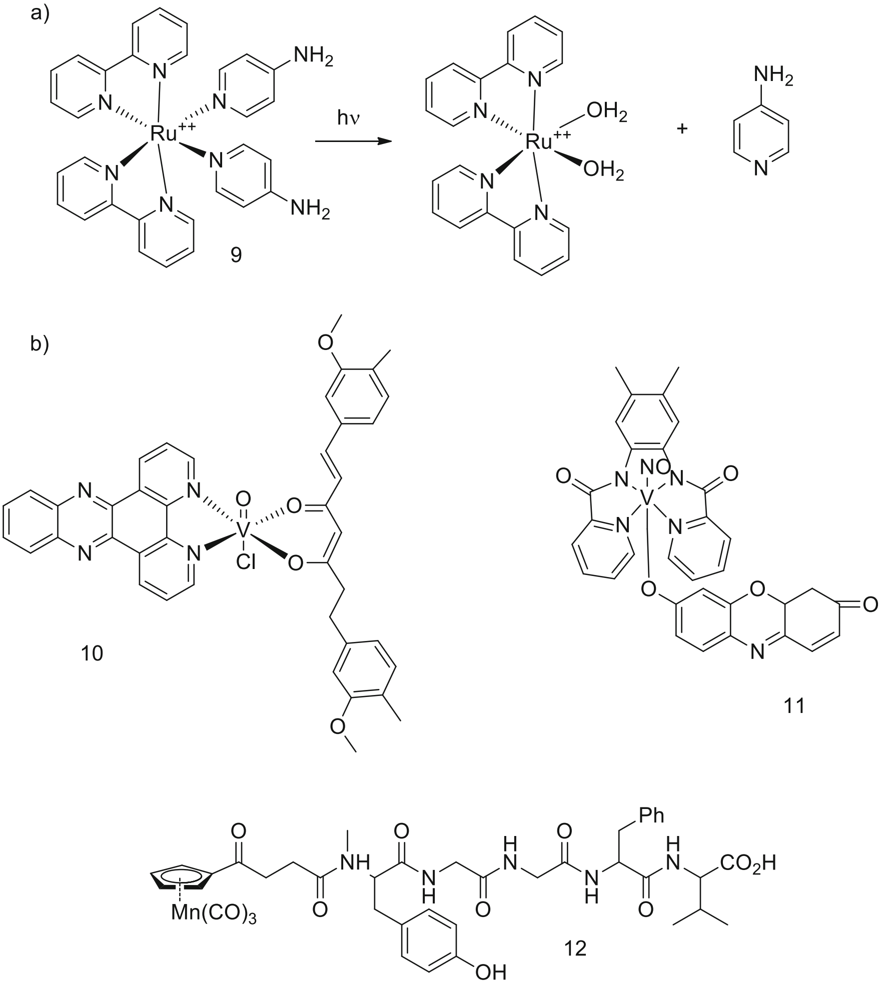
Fig. 9.2 Membrane barrier in liposomal medicine. Reprinted with permission from [18]



Scheme 9.2 Photoactivatable phosphatides **5**–8

9.1.5 Transition Metal Complexes

The role of transition metal complexes in pharmacology is increasing, because of their improved solubility and bioavailability. Activation by light is an appealing issue also in this field (see Sect. 9.1.1). Thus, many transition metal complexes that are inert in the ground state, particularly those with d^3 and d^6 electronic configurations, undergo smooth ligand dissociation when excited by visible light of a suitable wavelength. Phototriggered drug release has thus expanded among transition metal complexes, several of which (an example in Scheme 9.3a for the ruthenium complex **9**) have been found to be cytotoxic in combination with light (Scheme 9.3a) [19].



Scheme 9.3 Photoactivatable metal complexes considered as prodrugs

Complexation of curcumin with dipyridophenazinevanadium(oxa)chloro makes this drug (**10**) much more resistant to hydrolysis and of low toxicity, but irradiation leads to the free drug, much more active than in the complex (Scheme 9.3b) [20]. Some complexes considered as photoactivatable drugs (**11–12**) are also indicated in Scheme 9.3b.

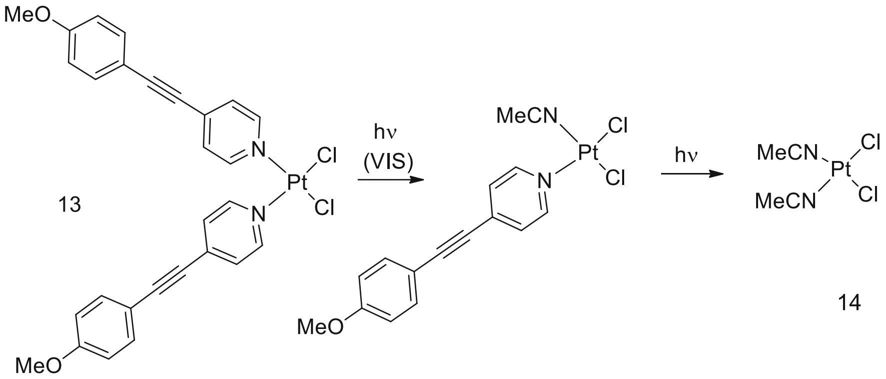
9.2 Photochemical Internalization

Again on the same issue, a typical problem encountered for the use of therapeutic macromolecules is the membrane barrier of the endocytic vesicles. Photochemical internalization (PCI) is a novel technology for release of endocytosed macromolecules into the cytosol, based on the use of photosensitizers located in endocytic vesicles that upon activation by light release macromolecules from their compartmentalization in endocytic vesicles. This applies to protein toxins and DNA polyplexes, as well as gene therapy vectors (e.g., viral vectors), peptide nucleic acids (PNA), small interfering RNA (siRNA), polymers, nanoparticles, and some chemotherapeutic agents [21]. Another possibility is antibody-directed phototherapy that is utilizing antibody conjugation to deliver photosensitizers to the tumor via tumor-associated cell receptors which appears to be able to increase both specificity and potency of a drug, as well as its pharmacokinetics [22].

9.3 Upconversion for the Photoactivation of Drugs

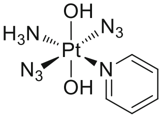
The main advantage in achieving upconversion in drug release is the increased penetration of low-energy photons that allow to reach inner tissues and liberate there the active molecule. Ford and colleagues have used lanthanide-doped upconversion nanoparticles to mediate nitric oxide (NO) release from Roussin's black salt anion $[Fe_4S_3(NO)_7]$—using NIR light from a simple diode laser operating at 980 nm [23]. On the other hand, protection (of the instrument and of the experimentalist) from strong laser light is also an issue, and some useful complexes have been reported [24, 25].

Tetrahedral Pt derivatives are well-known anticancer drugs and the active complex is generated by ligand solvation, as indicated on the model compound **13** at 600–740 nm (Scheme 9.4) [26].



Scheme 9.4 Photoinduced solvolysis of metal complexes

In the case of the Pt complex **15**, two-photon excitation is effective down to a femtoliter-limited concentration (Scheme 9.5) [27].



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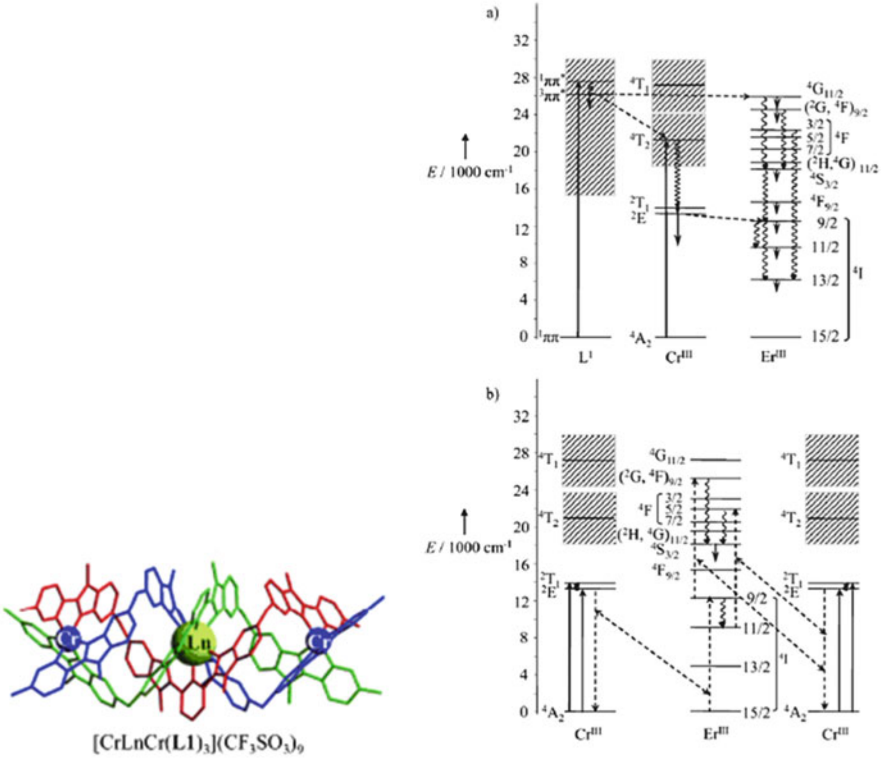
Scheme 9.5 A Pt complex activated by two-photon excitation

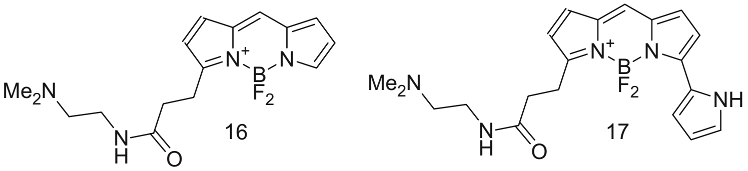
In another example, a self-assembled cation bearing two Cr^{III} sensitizers that connect a central Er^{III} acceptor has been reported. The structure of the complex provides high local metal concentrations that favor efficient nonlinear energy transfer and upconversion luminescence. When this d–f–d complex is irradiated by a low-energy NIR light involving the Cr^{III}-centered transitions, the complex exhibits molecular two-photon green Er^{III}-centered emission (Scheme 9.6) [28].



Scheme 9.6 State diagrams for the different chromophores present in [CrErCr(L1)$_3$](CF$_3$SO$_3$)$_9$ showing (**a**) the linear downconversion luminescence (excitation, *full upward arrows*; internal conversion, *curled down arrows*; energy transfer, *dotted arrows*; emission, *full downward arrows*) and (**b**) the nonlinear upconversion luminescence (excitation, *full upward arrows*; internal conversion, *curled down arrows*; ETU, *dotted arrows*; emission, *full downward arrows*). Reprinted with permission from [28]

9.4 Diagnostic Applications: Two-Photon Fluorescence

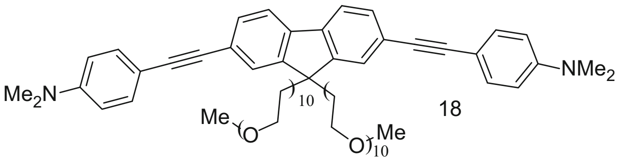
Microscopic investigations of cell organelles, e.g., lysosomes, are important in the diagnosis of a variety of diseases, including solid tumors. Fluorescence is the most sensitive method. Endogenous fluorophores are not satisfactory, because of the low fluorescence quantum yield, and on the other hand, one-photon fluorescence requires the use of dyes that absorb at a rather short wavelength and thus suffer from a large disturbance by the matrix. Excitation by two photons is thus an important possibility and the above characteristics are even more important for the application to biological materials. This is demonstrated by the development of two-photon laser scanning microscopy, where fluorescence is induced by two-photon excitation in the near-infrared region (700 to ca. 1100 nm, more precisely 760–1000 nm within the tuning range of commercial Ti–sapphire lasers) profiting of the relative transparency of cell components in this region. This technique has been introduced in 1990 and purposely designed microscopes and ultrafast compact laser sources are commercially available. Imaging of various organs and the use as a noninvasive diagnostic procedure have been explored and two-photon absorption cross section and new organic fluorescent probes have been introduced. In fact, a number of convenient dyes are available commercially, such as Lysotracker green and Lysotracker red (structures **16** and **17**). Search for new probes is active, and probably large improvements are expected. An ideal probe must have appropriate characteristics and exhibit not only a high two-photon fluorescence quantum yield but also a high photostability, which is not always satisfactory among organic molecules. A figure of merit has been proposed as the product of the fluorescence quantum yield (Φ_f) for two-photon absorption cross section (δ) and the photodecomposition quantum yield (η) in order to take into account all of the aspects (Eq. 9.1, Scheme 9.7) [20].



Scheme 9.7 Dyes for two-photon fluorescence

$$F_M = \Phi_f \delta / \eta$$

As an example, the fluorene derivative **18**, where the poly(ethylene oxide) chains impart hydrophilicity and lessen cytotoxicity, has been shown to be a selective probe for the lysosomes of human colorectal carcinoma cancer cells in two-photon fluorescence microscopy (Scheme 9.8).



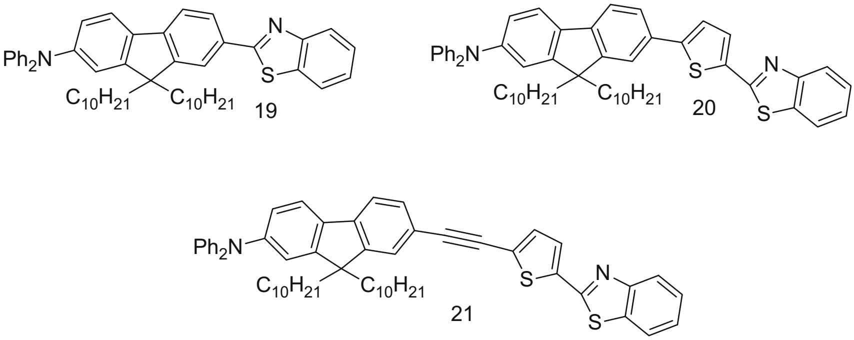
Scheme 9.8 Dyes for two-photon fluorescence

This molecule localized similarly to commercial dye Lysotracker red (colocalization coefficient 0.98), but exhibited a high two-photon absorbance (more than 1100 GM), good quantum yield of fluorescence, and, importantly, slow photodecomposition, which led to a much higher figure of merit (see Table 9.1) [29].

Table 9.1 Comparison of dyes for two-photon fluorescence

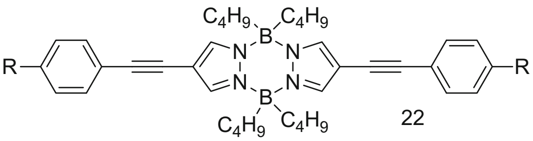
Fluorescent dye	$\lambda^{a}_{max}/\lambda^{b}_{max}$	$\varepsilon \times 10^{-4}$ (M^{-1} s^{-1})	Φ_F	δ (GM)	$\eta \times 10^{-6}$	$\Phi_F \times \eta$	$F_M \times 10^{-6}$
16	502/510	6.3	1.0	17	3.70	17	4.6
17	575/591	4.9	0.07	33	5.31	2.3	0.4
18	387/501	7.7	0.38	1135	0.94	431.3	458.8

A further problem is that most of the best candidates are, as one may expect, strongly hydrophilic. As usual in biochemistry, the addition of some dimethyl sulfoxide overcomes this limitation, but specific media have also been developed. Good results have been obtained with block polyesters polyamides that form micelles shown to be efficient nanocarriers for typical two-photon absorbing fluorescent dyes (see compounds **19–21** in Scheme 9.9) [30–32].



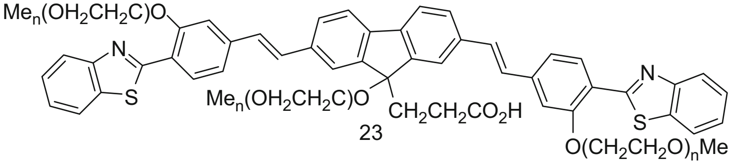
Scheme 9.9 Structure of some molecules (**19–21**) that are efficient probes for two-photon fluorescence microscopy

Molecules that are suitable as probes for two-photon fluorescence microscopy in terms of efficient emission, solubility, and nontoxicity are being rapidly developed and have been applied to various fields. Compounds above (Scheme 9.9) and further analogs show $\Phi_f > 0.86$, $\delta > 200$ GM in the NIR region, are rather photostable, and have been shown to localize specifically in distinct areas of the cell. On the other hand, boron-containing compounds of structure **22** (Scheme 9.10) are also taken up by cells, likewise show $\delta > 200$ GM in the NIR region, and have the additional advantage of the possible use in boron neutron capture therapy [33].



Scheme 9.10 A boron-containing probe for two-photon fluorescence spectroscopy

Fluorene derivatives like **23** and its block copolymers with Arg–Gly–Asp (RGD) peptide conjugates have been used in two-photon fluorescence microscopy for deep ex vivo imaging of tumor vasculature in “whole” excised tumors obtaining excellent three-dimensional reconstructed images up to the depth of 830 μm that clearly revealed the tumors. The peptides that targeted $\alpha_\nu\beta_3$ integrin are considered a biomarker of tumor malignancy. Interestingly, the copolymer gave a clear, uninterrupted image of the blood vessel network with high sensitivity, while the small-molecule conjugates showed interrupted images of the vessels. This was hypothesized to result from the lower residence time in the vessels of the small molecule that responded to the inhomogeneous nature of the tumor’s vasculature and thus to the varying levels of $\alpha_\nu\beta_3$ integrin expression [34] (Scheme 9.11).



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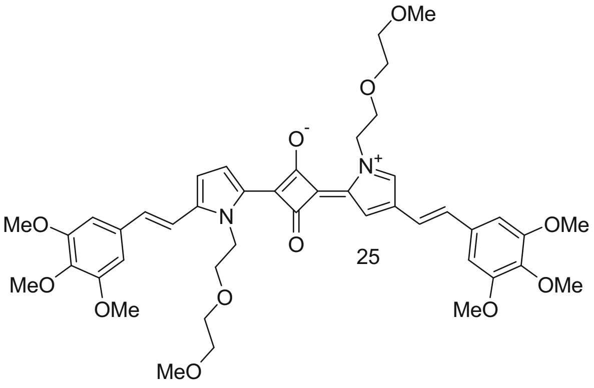
Scheme 9.11 A fluorene derivative for two photon fluorescence microscopy

Many other donor acceptor systems have been considered, as an example cyanines, which however are often photochemically degraded, in particular the highly conjugated derivatives that would be the most interesting cases. Squaraines are more promising, at least to judge from the case of squaraine **24**, which exhibited a very high two-photon absorption cross section of ca. 20,000 GM at 800 nm and ca. 1000 GM at wavelengths just over 1000 nm, thus offering several possibilities for two-photon-based imaging at different excitation wavelengths. Notice further that these dyes were considerably more photostable than a typical (commercially available) NIR dyes [35] (Scheme 9.12).



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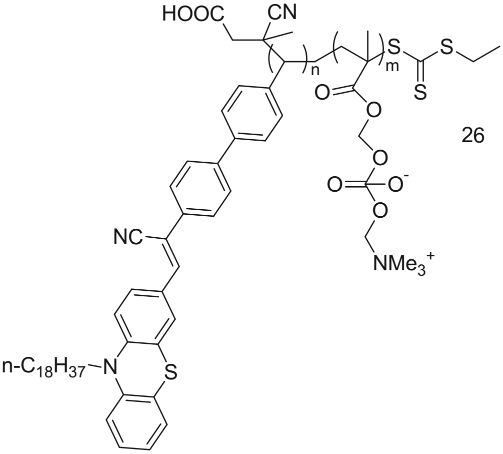
Scheme 9.12 A squaraine derivative for two photon fluorescence spectroscopy

9.5 Diagnostic Applications. Aggregation-Enhanced Fluorescence

Microscopy is one of the key diagnostic techniques of the future and ensures a high detail, almost at the single-molecule level. However, this cannot be obtained by excitation by an intense irradiation of a highly concentrated dye, because of effective reabsorption. However, some classes of dyes undergo no self-quenching and rather exhibit solid-state or aggregation-enhanced fluorescence (compare Sec. 11.1.1). This phenomenon contributes to the overall luminescence and often in the past was not recognized. Particulate nanoprobes are produced as a water-dispersed formulation, dispensing from the need of chemically functionalizing the molecule for solubility. Furthermore, nanoparticle formulation offers the possibility of tuning the cell permeability or achieving specific targeting of some biomolecules. As an example, it is observed in conjugated DA molecules **26**. In this compound, the fluorescence of the aggregate in 95-5 water THF is two orders of magnitude more intense than the solution in THF, and the systematic examination has shown that introducing further substituents increases the intensity (Scheme 9.13) [36–38].



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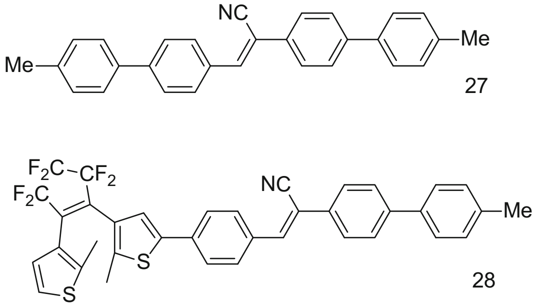
Scheme 9.13 A molecule undergoing aggregation-enhanced fluorescence

A variety of luminescent nanoparticles have been specifically devised for confocal and multiphoton microscopy. These include nanomaterials, such as silica-based nanoparticles doped with two-photon-absorbing fluorophores, able to exhibit aggregation-enhanced fluorescence, gold nanoparticles, semiconductor nanocrystals (quantum dots/rods), and nanophosphors, viz., ceramic nanoparticles containing luminescent lanthanide ions.

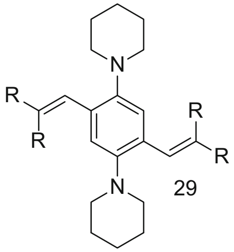
In the solid state both the shape and the efficiency of fluorescence are affected, due both to the fact that large motions are inhibited and to specific interaction between some moieties of the molecules. In π−conjugated systems the main absorption band corresponds to the S_0–S_1 transition, where the transition moment is mainly oriented along the long axis of the molecule. In the solid state, molecules are oriented side by side, with small displacement along the long molecular axis. This transition is dipole forbidden and aggregation causes a hypsochromic effect and quenching of the emission, often weak in solids even when strong in solution. The insertion of a disturbing group that hinders planarity reverses the situation, however. Thus, conjugated cyanostilbenes such as 1-cyano-trans-1-(4-′-methylbiphenyl)-2-[4′-(2′-pyridyl) phenyl]ethylene are nonplanar in solution, due to the repulsion between the cyano group and the *ortho* hydrogens, and torsion-promoted non-radiative deactivation strongly inhibits fluorescence (Scheme 9.14).



Scheme 9.14 Molecules undergoing aggregation enhanced fluorescence. The cyano group in stilbene derivatives such as **27** and **28** imparts a “twist” outside planarity in solution, while aggregation causes planarization. Molecule **28** also incorporates a dithienylethene moiety for dual stability

On the contrary, aggregation causes planarization of the structure due to the π–π interaction between cyano groups and biphenyl system, with both an increase of the radiation rate and a decrease of the non-radiative decay. This results in a bathochromic shift (J aggregates) and a dramatic enhancement of the emission efficiency (aggregation-induced enhanced emission). Strongly emitting colloids are obtained by simple reprecipitation, e.g., from tetrahydrofuran/water mixture, and are stable for months (due to the effect of polar cyano groups), while ordered mono-, di-, or tridimensional structures could be prepared by various techniques. Applications were developed for organic semiconductor lasers, optical memory, sensors, and conducting cables. Besides colloidal fluorescent nanoparticles, nanotailored nanoengineered structures built on this base included a variety of materials with strictly controlled optoelectronic properties [39].

In general, strongly emitting molecules contain extensive conjugated π-systems and emission in the NIR can be achieved from the condensation products from aromatic aldehydes and active methylenes [40]. However, relatively small fluorophores may give useful results. Thus, bis(alkenyl)-dipiperidino benzenes have been found to emit visible light in solution (quantum yield 0.09–0.66) and, more strongly, in the solid state (0.43–0.98) as a thin film or incorporated in a polystyrene films (0.43–1.00, Scheme 9.15) [41].



29

Scheme 9.15 Simple molecules undergoing aggregation enhanced fluorescence

9.6 Antimicrobics

UV light per se has an antimicrobic effect. Treatment by a pulsed UV irradiation effectively kills microorganisms [42]. The excellent properties of singlet oxygen as bactericidal are exploited in a variety of convenient materials. As an example, nanofabric fibers bearing tetraphenylporphyrin as sensitizer have been deposited from a solution of polyurethane and the dye. The polyurethane nanofabric obtained had a 0.03-mm thickness and contained 0.12% dye. The absorption and emission spectra of the fabric were strictly similar to those of the dye in solution, attesting that it remained in the monomolecular form. Bacterial colonies of *E. coli* were completely eliminated upon exposure to light (see the agar plate in Fig. 9.3) [43].

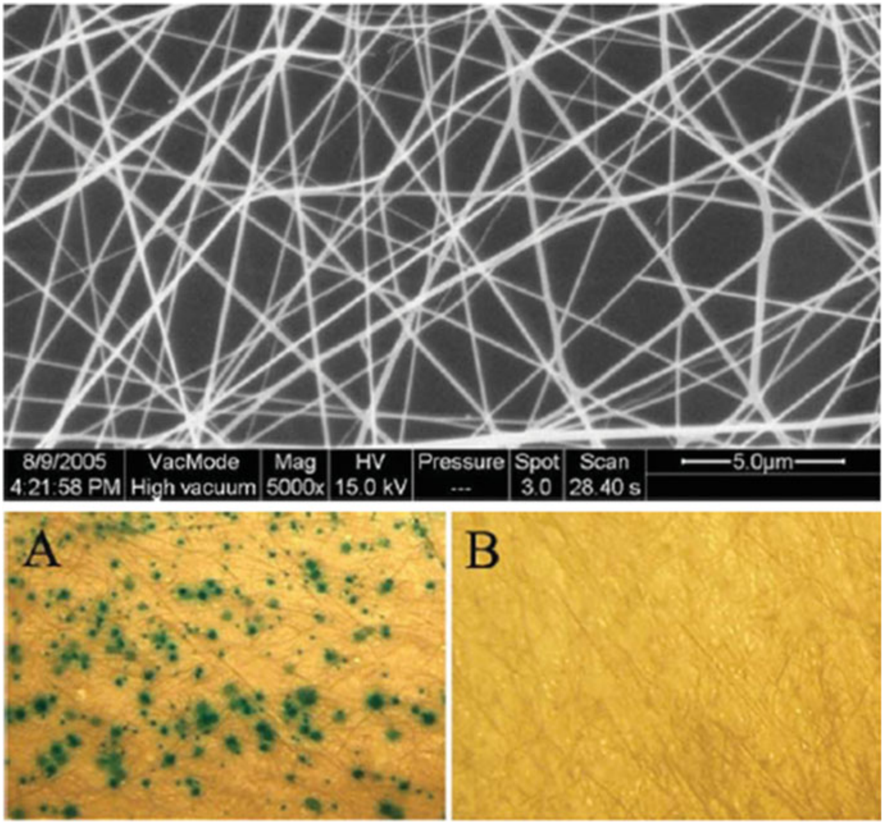


Fig. 9.3 Scanning microscope image of fibers bearing tetraphenylporphirin. Average fiber diameter, 460 nm. Reprinted with permission from [43]

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Chapter 10
Solar Energy Conversion

The problem that Ciamician, Bodenstein (see Chap. 4), and other scientists had confronted more than a hundred years ago has certainly not lost importance. Providing a sufficient amount of energy for the steadily growing needs of society and that in a sustainable way remains one of—or probably *the*—question of the future. Fossil fuels are a concentrated form of energy that mankind has learned to exploit more and more efficiently. On the basis of this source and of the technological advancement, the dramatic population increase over the last two centuries has been possible. However, fossils are nonrenewable and contribute heavily to global warming. There is no way out except finding alternative, carbon-neutral sources (all major CO_2-emitting countries agreed at Copenhagen in 2009 to a target of keeping global warming to less than 2 °C above preindustrial levels), with the added trouble that new energy demand is expected to occur in areas where large-scale energy infrastructures are less developed.

What had used to be the prophetic intuition by a few scientists has become a general belief not only among scientists but also among the society in general. The only possible answer has to come from the efficient use of solar irradiation [1–5]. As it has been repeatedly stressed, "solar energy strikes the Earth's surface in 1 h of each day than the energy used by all human activities in 1 year. World energy consumption is currently in the region of 450 EJ per year, but vastly more than this is the solar energy potentially usable at ~1.0 kW m^{-2} of the Earth" [3]. "Photosynthesis, the ultimate source of our oxygen, food and fossil fuels, has been operating on earth for 2.5×10^9 years. Much work has been devoted to various aspects, and in particular the mechanism of photosynthesis is now known in detail. As a consequence of this advancement, the present approach is much more diversified, both for the energy vector produced and for the photochemically active system. However, it could be hardly stated that we are close to the target.

Photosynthesis creates a global annual CO_2 flux of 1.24×10^{11} tonnes per year and an annual O_2 flux of ~10^{11} tonnes per year. In its present technologically unenhanced form, photosynthesis already traps around 4000 EJ per year of solar energy globally in the form of biomass. The global biomass energy potential for

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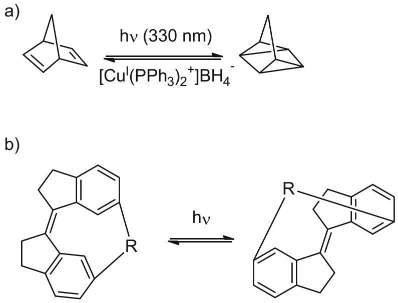
Table 10.1 Energy consumption on Earth [3]

Global energy per year	Joule per year
Energy consumption	4.5×10^{20}
Solar energy	3.9×10^{24}
Energy trapped in the form of biomass	4×10^{21}
Energy of biomass suitable for human use	$\sim 4.5 \times 10^{20}$

human use from photosynthesis as it currently operates globally is approximately equal to human energy requirements (450 EJ per year)" (Table 10.1) [3]. The possibility of more fully exploiting vegetation and producing fuels from the part that is not used as food has demonstrated to be viable under particular conditions, for appropriate geopolitical situations. However, a more detailed consideration of photosynthesis for the production of biofuels, whether in plants or in algae, shows that it is neither very efficient in solar energy conversion nor carbon neutral (since it requires much infrastructure). Perhaps more importantly, the availability of land is likely to be a limiting factor, particularly in densely populated and highly developed countries, while importing solar-produced fuels from less-populated countries may have to overcome political barriers.

10.1 Non-photosynthetic Strategies

Strategies that avoid having recourse to photosynthesis have an equally important role and include conversion of solar energy to electrostatic gradients (photovoltaic) [6], to thermal gradients sufficiently high to drive turbines (photothermal) [7], and to electrochemical gradients by causing chemical reactions (photochemistry and photocatalysis). Chemical reactions are applied for the synthesis of fuels, in particular CH_4 and CH_3OH from CO_2 and H_2 from H_2O, thus extracting the free energy content but consuming O_2 and producing CO_2. This is an open-system solar-fuel cycle. However, a closed system is also possible, where photon absorption causes an endoergonic unimolecular isomerization into a metastable isomer that act as the fuel. The energy stored in such isomer is released when this is converted back to the precursor form through a thermal, catalytic, or photochemical reaction, not exchanging any material with the environment [8]. Although this basic idea has been followed for many years and applied both to small molecules and to polymers, convenient compounds where the energy stored is a high enough fraction of the solar flux and can be then obtained over a not-too-large barrier pertain to a limited choice of models that does not seem to be easily extended, even if modifying the existing models may bring significant advantage. In practice, all of the known systems are based on strained small-ring systems or on putting a rigid constraint over an isomerization-liable double bond (Scheme 10.1) [8–11].



Scheme 10.1 Energy storage in the form of a strained chemical bond [8, 9]

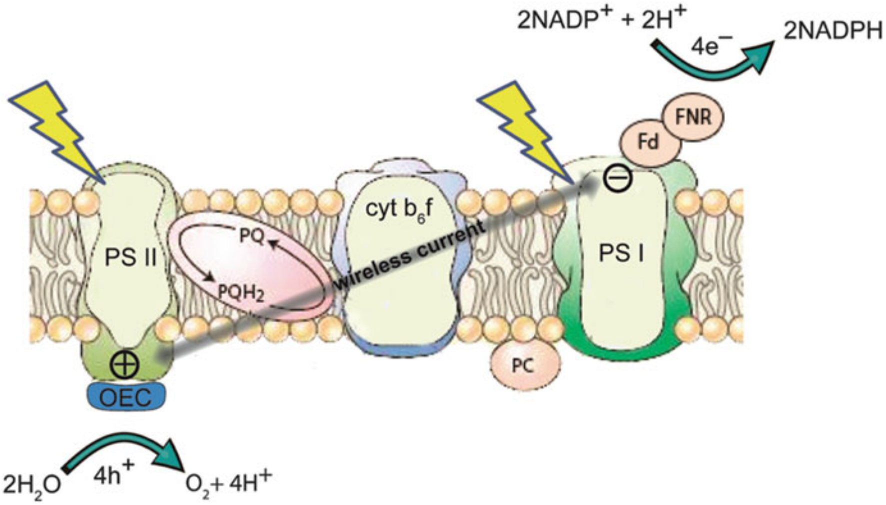
10.2 Artificial Photosynthesis

Artificial systems mimicking photosynthesis [12, 13] are actively investigated. Synthesizing a sugar is essentially equivalent to water splitting, as shown by the close one-to-another potential at which reactions (10.1) and (10.2) occur and thus the actual energy-storing step can be taken as that of photochemical water splitting, disregarding the ensuing steps forming carbohydrates.

$$H_2O \rightarrow H_2 + ½O_2 \quad E_0 = 1.23 \;\; \mathrm{V} \tag{10.1}$$

$$CO_2 + H_2O \rightarrow 1/6\,C_6H_{12}O_6 + O_2 \quad E_0 = 1.24 \;\; \mathrm{V} \tag{10.2}$$

Solar photons cause charge separation that is exploited by redox cofactors at the terminus of the charge-separating network and causes water splitting [14]. Light absorption in the photosynthesis PSII system transfers four electrons to plastoquinol, plastocyanin, and cytochrome b_6f and finally to ferredoxin bound to PSI to form “reducing power” in the form of four molecules of NADPH, which in turn enters the Calvin cycle where it is fixed with CO_2 to produce carbohydrates. The four holes are transferred to the oxygen-evolving center in PSII which splits water liberating a molecule of oxygen and four protons. The intrinsic complexity of the system results from the fact that the energy of the photon absorbed can’t be too large, in order to use a fraction as large as possible of the solar light spectrum, but at the same time must be large enough to cause both water-splitting and $NADP^+$ reduction. This limits the operation of PSI and PSII that can only generate one electron/hole pair for each photon. However, water splitting is a four-electron/hole process, while $NADP^+$ reduction is a two-electron proton reaction. Thus, the function of light collection and conversion must be supplemented by catalytic active centers at the termini of the charge separation network so that the multi-electron process occurs (see Scheme 10.2). The all-important oxygen-evolving center (OEC) is based on a Mn_4Ca cluster that self-assembles under oxidizing conditions when Mn^{2+} is photooxidized to Mn^{3+} that is bound to the apo-coordination environment of the PSII complex, a step that involves the same path via PSII that is used for water splitting after the OEC is assembled.



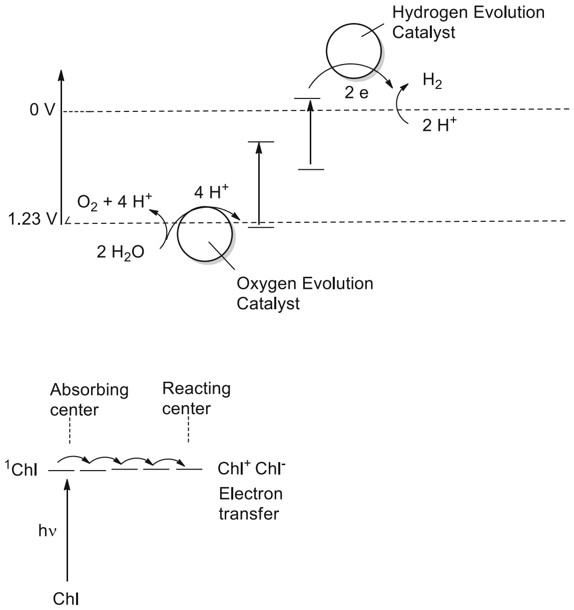
Scheme 10.2 Photosynthetic Z scheme. Reprinted with permission from [14]

As it has been remarked, the OEC operates at ambient conditions of temperature and pressure and at neutral and near-neutral pHs and uses Earth-abundant elements. This contrasts with the artificial photocatalytic water-splitting systems that often involve the use of rare elements [14–16].

At any rate, it would seem not reasonable to embark in an attempt to reproduce such a complex structure. A still formidable goal would be the production of a convenient energy vector, such as hydrogen (a clean fuel, oxidation product is only water) by photolysis of water, abundant on the planet, and under conditions inspired to nature, although much simplified.

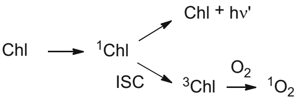
Thus, the question is how to develop a reasonable way for converting solar energy into chemical energy that can be stored [12, 13, 17, 18]. Artificial photocatalytic water splitting is understood as the generation of hydrogen and oxygen in stoichiometric amounts from a molecule of water. This is possible through an approach that mimics oxygen-generating chlorophyll photosynthesis. Thus, the 1.23 V gap required for splitting a molecule of water (at pH 0) may be provided through the absorption of a photon that corresponds to ca 800 nm. However, it is not obvious to find a sensitizer that matches the gap required and thus imitates nature; it is more practical to have recourse to two different sensitizers, one that drives oxidation in the excited state (E^*_{red} is more positive than the reduction potential of water) and one that in the ground state reduces it (E_{red} is more negative than reduction potential of water). Absorption of light generates charge-separated species and the positive charge is transferred to an oxygen evolution catalyst to oxidize water into oxygen and protons. Liberated electrons are transferred efficiently through a connection to a hydrogen evolution catalyst that reduces protons into hydrogen. However, in order to simplify the problem, the large majority of published studies involve a half-reaction only and the use of a sacrificial electron donor or, respectively, a sacrificial electron acceptor in the assumption that joining the two half-reactions and eliminating the sacrificial partners will lead to a self-supporting system. Notice further that absorption of a photon causes a single event, but more photons are required for both photosynthetic steps and the system has to be efficiently catalytic (high turnover number). The versatile preparation of polynuclear metal complexes (including dendrimers) has been a convenient approach to directional energy transfer [19].

At any rate, every step has to be appropriately developed, from the antenna for absorbing as much as possible of the radiation and hindering back electron transfer to the hydrogen- and oxygen-evolving centers in a structure that ensures directional electron transfer (see Scheme 10.3).

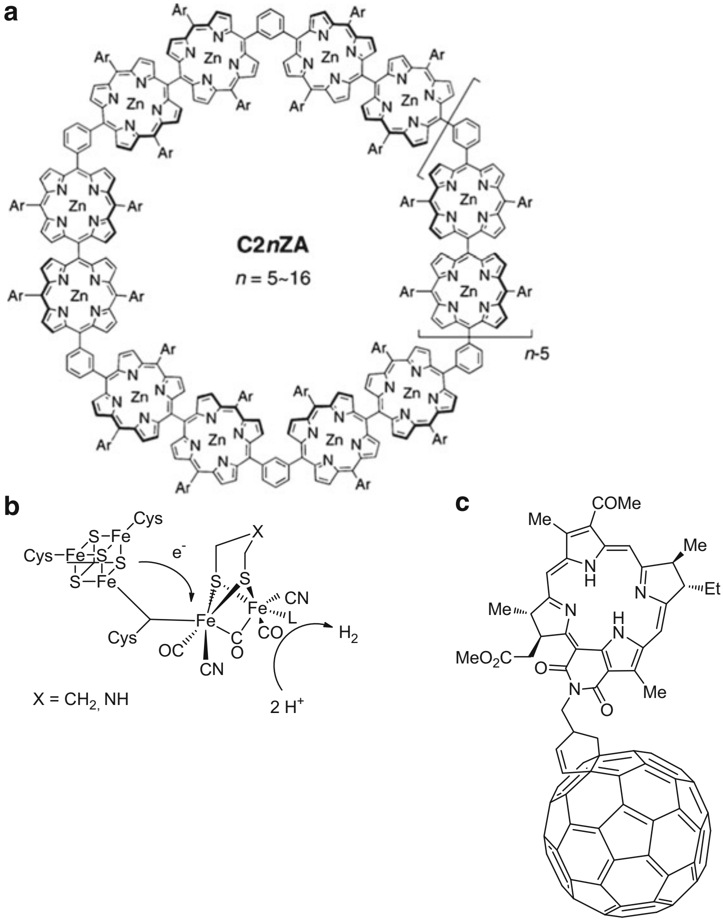


Scheme 10.3 Operation of chlorophyll photosynthesis (*above*) and energy transfer between chlorophyll molecules in the chloroplast until electron separation takes place (*below*)

As indicated in Scheme 10.4, none of the key functions of photosynthesis can be confined to chlorophyll as a molecule. In photosynthesis, "the absorption of a photon by light-harvesting (antenna) complexes made up of a large number of protein embedded pigments initiates photosynthesis. Subsequently the many pigments within the antenna system shuttle that photon via an efficient excitation energy transfer (EET) until it encounters a reaction center" [20]. The molecules are closely arranged in a convenient way so that virtually no photon is lost. The efficiency of this process is vital, and indeed nature does this with an incredible efficiency, >95 %, since EET is very fast between close-lying chlorophyll molecules (see Scheme 10.5). Recent research has evidenced that cyclic arranged chromophoric assemblies may have a role. This is the case for bacteriochlorophyll a [23, 24]. Artificial metal complexes or supramolecular systems that have an equivalent performance have been devised. In particular, interesting results have been obtained with porphyrins [20]. Well-characterized derivatives have been built by covalent or noncovalent bond and the decay mechanism identified as electronic energy transfer (EET) which in some cases, such as dye CZ8, reaches a rate $>10^{12}$ s^{-1}. Furthermore in non-coordinating solvents, self-assembling has been found to give specific oligomers with rigorous self-sorting of homochiral components.

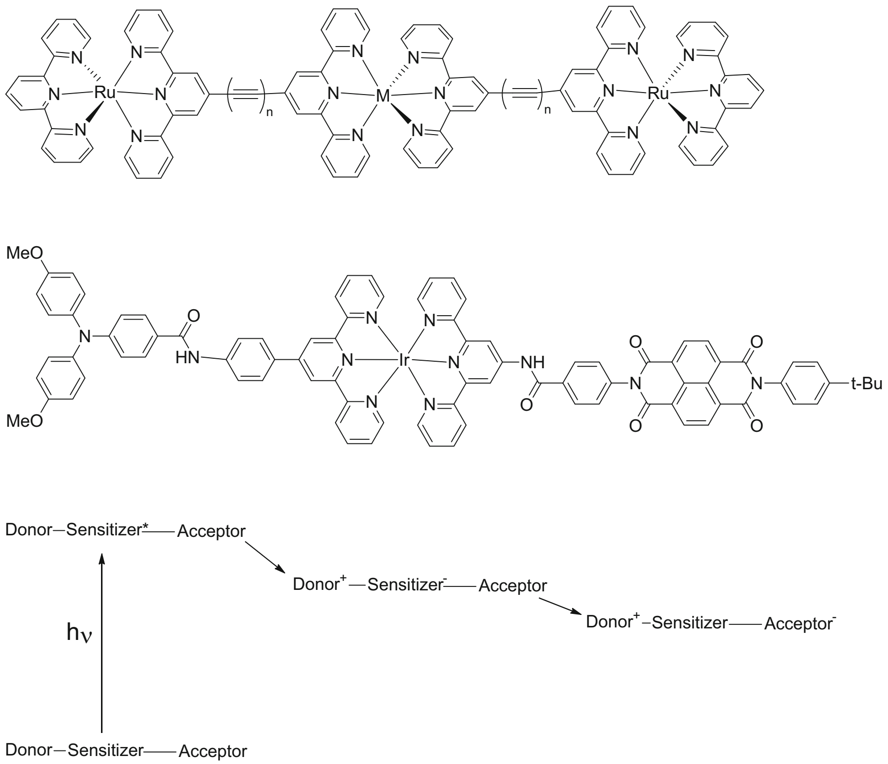


Scheme 10.4 Chlorophyll (Chl) photochemistry in solution

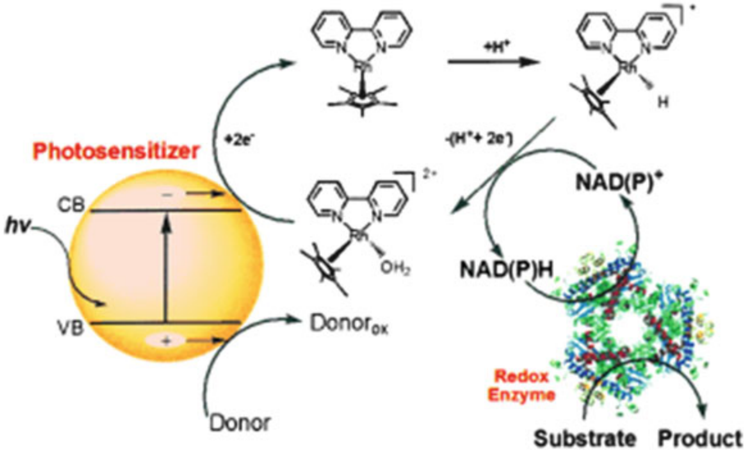


Scheme 10.5 Mimicking chlorophyll photosynthesis. (**a**) A cyclic chromophore for mimicking the antenna (reprinted with permission from [20]); (**b**) active site of the Fe–Fe hydrogenase (from [21]); (**c**) a dyad for long-lived charge separation (from [22])

Models for directional excitation migration have been developed on the basis of both energy and electron transfer, as exemplified in Scheme 10.6 [21, 22, 25–27], and have been applied also to direct activation of biocatalyzed redox processes (Scheme 10.7). Likewise, viable models for the water oxidation center and the formation of reductants have been developed. Further following this path, actual "artificial leafs" have been built where the different functions have been assembled [14, 28]. Therefore, it is natural that a major effort is directed toward "the development of a renewable fuel source that can meet the nation's energy demand while reducing carbon dioxide emissions "that" is critical to the energy security, environmental protection, and economic well-being of the United States." This is the stated target of the Joint Center for Artificial Photosynthesis recently (2010) established at Berkeley [29]. The ambitious mission of this center "is to develop a manufacturable solar-fuels generator, made of Earth-abundant elements, that will use only sunlight, water, and carbon dioxide as inputs and robustly produce fuel from the sun ten times more efficiently than current crops. Such an achievement would minimize trade-offs between food and fuel, would allow for installation of the systems in a diverse range of sites and environments, and would provide the direct production of a useful chemical fuel from the sun." Apart from confronting a number of basic scientific issues, the technical aspects to be coped with for designing and assembling a device able to produce energy-dense fuels, such as hydrogen and carbon-based fuels using only sunlight, water, and carbon dioxide as inputs, are a formidable challenge. At present, a system that would be both sufficiently efficient and sustainable and furthermore economically viable and suitable to be scaled up is nowhere in sight, but taking this opportunity could have a revolutionary impact on our energy system. The target photosynthetic system should be significantly more efficient than biofuel production processes and should be "easily deployable almost anywhere," not requiring arable land or substantial inputs of energy or water. Again, this reminds of Ciamician's dream.



Scheme 10.6 Using polynuclear metal complexes for directional excitation transport



Scheme 10.7 Electron transfer on an artificial system leads to a chemical activation of an enzymic redox process. From [25]

This goal is pursued by different themes, viz., semiconductors that are able to provide sufficient voltage for water-splitting and carbon dioxide reduction chemistry while being stable to photocorrosion. As an example, illuminated photoelectrodes made from tungsten diselenide with noble metal catalysts deposited on the surface can produce hydrogen from water with energy-conversion efficiencies of more than 7 % and are chemically stable in both high- and low-pH environments [30].

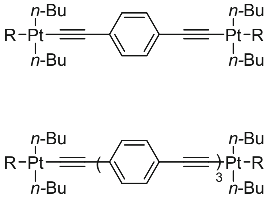
In a large institution such as the Joint Center for Artificial Photosynthesis, this is done by using theory, modern surface-science methods, and synchrotron-based techniques, for establishing the mechanism of the homo- and heterogeneous catalysis, combinatorial techniques that can produce new alloys, rapid screening methods that can identify high-performing light absorbers and catalysts, and surface-science analysis tools that can characterize the structure and composition of promising materials. The system is now being integrated into a discovery pipeline that will produce tens of millions of new candidate materials for solar-fuel generation systems. In turn, these materials should allow the implementation of strategies and tools for linking individual components into fully functioning, nanoscale artificial photosynthetic assemblies. Key points are:

- Overcoming the inefficient charge transport between light absorbers and catalysts and, in particular, between the sites of water oxidation and fuel-generating half-reactions.
- Methods for orienting, assembling, and interconnecting nanoscale functional assemblies containing catalysts, light absorbers, and support matrices into fully functional photoelectrochemical systems.
- To develop a knowledge foundation of structure–function relationships for photoelectrochemical layers that allows for prediction and control of transport phenomena in macroscopic solar-fuel generation systems.
- Identifying gaps revealed by real-world implementation of an integrated solar-fuel generator based on artificial photosynthesis. The current development work in the program is focused on the design of prototype models that use dual-light absorber (tandem) configuration cells.

10.3 Dye-Sensitized Solar Cells

The most important application is dye-sensitized solar cells, where electron injection from an excited complex adsorbed onto a semiconductor, normally TiO_2, is the key process. Ruthenium complexes were shown to inject electrons in titanium dioxide on the $<$10-ps scale [31] (see Chap. 6).

Two-photon absorption and ultrafast dynamics of spin photoexcitations have been used for the characterization of conjugated polymers containing platinum atoms (Scheme 10.8). These complexes show a record intersystem crossing time of 1 ps (with one phenyl spacer) and 6 ps (with three phenyl spacers). This tunable ultrafast intersystem crossing determines the intensity ratio of the phosphorescence and fluorescence emission bands and is potentially useful for applications for white OLEDs [32].



Scheme 10.8 Pt complexes with exceptionally fast ISC

10.4 Comparing Different Approaches

Photocatalytic water splitting to produce hydrogen and oxygen is considerably advancing. Some of the systems studied involve a single visible-light-responsive photocatalyst that has a suitable thermodynamic potential for water splitting, as well as a sufficiently narrow bandgap to harvest visible photons and stability against photocorrosion, conditions that are met only by a few materials. The alternative approach is to apply a two-step excitation mechanism by using two different photocatalysts following the trail of natural photosynthesis in green plants. In this case, the ΔG required for each photocatalyst is reduced, allowing a wider choice of appropriate materials, and further it is possible to use catalysts that have the required ΔG only for the reduction or oxidation side, but it must be taken care that electron transfer between two semiconductors is efficient [33].

Domen has evaluated that in order to provide one-third of the expected energy needs of human society in 2050 from solar energy, approximately 10,000 "solar plants" with an area of 5 km × 5 km and a solar energy-conversion efficiency of 10 % should be built. Overall, this would require a 250,000-km^2 area, that is, the 1 % of the Earth's desert area. Five hundred seventy tons of H_2 gas would be produced and would be available for use either as a "recyclable" reactant in fuel cells or as a raw material for the production of important chemicals. This implies that an efficient technology allowing to separate simultaneously produced H_2 and O_2 is available. A study by the US Department of Engineering considered the technical and economic aspects of the photochemical production of hydrogen and concluded that a bag made of inexpensive flexible clear plastic containing the reactant solution and the photocatalyst may be a practical solution [34, 35].

Nature is obviously the model, but the system it has evolved, viz., oxygenic photosynthesis, is not necessarily the best possible one for an artificial use. Photovoltaic cells represent the most diffuse way for exploiting solar energy, although the contribution to the global energy produced is limited to a fraction of percent. However, in order to have energy available at the time and in the way required, one has to transform electricity into chemical energy, and the most viable solution is hydrolyzing water and producing hydrogen, a convenient energy vector. The power conversion efficiency is conveniently evaluated as the ratio of the power afforded divided by the solar irradiance. For a single-junction (i.e., operating with a single photosystem) silicon solar cell modules, this value averaged over a 1-year cycle is around 17 % at present. Water electrolysis can be carried out with an 80 %

efficiency and further losses intrinsic to the use of photovoltaic modules arranged in series amount to 20–30 %. Summing up, the efficiency of water splitting is around 10–11 %.

In photosynthetic organisms, energy is stored as chemical bonds. The efficiency is then the ratio of the heat of combustion of glucose produced divided that of carbon dioxide consumed. With this definition, the energy conversion amounts to 1 % or less for spontaneously growing plants but is higher for microalgae (3 %). These are average values, since organisms accumulate more energy during the growing period, and the low values are not unexpected, since obviously the target of evolution has not been producing food for mankind but rather reproducing the organism. In artificial systems, efficiency can be increased in various ways. A fundamental issue involves excitation. Natural photosynthetic pigments absorb in the visible, and this limits the part of solar spectrum absorbed to ca. 50 %, a large part of which is wasted due to the loss of the part of the photon energy overcoming the minimum value corresponding to the S_0–S_1 transition, because of the ultrafast internal conversion from the higher excited states initially formed. Furthermore, both photosystems are based on chlorophyll and their absorption spectra are quite similar. While guaranteeing a lower loss by charge recombination, this arrangement causes a competition between both systems for the same spectral region. In the two photosystems arrangement, this corresponds to a limit efficiency of 12 %, and, when taking into account loss in light absorption, competition with oxygen (i.e., respiration) and overpotential, efficiency drops to 4.6–7 % according to the type of vegetal. The limit may be overcome by extending the absorption further toward the red. A great breakthrough would be having two systems with non-superimposed spectra and engineering the structure in such a way that each antenna transfer energy to a different reaction center.

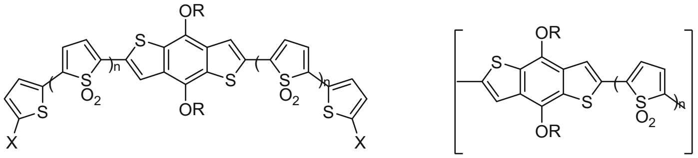
Likewise, semiconductors absorb photons of energy higher than that of the energy gap between valence and conduction band, but again any energy higher than the minimum is lost. Silicon used in photovoltaic cells absorb over a large range, from UV to near IR, but the above consideration shows that the energy actually available is ca. 32 % and, when one takes into account overvoltage, 24 %. One can make better, however. A way is substituting single-junction cells with tandem systems, each separately optimized for hydrogen and, respectively, oxygen evolution [35].

Although solar cell technology is advancing steadily and laboratory advancement is rapidly converted into applications, resulting in greatly increased production volumes and greatly reduced costs, alternative approaches are gaining momentum [36, 37]. Organic compounds offer a great versatility for bulk heterojunction photovoltaics. Conjugated polymers are largely used as the donor material and fullerenes and conjugated polymers as electron acceptors. Indeed, polymer/fullerene blends have allowed large advancements provided that donor and acceptor energy levels were appropriately tuned, in order to extend the absorption spectrum to lower energies while limiting voltage losses in the device [38]. Polymeric materials with an excellent performance are being developed [39, 40].

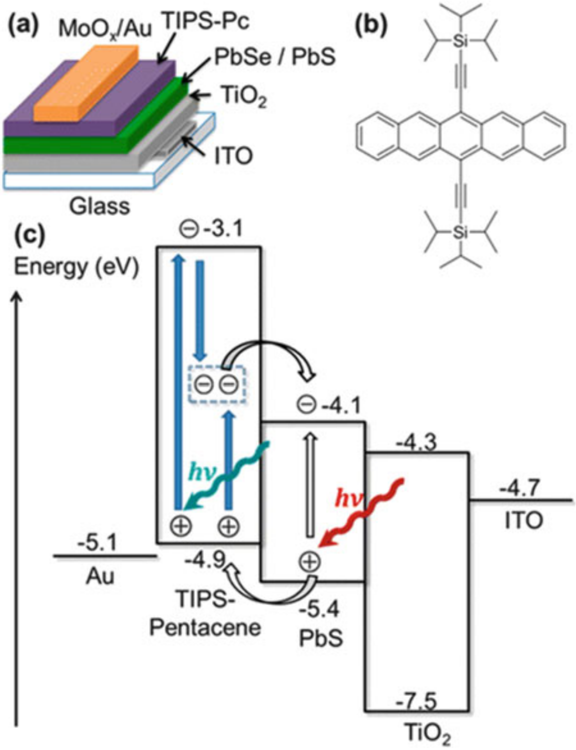
10.5 Singlet Fission

As hinted above, the amount of solar energy that can be converted in electric energy is limited even under optimal conditions (Shockley–Queisser limit, slightly above 20 % in the case of silicon). “Tandem” cells with different bandgaps, each of them optimized for the range of light absorbed, can be connected in such a way that their voltages add in series. A conceptually simpler alternative would be the generation and use of more photons within a single cell. A singlet exciton may undergo a fission process to form two triplet states, as mentioned a spin-allowed process, which thus is potentially fast and efficient. Singlet fission allows a large increase of efficiency of dye-sensitized solar cell, since it exploits energy that would otherwise be lost. As an example, pentacene is known for undergoing efficient singlet fission (the singlet energy is almost exactly twice that of the triplet), although the pentacene triplet is non-emissive and this makes a precise determination of its energy difficult. Measurements of pentacene triplet energy have been obtained by fabricating a series of bilayer solar cells with IR-absorbing nanocrystals of varying bandgaps, which has established triplet energy between 0.85 and 1.00 eV in operating devices. Under these conditions, the power conversion efficiency is 4.7 %, which supports that fission-sensitized solar cells are a favorable candidate for third-generation photovoltaics [41].

Donor–acceptor systems are likewise effective (Scheme 10.9) [42] and still more are quantum dots (nanomaterials small enough to exhibit quantum properties) [43, 44]. A hybrid organic/inorganic architecture has been demonstrated to be able to collect high-energy photons in pentacene, where these are transformed into low-energy photons, while at the same time low-energy photons are collected [45] (Scheme 10.10).



Scheme 10.9 A study on both small molecules and polymers showed that strong donor–acceptor interactions, such as that between thiophene and thiophene dioxide, undergo effective singlet fission, with a triplet yield around 170 % [42]



Scheme 10.10 (**a**) Architecture of a nanocrystal–pentacene photovoltaic device, (**b**) chemical structure of the bis(silylethynyl)pentacene used, (**c**) alignment of energy levels in the device. *Blue arrows* illustrate the singlet fission process in the pentacene upon photoexcitation. Singlet excitons are rapidly converted into low-energy triplet excitons, potentially doubling the photocurrent obtained. The excitons are captured by small bandgap PbS or PbSe nanocrystals. Reprinted with permission from [45]

As easily happening in rapidly growing fields, results are sometimes not easily reproduced from lab to lab. It is therefore important that experiments are carried out under rigorously controlled conditions and that any report that claims a new record of best energy-conversion efficiency in its field is independently certified by a qualified public test center [46, 47].

10.6 Hydrogen as an Energy Carrier

Adopting hydrogen as an energy carrier is appealing since combustion with oxygen is a clean process and gives water as the only product (but burning in air produces also nitrogen oxides) [48, 49].

Hydrogen can be generated photochemically through water splitting by artificial photosynthesis, by photobiological methods based on algae, by thermal water splitting, accessible at high temperatures obtained by nuclear or concentrated solar power plants, or by water electrolysis. The last approach involves using enormous amounts of electric power that has in turn to be generated. Then, the use of hydrogen leads to further problems, among which what to do of coproduced

O_2 and how to store and transport hydrogen. Research has devised promising approaches but is still far from practical applications, and in the next decades producing electricity by burning fossil fuels will still have a key role. Hydroelectric power can give but a very modest contribution. Therefore, it will be necessary to generate large amounts of electric power by nuclear energy of by renewable energies.

A hydrogen economy based on nuclear electricity would imply the construction of thousands of fission reactors, with the attending technic and polytic issues (proliferation, plant decommissioning, and uranium shortage). In principle, wind, photovoltaic, and concentrated solar power have the potential to produce enormous amounts of electric power, but, except for wind, such technologies are too underdeveloped and expensive to tackle such a big task in a short period of time. A full development of a hydrogen economy needs also improvement in hydrogen storage, transportation, and distribution. Hydrogen and electricity can be easily interconverted by electrolysis and fuel cells, and which of these two energy carriers will prevail, particularly in the crucial field of road vehicle powering, will depend on the solutions found for their peculiar drawbacks, namely, storage for electricity and transportation and distribution for hydrogen. Coping with these issues will play an essential role in phasing out fossil fuels [50, 51].

10.7 Socioeconomic Issues

It would be difficult not to concur with the idea that the main thing both citizens and scientists expect from photochemistry is a serious advancement that exploits such a clean and abundant source of energy as solar light and makes available a boundless amount of fuel that way. It is certainly true that solar light impinging on our planet is much more than required in any foreseeable future, but this is so sparse and intermittent that its practical use is not straightforward. Judging whether the glass is half filled or half empty, particularly when attention is given to practical application and perspective, finds quite different answers in the literature. A recent example is a series of papers that appeared in 2013 in the Philosophical Transactions of the Royal Society. The inequality in the distribution of energy is well known, and when the energy consumed (kWh per person per day) is compared with the density of population (people per km^2), it appears that countries with both low parameters have plenty of space to use, but the situation is well different where the amount of energy consumed is high, as in the UK or Germany. In the UK, the average production of energy is 1.25 $W\ m^{-2}$, which is a value close to the average power density available from many renewable sources. This would mean that in order to ensure the present level of energy, one could not use less land than is used presently for agriculture, and highly populated countries such as India and China are “progressing” in the same direction [52].

Tables for the evaluation of electrochemical cells are consistently published [53]. Another evaluation carried out by a commission of the US Department of

Energy detailed the technoeconomic evaluation of photoelectrochemical hydrogen generation prepared by a working group connecting a number of laboratories. Results of this study place the average cost of hydrogen for these systems between \$1.60 and \$10.40 per kg H_2, indicating that commercial-scale implementation of this method could be cost competitive with fossil-based fuels. These evaluations suggest that it is not so much a technical deficiency that inhibits the adoption of artificial photosynthesis, but rather the habit of 150 years in which mankind has learned to exploit fossil fuels that make difficult a complete change [54].

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Chapter 11
Actuators

Light-sensitive molecular tools can be used to monitor/cause a change in a system.

11.1 Photochromism

Photochromism has progressed a long way since the discovery of fulgides by Stobbe at the beginning of twentieth century. As the name implies, this phenomenon involves the interconversion between different chromophores that correspond at the molecular level to a change in the shape, dipole moment, polarizability, or electronic features of the photochromic species. This leads to a change in a large number of macroscopic properties that can be exploited for applications, such as refractive index, transmission of polarized light, reflectivity, light dispersion, polarization, charge transport capability, and dielectric properties [1]. The experiment can be extended to the single-molecule level, and indeed single-molecule fluorescence spectroscopy is being largely explored as are new applications, such as “single-molecule photoswitch” or “superresolution fluorescence imaging” [2, 3].

11.1.1 Fluorescent Switches

Dyes that are highly fluorescent and have large absorption coefficients have been the favored subject of early studies and again are of recent advancements. Photochromic rearrangements that lead to fluorescent species are intensively studied as higher-sensitivity probes. Several classes of such photoswitchable or photoactivatable fluorescent dyes have been reported, as an example non-emitting sulfone derivatives of 1,2-bis(2-ethyl-6-phenyl(or thienyl)-1-benzothiophen-3-yl)perfluorocyclopentene (**1**, Scheme 11.1) that under UV light irradiation are activated to emit green or red fluorescence. The introduction of a phenyl and, still more strongly, a thienyl

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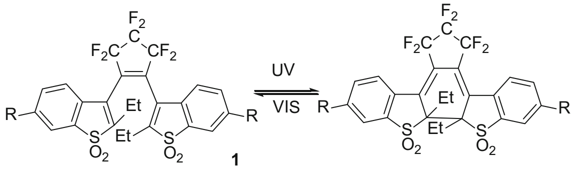
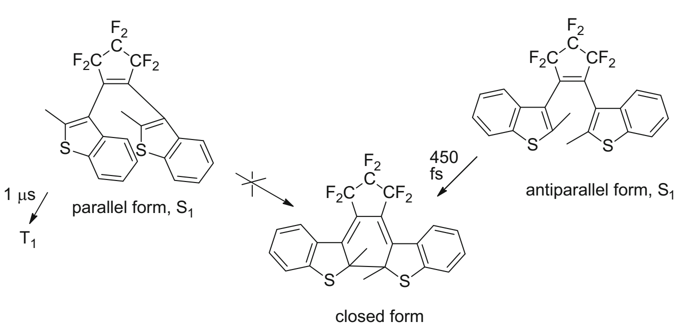
substituent shifts the photochromism toward the colored close form and increases the fluorescence. This in situ activation is potentially applicable to ultrahigh-density optical memory media as well as superresolution fluorescence imaging. The thienyl-substituted derivatives exhibit an excellent fatigue resistance [4].



R	$\Phi_{O\text{-}C}$	λ_{max},nm	$\Phi_{C\text{-}O}$	Φ_F	τ_F, ns
H	0.28	414	0.18	0.22	1.2
Ph	0.42	456	0.0004	0.87	3
C_6H_4COMe	0.51	456	0.0003	0.87	2.8
$C_6H_4CH_2OH$	0.43	463	0.00016	0.88	2.9
C_4H_2SMe	0.21	506	<0.00001	0.78	2.6
C_4H_2SCOMe	0.32	485	<0.00001	0.61	1.9

Scheme 11.1 Appropriate substitution makes the closed form of a series of diarylhexafluorocyclopentenes strongly fluorescent and predominating in the chromophoric equilibrium

New techniques have demonstrated how fast a cyclization can be. Thus, investigation by means of femtosecond–microsecond transient absorption spectroscopy and a time-correlated single-photon counting method of the photoreaction of 1,2-bis(2-methyl-3-benzothienyl)perfluorocyclopentene in nonpolar alkane solutions with different viscosities revealed that a ring closure rapidly occurred with a time constant of 450 fs from the antiparallel form, while from the triplet the predominating path was intersystem crossing to the T_1 state [5] (Scheme 11.2).

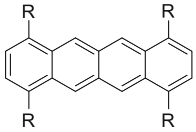


Scheme 11.2 Role of singlet and triplet in di(benzothienylcyclopentenes)

Many organic chromophores emit strongly in dilute solution but less so when increasing the concentration or in the solid state (concentration quenching, due to the predominance of non-emissive paths due to aggregation compare Sect. 9.5). However, some molecules exhibit the contrary behavior and emit from aggregates (aggregate-induced emission). This has been rationalized by Kasha on the basis of the exciton theory applied to one-dimensional aggregates and the dependence of the exciton displacement energy on the mutual orientation and separation of two neighboring molecules [6].

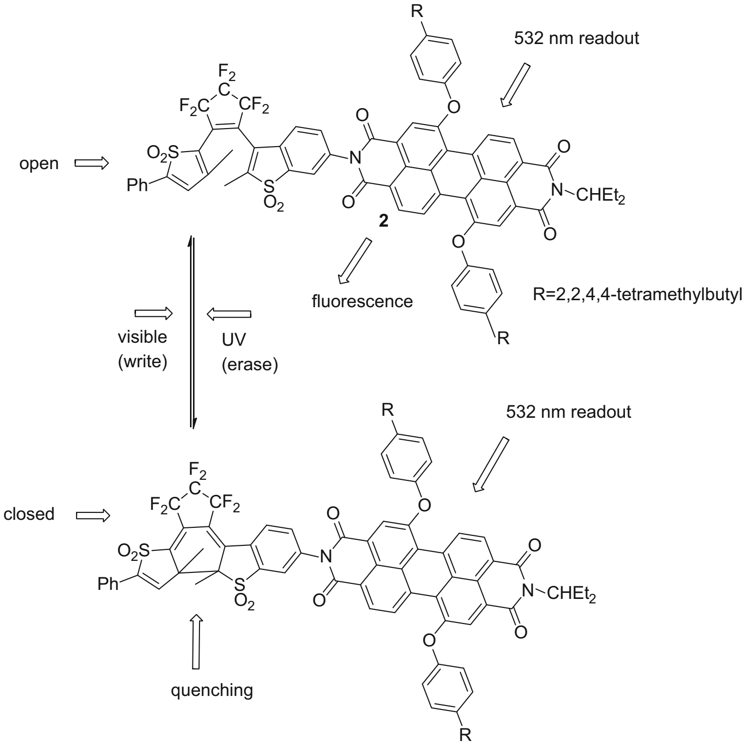
The theory has been extended to the three-dimensional case by Kitamura and explained the observed shifts [7]. Tetracenes bearing alkyl substituents in the A and D ring (Scheme 11.3) form aggregates that are highly fluorescent in the solid state. In particular, introducing alkyl groups in positions 1, 4, 7, and 10 red shifts the emission from yellow to orange and red with an increase of the emission quantum yield from 0.01 to 0.9.

Scheme 11.3 Solid-state fluorescence of some tetrasubstituted tetracenes



R	λ_{em}	Φ_F
Me	578	0.21
Et	564	0.40
Hex	623	0.28
i-Pr	566	0.90

Indeed, several fluorescent photochromic molecules and fluorescent proteins have been applied to optical memories and super-high-resolution imaging. However, a further aspect has to be confronted, viz., the “fluorescence readout capability” that has to be “nondestructive” in order to ensure a satisfactory performance. For example, in the case of molecule **2** (Scheme 11.4, Fig. 11.1), the readout at 535 nm involves the perylenebisdiimide unit that emits fluorescence at 568 nm but is quenched by electro-transfer with the closed dithienyl dioxide function within 180 ps. Both open and closed isomers showed a long persistence (no change after 120-min irradiation at 535 nm). Ring closure (445 nm) and opening (360) thus give a nondestructive fluorescence readout system at the single-molecule level, as demonstrated in samples in poly(methyl methacrylate) films, with ultrahigh-density memory (at the level of Tbits per inch^2) and super-high-resolution imaging [8].



Scheme 11.4 A highly photostable chromophoric molecule

The bichromophoric dye **3** (Scheme 11.5, the diphenylethynylanthracene moiety functions as sensitizer for the dithienylethene photochromic system) has been used for generating a "digital" fluorescence at the single-molecule level. Thus, visible-light irradiation of compound **3** for 10 s caused the switching of four molecules to the fluorescent "on" state, as revealed by confocal fluorescence. Irradiation with weak ultraviolet light for 3 s led then to the nonfluorescent "off" state, but the phenomenon could be repeated by irradiating with visible light for 10 s [9].

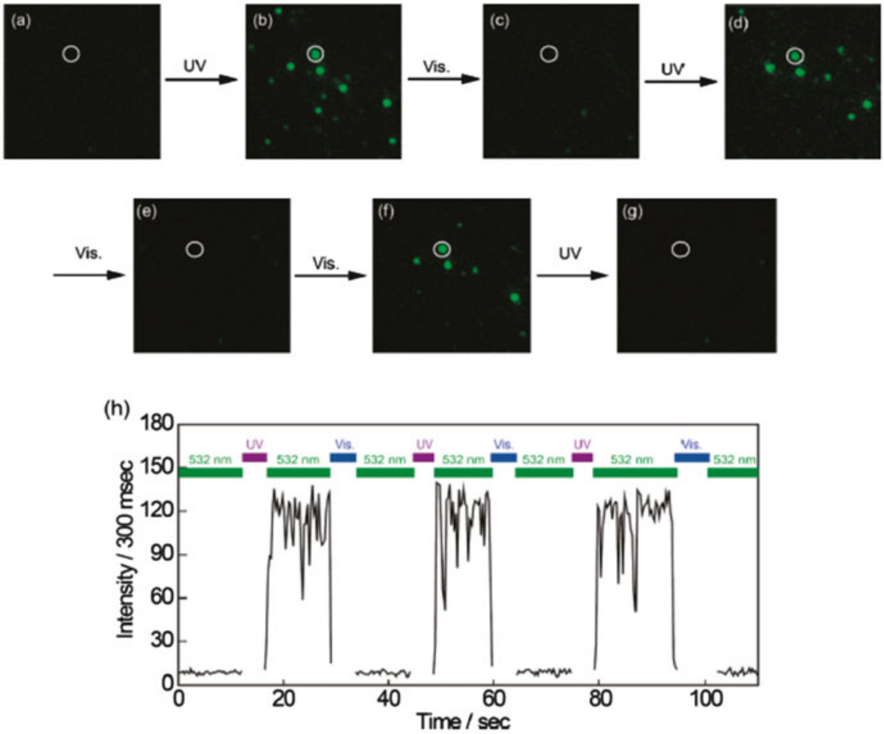
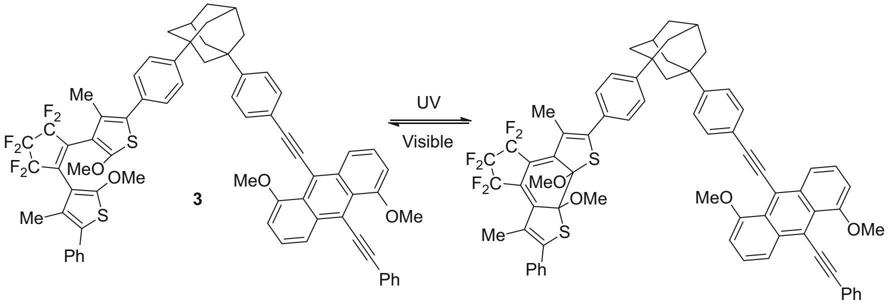


Fig. 11.1 Single-molecule fluorescence photoswitching in a poly(methyl methacrylate) thin film. At the bottom is the time trace of fluorescence intensity of a single molecule of compound **2**, indicated by a *circle* in the figure at the *top* under alternate visible and UV irradiation. Reprinted with permission from [8]

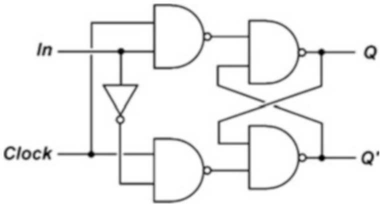


Scheme 11.5 Intramolecular sensitization of photochromism in a bichromophoric molecule

11.1.2 Electrical Functions of Photochromic Molecules

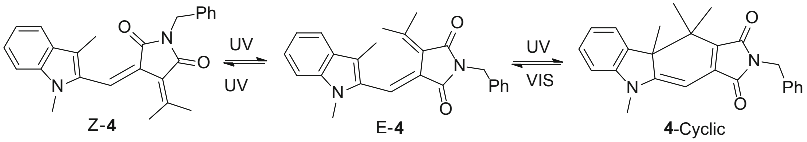
Films of (or films doped with) photochromic molecules as well as polymers containing photochromic moieties in the main chain have been shown to undergo changes in conductivity upon irradiation. Optical memories and electric circuitries have been built on this base [10].

The bistability of photochromic systems makes them par excellence candidates for the implementation of molecular switches in general, including all-photonic sequential logic switches, with the advantage of easy spatiotemporal control and the independence from many variables (while, e.g., chemical inputs are limited by diffusion). Indeed, molecule-based systems that mimic the conventional silicon circuitry have been developed. Thus, in electronics a flip-flop is a circuit that has two stable states and can be used to store information. Control inputs cause a change in the state and will have one or two outputs. Flip-flops are the basic storage element in sequential logic and store a single bit of data, a state representing a “one” and the other one “zero” (Scheme 11.6) [11].



Scheme 11.6 A flip-flop circuitry. Reprinted with permission from [11]. Open access

The functional integration with a molecule-based system is illustrated in Scheme 11.7 by using fulgimide **4**. Q' symbolizes the complementary output [11].



Scheme 11.7 A molecular equivalent of a flip-flop circuitry

The open E-**4** form has an absorption maximum at 374 nm and irradiated at 366 nm gives the colored closed form (523 nm). The absorbance of the colored form or its fluorescence (644 nm) can be used. As shown in the scheme, the fundamental wavelength of an Nd:YAG laser (1064-nm IR light) is taken as data input *In* and the second harmonic (532 nm) produced by the second-harmonic-generating crystal as *Clock* input. Application of both input wavelengths will produce 355 nm UV light via a third-harmonic-generating crystal. Schematically, the following cases result:

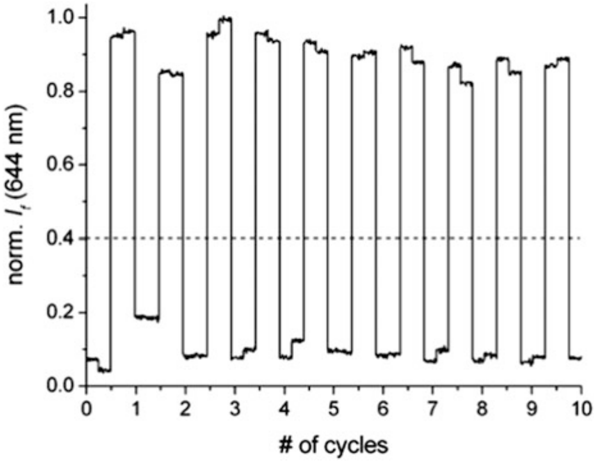


Fig. 11.2 Switching cycles of fulgimide **4** when operated as a D flip-flop. The fluorescence output (λexc = 550 nm, λem = 644 nm) with associated noise is shown for ten cycles. One cycle consists of the following action sequence: (1) irradiation with 1064-nm IR light; (2) simultaneous irradiation with 532-nm light and 1064-nm light via a THG (effectively corresponding to 355-nm light); (3) irradiation with 1064-nm IR light; (4) irradiation with 532-nm light. Each irradiation step was performed for the constant time of 45 s, and the fluorescence output was monitored for 5 s. The *dashed line* represents the threshold level used to distinguish output = 1 from output = 0. Reprinted with permission from [8]

Clock = *In* = 0, no irradiation, the switch (E-**4** or **4**-cyclic) and the fluorescence from it remains unchanged; hence, *Q*current = *Q*next results.

In = 1, *Clock* = 0, again no effect on the switch, *Q*current = *Q*next.

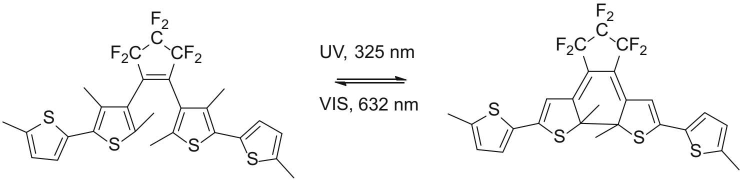
In = 0, Clock, then always the nonfluorescent open-form E-**4** prevails. Hence, *Q*next = 0 applies, regardless whether E-**4** or **4**-cyclic is irradiated.

Clock = *In* = 1355-nm UV light is generated via the third-harmonic-generating crystal; E-**3** is converted to **4**-cyclic, while the latter isomer is unaffected. Thus, fluorescence is observed (*Q*next = 1). As the authors conclude, “whenever the 532 nm light is avoided (*Clock* = 0), the flip-flop is not enabled and the current state (form) of the photochrome persists (*Q*current = *Q*next) and whenever *Clock* = 1 applies, the state of the data input (*In*, 1064 nm IR light) is directly transmitted to the output. These binary logic characteristics are coincident with the D flip-flop” [11] (Fig. 11.2).

11.2 Two Color/One Color

Traditionally, the pattern resolution is limited to about a half of the wavelength used. However, this limit can be overcome, e.g., by adopting a technique called absorbance modulation [12]. In this case, a thin film of a photochromic material

(Scheme 11.8) is placed on top of the photoresist layer. The molecules chosen adopt two forms that are interconverted by UV (λ_1) and, respectively, visible (λ_2) light. The irradiation with both colors is then carried out in an interference pattern that overlaps peaks at λ_1 with nodes at λ_2. Absorption at λ_1 causes some ring closure to give the isomer transparent to that wavelength, but absorption at λ_2 reverts back to the ring-opened form that continues to absorb λ_1. At λ_2 nodes, however, a stable population of the ring-closed form and thus a transparent area build up. Light at λ_1 penetrates this area and patterns the underlying photoresist. The size of the aperture deceases as the ratio of the intensity at λ_2 to that at λ_1 increases and thus confines light at a dimension far smaller than that of the wavelength.



Scheme 11.8 Isomerization of a photochromic material to produce absorbance modulation [12]

Thus, the switching between the two forms is obtained by using two light sources of different colors. However, using a single source is also possible by having recourse to multiphoton absorption. In fact, the transition probability of nonresonant simultaneous multiphoton (n photon) absorption processes is dependent on the power of incident light intensity, I, as I^n. Thus, one may expect that the level of electronic states attained by the multiphoton absorption can be controlled by the light intensity. For instance, when using a near-infrared light with a rather weak intensity, two-photon absorption would lead to the energy level of $2h\nu$, in the visible, while three-(or more)-photon absorption would lead into the UV. The latter process would become dominant if the light intensity would be increased. In fact, this has been proved by the Irie group. In the experiment, the dithienylethene derivative **5** as an amorphous solid has been excited by an NIR femtosecond laser microscope. This provided the pulse duration of 35 fs when using the femtosecond Cr/forsterite (Cr:F) laser at 1.28 μm through a tightly focused objective. This resulted in a high peak intensity of ca. 10^{31}–10^{32} photons cm^{-2} s^{-1}, despite the rather weak output energy of the laser (typically, <1 nJ/pulse). As it is shown in Fig. 11.3, when an amorphous film of the compound prepared by spin coating was irradiated for 50 ms (100 kHz), coloration was induced (i), while the exposure with the weaker intensity of 48 pJ/pulse (100 kHz) for 180 s led to decoloration (ii). This colorization and decolorization could be repeated (iii and iv). It was further shown that the system could be applied to the space-resolved patterning. In essence, the more intense central part of the beam induces the three-photon absorption, while the two-photon absorption is dominant in the boundary area with low intensity of the beam. The full width at half-maximum of the colored spot was ca. 600 nm. Such experiments support that high-order multiphoton process can be induced without large laser systems and that the submicrometer resolution can be

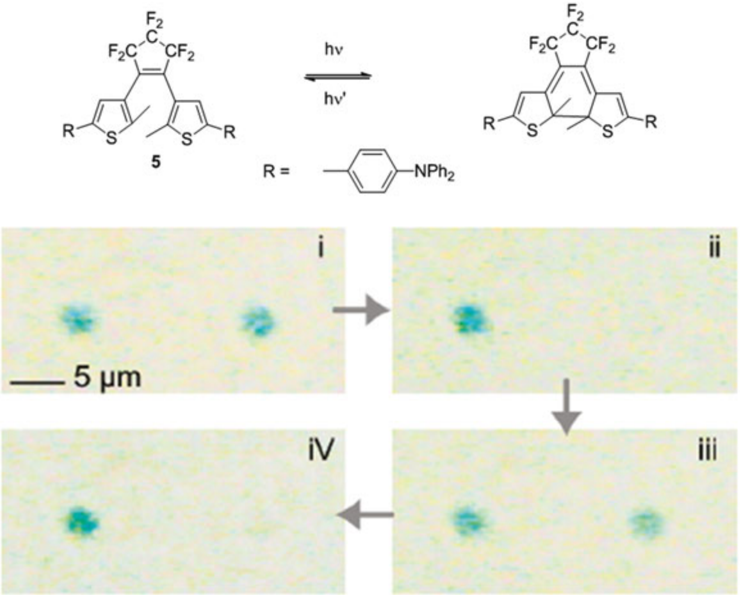


Fig. 11.3 Irradiation of the dithienylethene **5** by a Cr:F laser at 1.28 μm with 0.7 nJ pulses for 50 ms produces colorization (**i**), with the lower intensity of 48 ps for 180-s decolorization (**ii**) and the process can be repeated (**iii**, **iv**). Reprinted with permission from [13]

easily attained by using one-color multiphoton colorization and decolorization reactions. Photochromism induced by high-order multiphoton absorption in the NIR region may be advantageously applied for obtaining an increase in the memory density. The NIR laser light around 1.3 μm in the light-wave communication frequency could provide new applications of molecular memory systems directly coupled with the communication light wave. Furthermore, the viability of spatial patterning suggests that a combination of high-order multiphoton absorption processes could open a new maskless pattern formation by using photochromic materials (see Fig. 11.3) [13].

The very large variety of applications of popular classes of photochromic materials, such as dithienylethenes, find a limitation in the requirement of using visible or UV light. However, this limitation can be overcome and activation extended to near-infrared (NIR) light excitation to trigger the photochemical reactions via multiphoton absorption. This usually requires a powerful source. However, a rather elaborated system has been proposed based on the spatial differentiation of areas (Fig. 11.4). Core–shell–shell-type $NaYF_4$ nanoparticles are built which contain Er^{3+}/Tb^{3+} or Tm^{3+}/Er^{3+} cations in spatially different areas. Thus, light generated under high excitation power densities induces three-photon fluorescence and this is reached in UV, the suitable wavelength range for ring opening, while that generated under low excitation power density arises via two-photon excitation and is reached in visible, suitable for inducing ring opening.

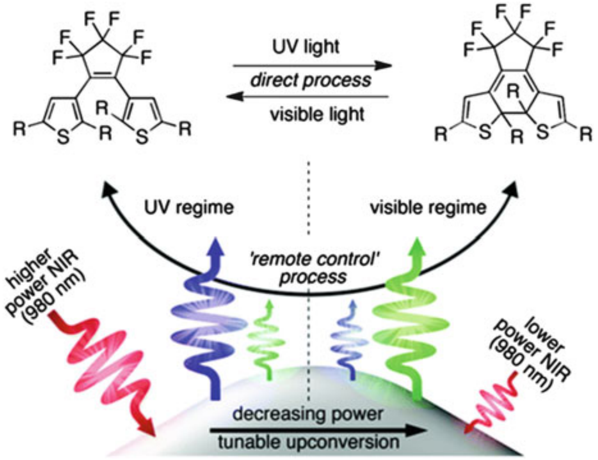


Fig. 11.4 The "direct" photoreactions of the dithienylethene derivatives are triggered by UV light (for ring closing) and visible light (for ring opening). These reactions can also be triggered in a "remote control" process using the UV light generated under high excitation power densities and the visible light generated under low excitation power densities when the core–shell–shell upconverting nanoparticles doped with lanthanide cations. Reprinted with permission from [14]

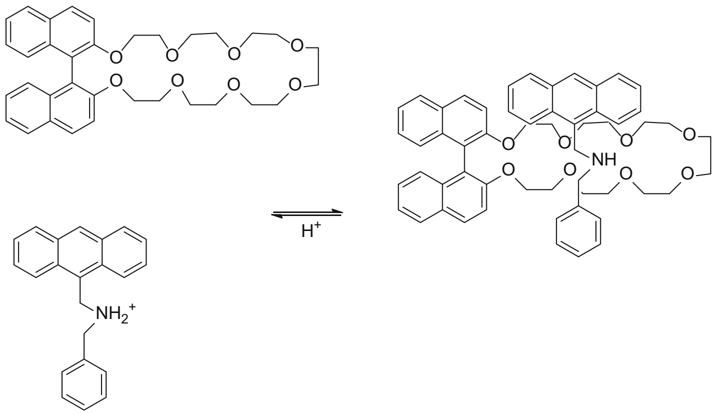
This achieves a "remote control" photoisomerization, operating by varying only the intensity, not the wavelength of the exciting light [14].

11.3 Photomechanical Actuators

11.3.1 Molecular Motors from Molecular Movements

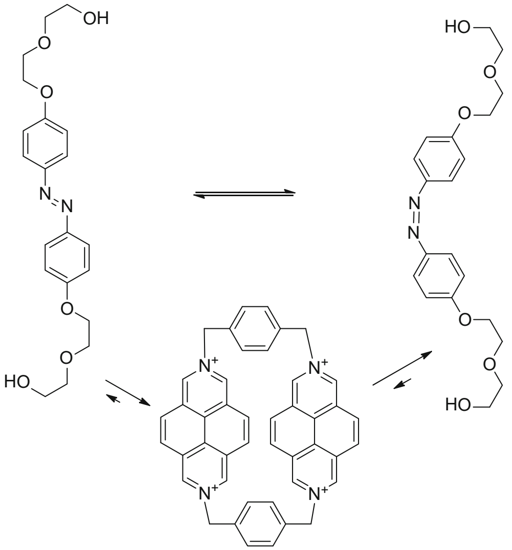
Chemical reactions involve a change in shape and properties of molecules. This microscopic change can be translated into a macroscopic effect, resulting in a change in the shape of an object or exerting a force that moves an object. Provided that the system is bistable, at least in the time scale of the effect considered, a change in the shape can be used either for detecting and registering a signal or for exerting a mechanical force. In both cases, nature is much in advance (think of the isomerization of rhodopsin in vision or the movement of a muscle) and for the moment is far above what chemists can device. In principle, photochemistry may have an important role in this field, having the advantage that the photon carries with itself a large amount of energy and leaves no waste.

An approach is through supramolecular chemistry by facilitating complexation. Thus, a donor such as an alkylamine is easily complexed by an acceptor, and this can be built in a system resembling a plug in/out of a wire, but an ammonium salt will not; thus a difference in fluorescence emission will be observed depending on pH (Scheme 11.9) [15].



Scheme 11.9 Amines thread in the crown ether, ammonium salts do not

On the same idea, a piston–cylinder system can be built, e.g., based on the different complexation tendencies of *E*/*Z* azobenzene into a diazapyrenilium cavity (Scheme 11.10) [15].



Scheme 11.10 *E* azobenzene derivative fits into a diazapyrenilium cavity, the *Z* isomer does not

11.3.2 Macroscopic Effects

Photochemical reactions may induce major macroscopic changes in objects. Another important system is based on chiroptical molecular switches built from overcrowded alkenes where light causes reversible interconversion between right-and left-helical forms and thus to applications such as high-density data storage. Even with a very low enantioselectivity, the use of chiral compounds such as the azo compound **6** as dopant in a low-molecular weight host nematic liquid crystal material was sufficient for obtaining chiral cholesteric liquid crystal films [16].

Furthermore, just as photochemistry is a clean way to cause a reaction, it may offer a clean way to cause a movement in a macroscopic object. As a matter of fact, this is an issue rarely adopted by nature, where direct conversion of light into mechanical energy is limited to a few cases in bacteria [16]. This does not preclude adopting this principle for artificial system. As an example, one may think of controlling and directing the Brownian motion of molecules in solution and to induce directional translational and rotary motion of molecules or of nano-objects. In other words, rotary and translational motors may be devised and used to power future nanodevices. For example, rotary molecular motors allow the transmission of motion in multicomponent systems as well as reaching out-of-equilibrium assemblies (see Fig. 11.5) [18].

The most used design is based on chiral overcrowded alkenes. Consecutive elaborations have led to new functions, as shown in Fig. 11.6. "First-generation" light-driven molecular motors consist of two identical chromophores linked through a central alkene which serves as the axle of rotation [17]. Two photochemical *cis-trans* isomerization steps that force the methyl substituents in an unfavorable pseudoequatorial position are followed by two thermal isomerization steps (energetically downhill) that reestablish the favorable pseudoaxial orientation of the methyl substituents. As the result, the motor functions the unidirectional 360° rotation of the upper half relative to the lower half through a four-step switching cycle and the directionality of the rotation is governed by the chirality of the two stereogenic centers. In "second-generation" molecular motors, a more sterically

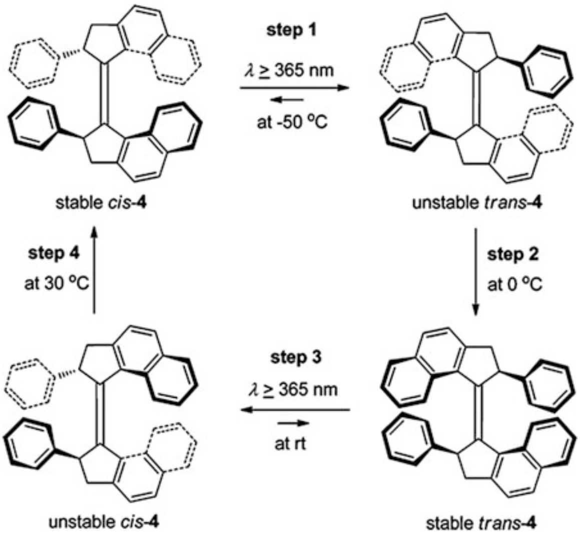


Fig. 11.5 Rotation around a double bond mimics the movement of a motor. Reprinted with permission from [17]

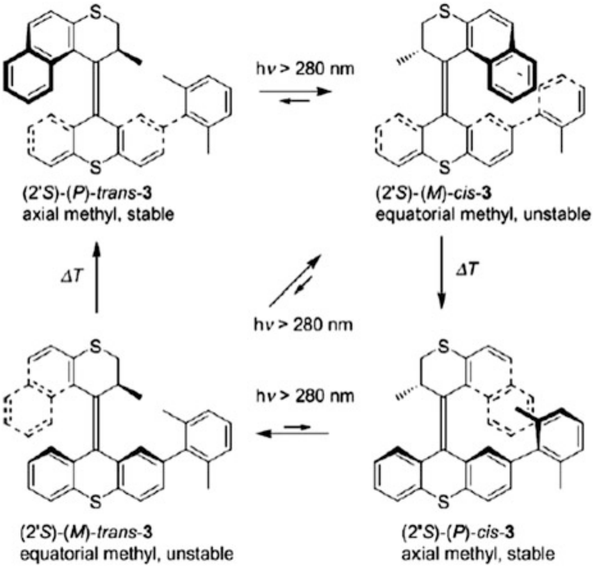


Fig. 11.6 Introducing a molecular gearbox. Reprinted with permission from [19]

demanding phenyl is substituted for the methyl group, thus hindering to a various degree the rotation [17]. The slightly increase in the barrier for the thermal helix inversion step demonstrated the transmission of motion. Thus, when embedded as chiral dopant in a liquid crystal film, this motor caused the rotation of a microscale object on top of the LC film. Another example of functional molecular motor is the so-called "molecular gearbox" motor (Fig. 11.7), where two rotary units are present, and a further molecular device controls intramolecular movement and coupling of motor and rotor functions of the device [19].

This principle has been developed and further implemented by extending the conditions of application and tuning the barrier to rotation, as well as by introducing new molecular tasks that can be performed in a sequential manner, with the sequence controlled by the directionality of a rotary cycle. Importantly, driving molecular rotary motors has been proved possible also by using visible light (530–550 nm) instead of UV light [21], an improvement that was achieved using palladium tetraphenylporphyrin as a triplet sensitizer rather than direct irradiation. Sensitization occurs more efficiently intramolecularly, by covalently linking the porphyrin to the "motor" structure. Light-driven "first-generation" molecular motors have been used also as molecular stirrers [22]. Unidirectional molecular rotary motors offer an appealing method for harnessing solar energy and converting it into mechanical motion [23].

A further dimension can be added by assembling such motors on a surface. This allows both to measure the properties of individual molecules in relation to the environment and to couple functions between assembled molecules [24].

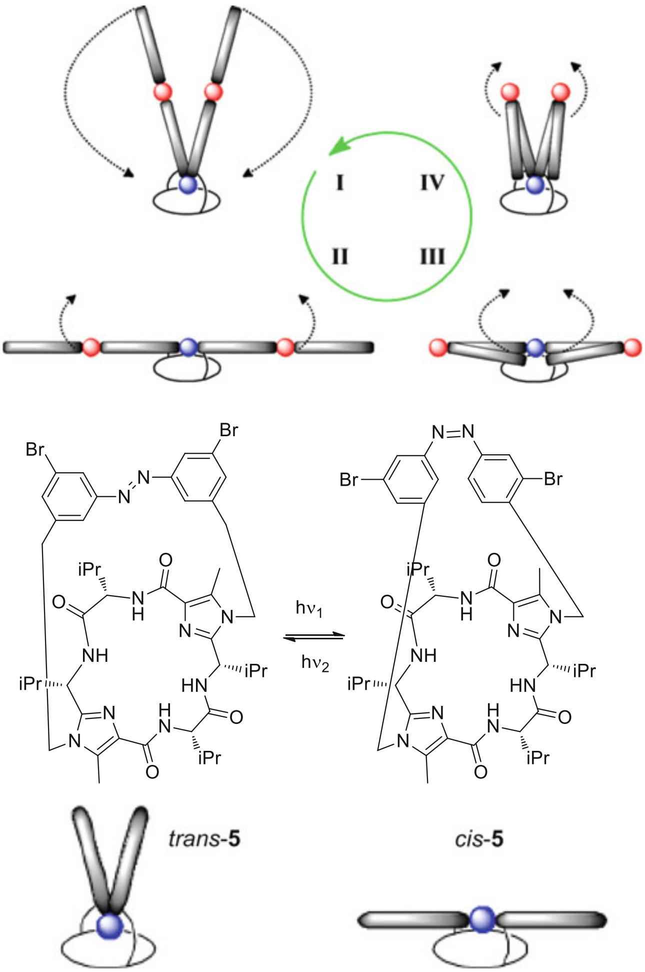


Fig. 11.7 Mimicking the movement of a swimmer, reprinted with permission from [20]

The movement of a human being swimming has been reproduced in a nanomachine capable of unidirectional, four-state switching cycles that are similar to the movement of a breaststroke swimmer. The nanomachine consists in a torso and two foldable "arms" (Fig. 11.7). The base is a peptidic, macrocyclic scaffold that controls the direction of the movement. The arms are rotated around one hinge and are stretched and folded by another hinge. The machine is moved by alternating addition of chemicals (complexation of a bipyridine by copper ions) and irradiation (isomerization of the azo function) [20].

11.3.3 Mechanical Work from Crystal Deformations Caused by Molecular Transformations

In the solid state, strain develops during the irradiation between reacted and unreacted crystal phases. Generally, this leads to fracture and crystal disintegration (the crystals "burnst," a phenomenon often observed, as several times mentioned in Chap. 4). However, if molecules are oriented in a crystal lattice, the microscopic change in the structure, thus in Angstrom range, may translate into a much larger change (micron to mm) [25]. Thus, during the reaction the exciting light leads to a gradient of reacted and unreacted molecules (Fig. 11.8). This makes a bimorph-type actuator, the motion of which is driven by a strain between the different phases and may be exploited for mechanical work. When the reaction is complete, a reconstruction to accommodate new packing arrangements of the product molecule might take place.

It is possible to design molecular crystal nanostructures where the directional response is "built in" by the crystal shape and molecular packing. As an example, a single crystal of 1,2-bis(2-ethyl-5-phenyl-3-thienyl)perfluorocyclopentene changes from a square shape to a lozenge shape in about 25 μs. On the other hand, a rectangular single crystal of 1,2-bis(5-methyl-2-phenyl-4-thiazolyl)perfluorocyclopentene contracts by about 5–7 %. In both cases the deformed crystals are thermally stable and return to the original shape when the photochemical reaction is reversed by visible-light irradiation. It can be taken advantage of this deformation for moving microscopic objects (see Fig. 11.9) [26].

Co-crystals composed of a diarylethene derivative and perfluoronaphthalene, with dimensions varying between 1 and 5 mm in length, 0.2 and 1.5 mm in width, and 10–50 μm in thickness bend upon irradiation, and enhance the tip by 1 mm

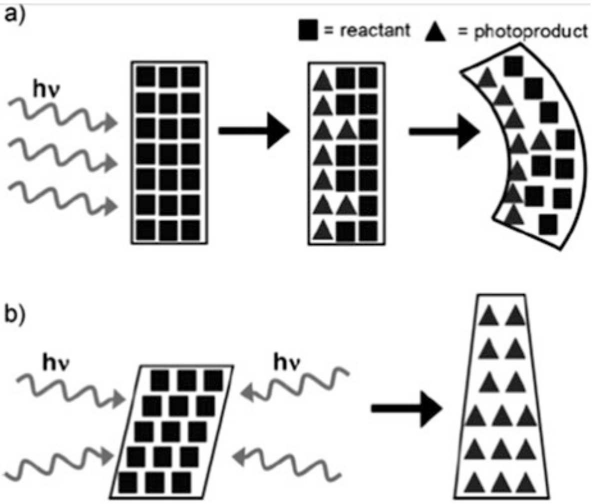


Fig. 11.8 (**a**) Attenuation of exciting light leads to a gradient of concentration during the photochemical reaction of a crystal; (**b**) complete photoreaction. Reprinted with permission from [25]

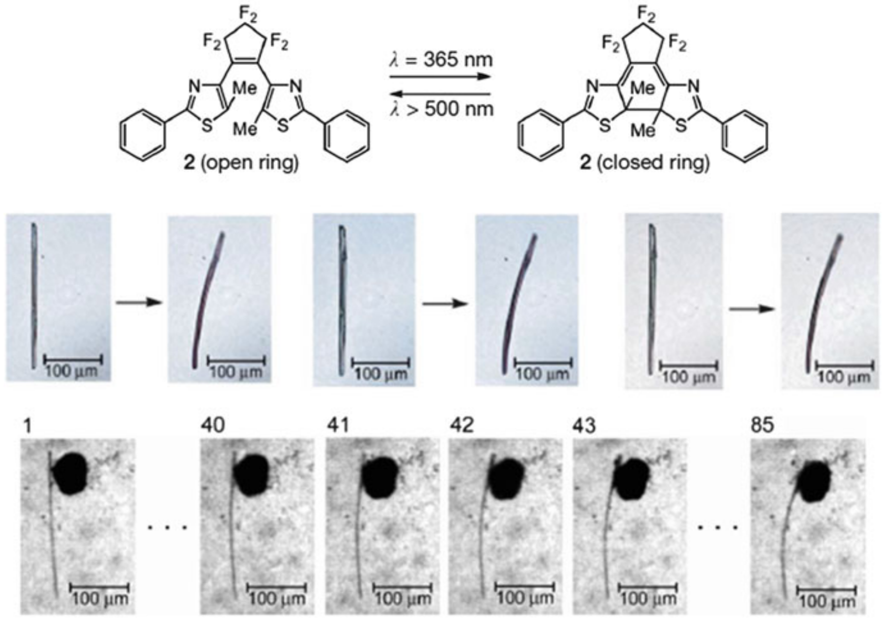


Fig. 11.9 (*top*) Alternate irradiation with UV (365 nm) and visible (>500 nm) light of rodlike crystals (225 × 7.5 × 5 µm) of dithiazolylethylene **6** causes reversible bending with the head moving as far as 47 µm. The bending–straightening cycle could be repeated up to 80 times. In the figure, pairs of images refer to the first, 5th, and 18th cycle. (*bottom*) Irradiation with 365-nm light of rodlike crystals (250 × 5 × 5 µm) causes bending. A gold microparticle 90 times heavier than the crystals is pushed as far as 30 µm. Reprinted with permission from [26]

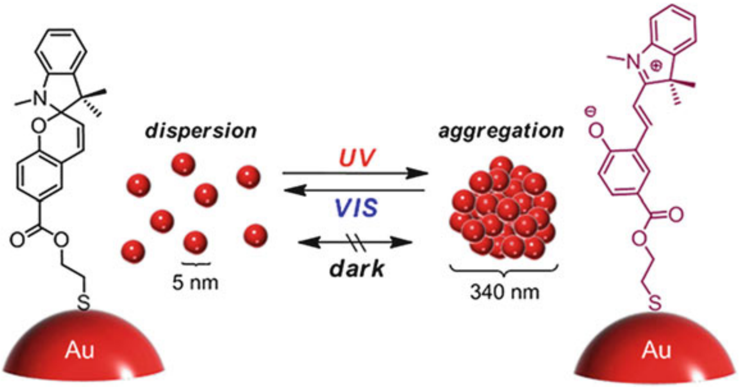


Fig. 11.10 The spiropyran isomerization affects reversibly the aggregation of gold nanoparticles. Reprinted with permission from [27]

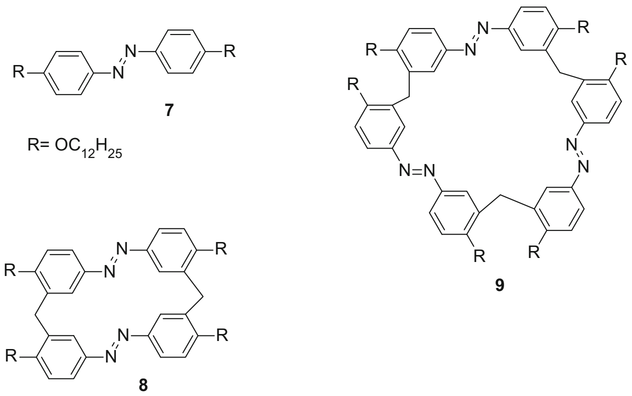
(Fig. 11.10). Still, the crystals remain strong enough to lift a 2 mm lead ball 275 times heavier than themselves and a 3 mm steel ball around 600 times heavier [28]. The crystals withstand a stress estimated at 44 MPa, much larger than muscles do (ca. 0.33 MPa), and this suggests that exploiting molecular movements to do real work on the macroscopic scale is possible [29, 30].

The integrity of the crystals during the photoreaction, and thus the possibility of harnessing mechanical work, is not granted, however. Thus, irradiation of solid dimethyl-2(3-(anthracen-9-yl)allylidene)malonate caused E/Z isomerization (DMAAM) and a pulse of visible light induced a curling motion in crystalline nanowires [31]. The phenomenon has been individuated also for different reactions, provided that very thin (<1 μm) crystals are used, presumably because the torsion constant depends on the crystal thickness, so that only very thin ribbons are susceptible to torsion. Thus, 4-chlorocinnamic acid (4Cl-CA) undergoes irreversible [2+2] photodimerization reaction with formation of a new crystal phase, but prolonged irradiation leads to an amorphous solid. However, microribbons with submicron thicknesses twist under irradiation, while no response is observed in crystals with thicknesses of 5–10 μm [32].

Likewise, oriented crystalline microribbons of 9-anthracenecarboxylic acid, a molecule that undergoes a reversible [4+4] photodimerization, rapidly twist when exposed to spatially uniform light irradiation. After that light is turned off, they relax back to their original shape in minutes, and the twist–relax cycle can be repeated. It appears that the reversible twisting involves the generation of interfacial strain within the ribbons between unreacted monomer and photoreacted dimer regions, with an interaction energy on the order of 3.4 kJ/mol [33]. Crystal nanorods of 9-anthroate esters—the crystal structure of which can support a [4+4] photodimerization reaction—react and undergo photomechanical deformations without fragmentation. The *tert*-butyl ester has been studied in more detail, and it has been found that a metastable intermediate is formed, probably the [4+4] photodimer that has not yet undergone the ester group rotations and repacking required to form the low-energy dimer crystal structure, which is then formed over weeks. This result shows that the photomechanical response of these molecular crystal nanostructures cannot be predicted based solely on knowledge of the equilibrium reagent and product [34].

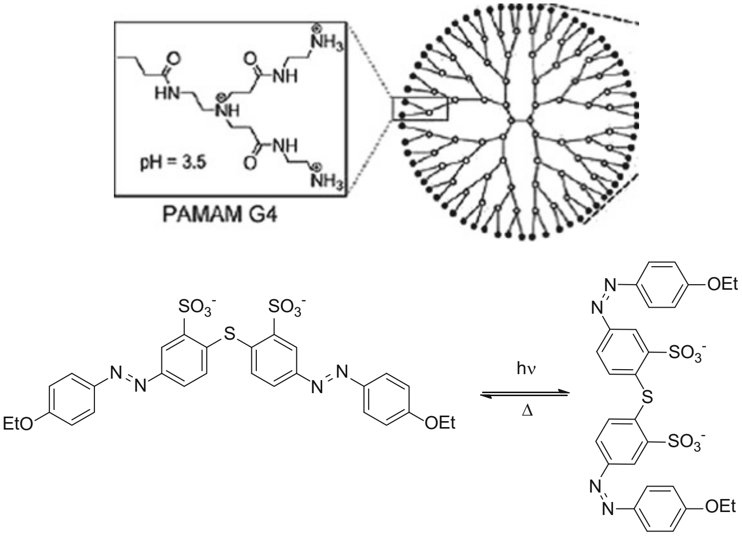
11.4 Self-Assembling

Controlling self-assembling leads to a variety of application. As an example, disk-shaped molecules are known for their tendency to self-assembling and to form liquid crystals. The molecular alignment required can be perturbed by altering the flat geometry of the molecules. An external stimulus, such as light, can thus switch on and off the properties. The azobenzene *E*/*Z* isomerization has proved to be well suited for this task. As an example, the cyclic polyazo compounds **7**, **8** (Scheme 11.11) form liquid crystals. Irradiation in solution shows that the initial all-*trans* configuration converts into a steady-state containing >95 % of the *cis* isomer. In the LC state, cyclic dimer **8** behaves as a rodlike molecule, but under irradiation, an isotropic phase transition from LC to isotropic occurs within seconds. Return to the LC phase occurs likewise in seconds when light is put off. Trimer **9** behaves as a disklike molecule and exhibits a photoinduced isothermal phase transition from columnar to isotropic by irradiation, in this case only slowly reversible. Such photoresponsible materials have potential applications in photolithography, photosensitive adhesives, and others [35, 37].



Scheme 11.11 Azo compounds that form liquid crystals

In another approach, *trans-cis* azo isomerization has been found to affect nanoparticles formed by the assembly of macroions with multivalent oppositely charged organic ions. A system based on electrostatically self-assembled nanoparticles consisting in a fourth-generation poly(amidoamine) dendrimer and an anionic azo dye (acid yellow 38). When mixing the solution of the components and adjusting the pH at 3.5, the amine group is protonated and associates with the anionic dye. Both 100 % *trans* and 80 % *cis* (obtained by irradiation prior to mixing) gave the same result. However, irradiation of the assembly limited isomerization (to 47 %) and produced a conspicuous change in the visual appearance because of light scattering. This was shown to be due to the remarkable increase in size of the nanoparticles, from 140 ± 15-nm diameter and 32 ± 9-nm height prior to irradiation to 480 ± 70-nm diameter and 180 ± 60-nm height for the irradiated samples, apparently due to a decrease in steric or electrostatic stabilization. Disassembling and reassembling into the original structure was achieved by appropriate pH changes [36] (Scheme 11.12).



Scheme 11.12 Azo compounds form salts with a polyamino dendrimer. Elaborated with permission from [36]

Another application of a photochromic reaction involves the reversible size control of gold aggregates in nanoparticles by using *S*-functionalized spiropyran derivatives. In the dark, the merocyanine form associates with each other, which suppresses the thermal rearrangement. Irradiation, on the contrary, accurately tunes the dimension due to the different electrostatic properties of spiropyran and merocyanine (Fig. 11.10) [27].

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Chapter 12
Photochemistry and Green Synthesis

Green chemistry is the answer chemists have given to the increasingly stringent demand for environment preservation. Key issues are "clean" reactions that can be adopted industrially in the place of "dirty" or unsafe methods, the banning of products that are in any way dangerous to human health and to the environment in general, that is leaving to our children a world not worse than that we are living in now. Green chemistry has both a preparative aspect and a destructive one, viz., a target is making available useful products from clean sources in a clean way and the other one is avoiding that pollutants remain in the environment by destroying (mineralizing) them. In both cases, the photon can be considered the green reagent par excellence in that if absorbed it causes a reaction, and often a deep seated one, while if it is not, no change is caused and light simply traverses the sample unaltered. Obviously, the perfect choice is using solar light, because producing artificial light is expensive in terms of resources. Furthermore, green photochemistry can help in transforming spontaneous growing materials into useful compounds. The use of a photocatalyst expands the range of active wavelengths and often allows to better control the processes.

12.1 Photochemistry for Bioresources

Modern society was born when the way to exploit high-energy density fuels, mainly hydrocarbons, from fossils, was found, and the market was flooded by cheap energy. Sustainability demands to revert the approach and that even low calorific, oxygen-rich sources are to be exploited. Thus, rather than consuming nonrenewable high-energy resources that have been formed in faraway eons, mankind should learn to use the renewable resources the environment produces every year. Thus, lignocellulosic biomass, such as "spontaneous" herbaceous or woody crops, industrial crops, forestry waste, agricultural residues, as well as municipal paper waste, should be used to generate energy or chemicals.

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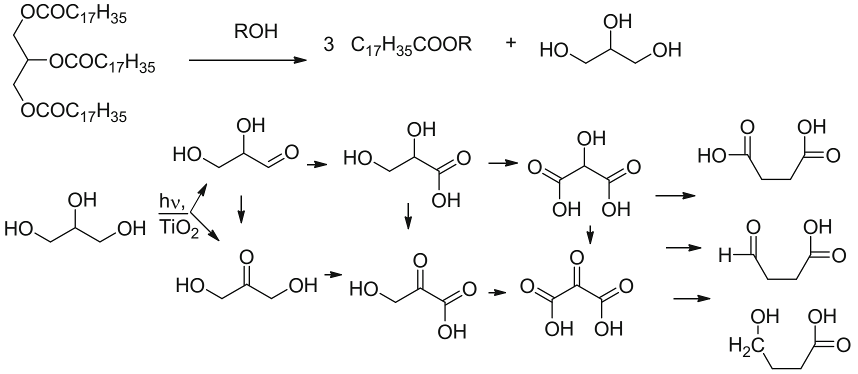
Several paths are available. Hydrogen production directly from biomass has been obtained by photofermentation, that is, by the action of photosynthetic bacteria. The biomass consisted in lactic acid or related materials, waste materials, and sugar biorefinery waste [1, 2].

Otherwise, the biomass may be converted into high-value chemicals after a series of reactions, but this demands that such complex structures (lignocellulose is composed of cellulose, a high polymer of glucose, held together by hemicelluloses and lignin) must first be decomplexed in order to use a more convenient starting compound. Photocatalysis under UV or solar irradiation has been shown to contribute effectively to such degradation [3–6]. The oxidation of aromatic alcohols and the oxidative degradation of acids have been studied as a model [7]. Another issue is the transformation of glycerol, a by-product from the conversion of oils and fats into methyl or ethyl alkanoates (biodiesel). The amount available is difficult to place on the market and it is more convenient to oxidize it, e.g., through photocatalysis to C3 and C2 derivatives, useful in synthesis (Scheme 12.1) [8].



Scheme 12.1 Glycerol, available in large amounts from the preparation of biodiesel, is transformed into useful chemicals

12.2 Preparative Photochemistry

12.2.1 Assessing the Green Potential

For the reasons outlined above, photochemistry is potentially an important part of green synthesis. However, most reported photochemical reactions have been developed with a mechanistic target, rather than having in mind maximizing preparative yields, let alone minimizing the use of resources, to begin with those consumed for firing artificial lamps used for irradiation. Thus, a literature process may have been reported as green, but it is advisable to reevaluate it as a green process, if this has not be done in the original publication. This may be conveniently carried out by

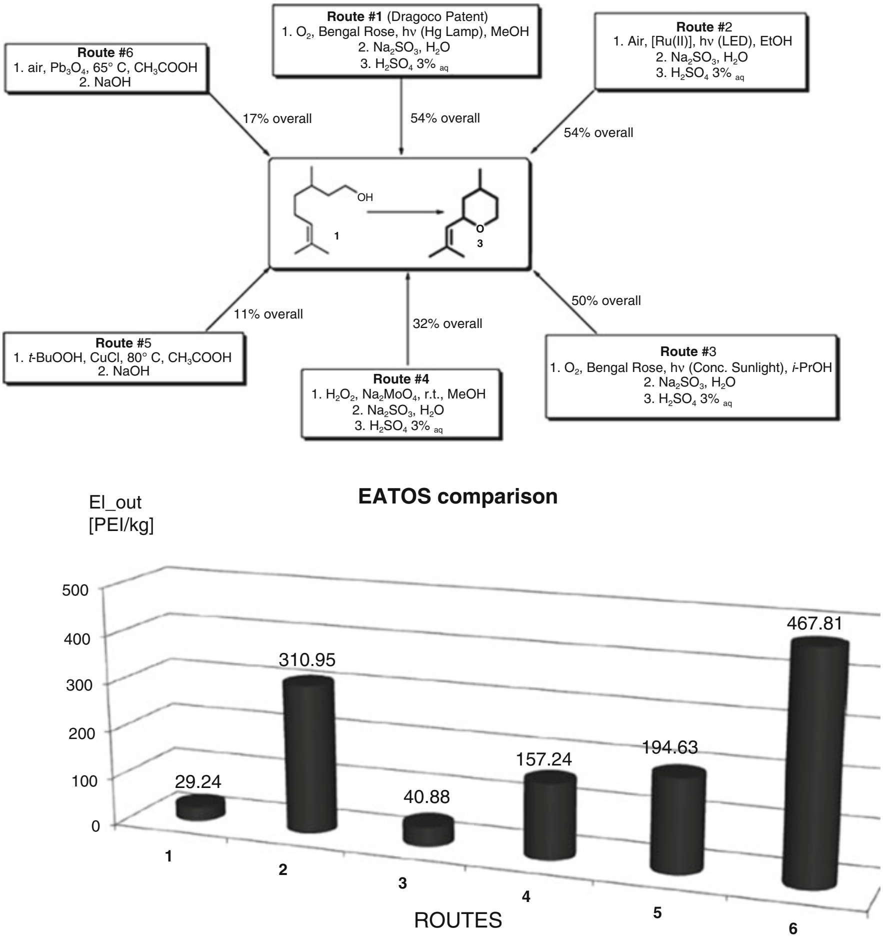


Fig. 12.1 Application of the EATOS metric to the preparation of rose oxide **3** from citronellol **1**. A penalty system is used for evaluating the environmental performance. Reprinted with permission from [10]

using either the full life-cycle assessment, which has however the limitation that the required parameters are available only for a few low-molecular-weight compounds of simple structure and large use. A metric of large application for fine chemicals is EATOS (Environmental Assessment Tool for Organic Synthesis) [9], which has been adapted to take in account also the energetic aspect [10]. This has been usually neglected, on the assumption that it is of little significance for fine chemistry. However, this is not necessarily true for photochemical reactions, where the electrical power consumption may contribute heavily.

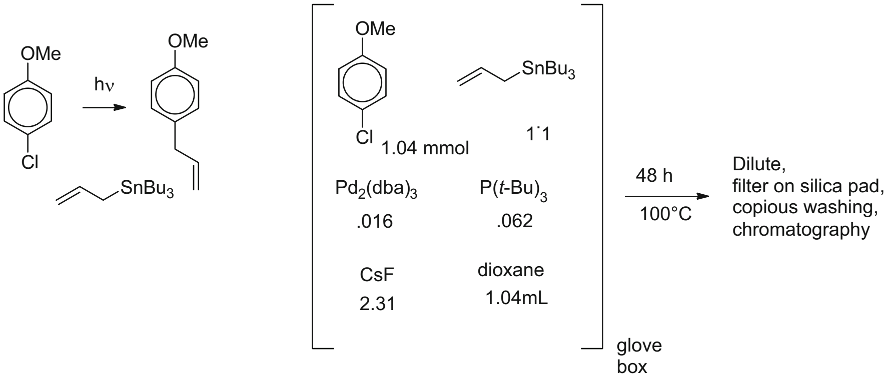
As an example, the EATOS metric is applied to the production of rose oxide (**3**) from citronellol in Fig. 12.1. In this approach, the Environmental Index of the process (EI-out) is expressed with a penalty system as Potential Environmental Impact per kg of product. As it appears, the environmental parameters of photochemical and thermal methods have been found to differ largely according to conditions, and in particular, for the first group, according to the mode of irradiation (in the example, mercury arc, LED, solar light). The importance of the geometry of the reactor in order to ensure a uniform excitation of the reagent will be never sufficiently stressed. The good performance of method #1 is essentially due the fact that this is the patented method resulting from an in-depth optimization, while in most published syntheses optimization has not been carried out and this affect all of the parameters.

12.3 What to Be Afraid of and What Not to Be Afraid of in Photochemical Reactions

The mere fact that photochemical reactions do not require the addition of chemicals as activators makes them good candidates for green chemistry. This indeed makes true the dream by Ciamician that by the action of light, chemicals are generated under mild conditions, comparable to those occurring in plants (see Chap. 4), provided that they are selective.

The future of preparative green photochemistry appears to be linked to two factors, namely, the still largely unexploited variety of excited state reactions on one hand and the overcoming of some characteristic limitations on the other one. A still diffuse prejudice among synthesis practitioners considers photochemical reactions as unsuitable because these would give only mixtures, would be very sensitive to conditions, and would require expensive apparatuses. Just to the contrary, photochemical reactions are usually clean because the short lifetime of the excited state cuts away all of the potential paths but one (see Fig. 12.1), provided that light is absorbed by the reagent (or by the photocatalyst, when this is present), and practically all of the reported failures are either cases where the reagent did not absorb any light or cases where a rapid sequence of photochemical reactions literally burned the reagent. The reverse side of the coin is that bimolecular reactions require a high concentration of the trap, often in a large stoichiometric excess. Also, it is difficult to catalyze an excited state reaction, because the activation energy is by definition already quite small.

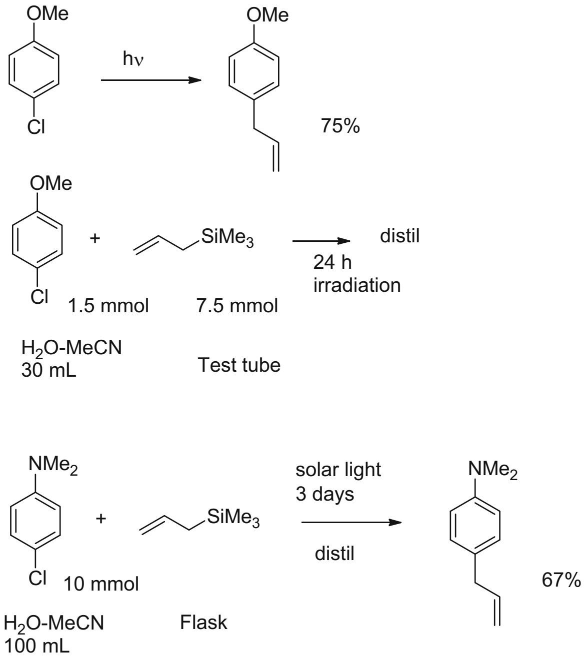
The enormous amount of energy injected in a molecule through the absorption of a photon makes its reaction relatively independent on conditions. Thus, often these can be chosen in a larger variety and less limitations must be considered. Let's take as an example the Stille coupling of aryl chlorides with stannanes, as in the allylation of *p*-chlorophenol in Scheme 12.2. This can be carried out in a Schlenk tube (or even in a nitrogen-flushed solution) by treating the anisole the appropriate solvent mixture with allylstannane in the presence of the palladium complex and a relatively abundant cocatalyst (a trialkylphosphine supposed to enhance the activity of the complex), a fluoride (supposed to enhance the reactivity of the organotin derivative) [11]. The workup is complex and requires filtration for eliminating the abundant precipitate and chromatographic separation. The reaction is appropriately considered a green reaction because it would not be possible, or only under very demanding conditions, to achieve the same transformation except by homogeneous catalysis. However, the environmental burden must be calculated by taking into account the relatively large amount of toxic, flammable, and moisture-sensitive reagents (Scheme 12.2).



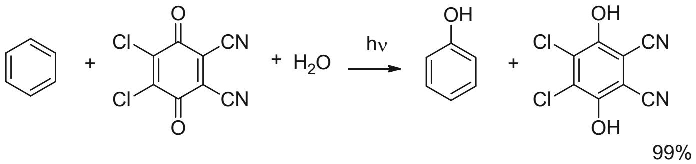
Scheme 12.2 Transition metal catalyzed allylation of chloroanisole. Cocatalysts are required and the mixture must be protected from air and moisture. Workup is rather complex

The same product can be obtained in a comparable yield from chloroanisole by using the corresponding allyltrimethylsilane, a “greener” reagent, by irradiation. In this case the product is obtained by mere distillation of the raw photolysate, no additive, no degassing being required, and water, far from being detrimental, actually enhances the reaction rate. In this case, more energy is invested in promoting the anisole to the electronically excited state, but then advantage is taken of the very fast heterolytic fragmentation of the carbon–chlorine bond and of the likewise fast trapping of the aryl cation formed [12]. As hinted above, the short lifetime of excited states and intermediates overcomes intramolecular conversion and competitive intermolecular processes, although this requires a large amount of trap. One is often worried about the effect by oxygen and in fact excited states, and in particular long-lived triplets, are quenched by oxygen. However, this is highly relevant for the irradiation of dilute solutions, under conditions exactly suited to reveal such quenching. If the simple precaution of stoppering the flask is taken, in many cases the oxygen dissolved will be consumed and the reaction be completed, as in the experiments by Ciamician (obviously this may lead to the unwelcome formation of peroxides, however).

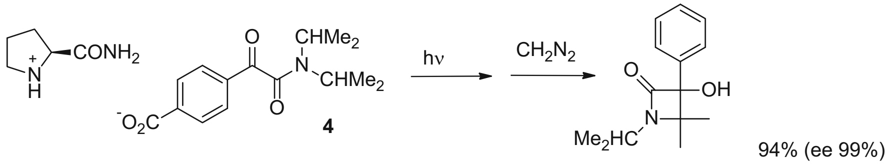
Solar light is of no use for the above reaction, because anisoles do not absorb solar light, but the related anilines absorb and react in a fully analogous way (Scheme 12.3) [13]. In general, the abovementioned insensitivity to the medium makes possible a “green” choice [14]. Examples are solvent-free reactions (see the photooxygenation of neat benzene by water in Scheme 12.4 [15]), solid-state processes (see the cyclization of the carboxylate **4** that occurs with high enantiomeric excess from the salt with proline, Scheme 12.5 [16]), and reaction in water or in eco-friendly organic solvents (e.g., oxygenation reactions carried out advantageously with an immobilized sensitizer in supercritical CO_2) [17]. A little more about synthetic perspective is given in Chap. 8.



Scheme 12.3 Photochemical synthesis of allylbenzenes by irradiation of phenyl chlorides. The reaction is not affected by the presence of oxygen or moisture and workup involves mere distillation. In the case of anilines, solar light is effective



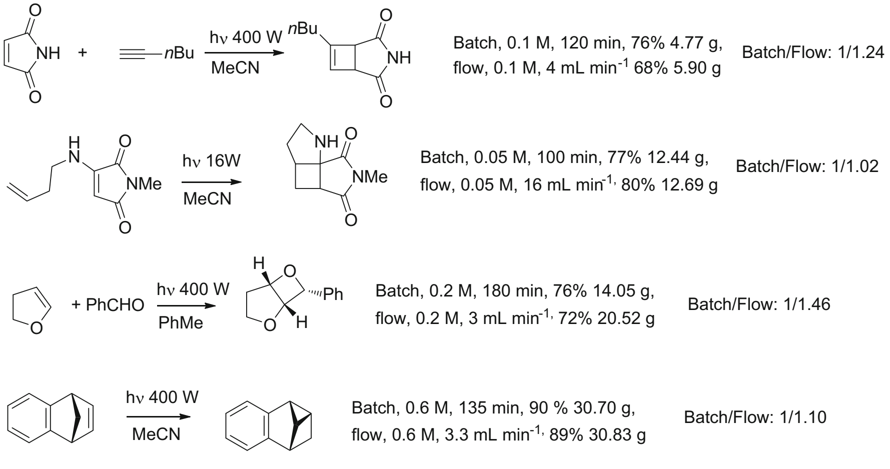
Scheme 12.4 Photocatalyzed hydroxylation of neat benzene



Scheme 12.5 Stereoselective cyclization

12.4 Method of Irradiation

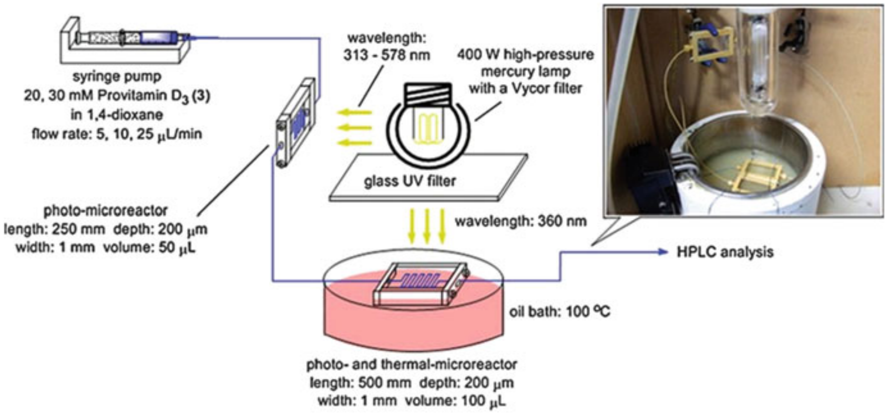
In the general trend toward the adoption of microtechnology for synthesis, photochemistry has a special place, because the short optical path makes nearer the target of uniform irradiation, impossible to reach under batch conditions [18, 19]. A large number of photochemical reactions of every class have been reported, where the adoption of microtechnology results in a large decrease of the irradiation time required or in an increased sensitivity. Which method will be most convenient is not obvious. Irradiations in batch are carried out in a cylindrical vessel (and thus, unsatisfactory results are often due to the (primary) photoproducts that react again). Flow reactions are carried out by circulating the solution in a thin tube wrapped around either a medium-pressure arc (optionally repeating wrapping), and thus, although the irradiation is more uniform, part of the light is lost because of the round form of the tube (and may be recovered by adopting multiple wrapping of the tube). An extensive study demonstrated that the isolated yield and productivity obtained by either method under the same conditions (that is, the same type of lamps is used at the same distance from the sample) were essentially identical (Scheme 12.6) [20].



Scheme 12.6 Comparison of the amount of photoproducts formed under batch and flow conditions

As pointed out by Booker-Milburn, it can be concluded that batch is best suited for 10–15-g scale, while flow reactors are best suited for a larger scale in a single run (or for specific indication, e.g., when a potentially explosive product is formed). However, each of the two methods may be preferred by taking into account the matching of light source and conversion, a statement the importance of which will never be sufficiently repeated, and is the cause of many disappointments (typical cases at both extremes, viz., either the reagent does not absorb significantly or the products are formed but are themselves destroyed).

Another application where miniaturization is useful is combining a photochemical and a thermal reaction that is convenient when using two microreactors. The long investigated synthesis of vitamin D has been further improved by controlling the photochemical equilibrium between lumisterol and tachysterol (Scheme 12.7) and pushing the equilibrium thermally [19].

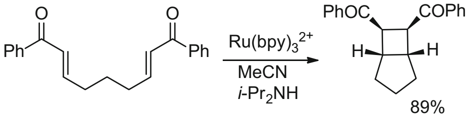
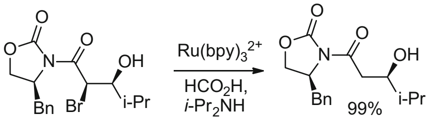
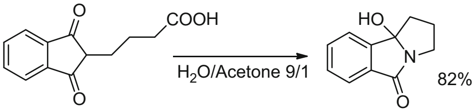
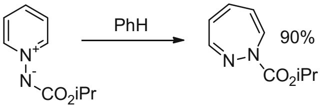
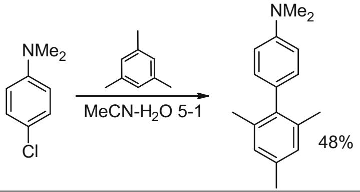
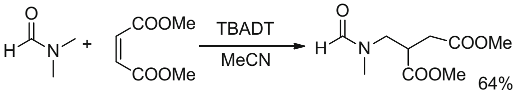
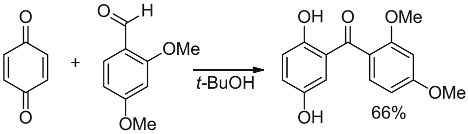
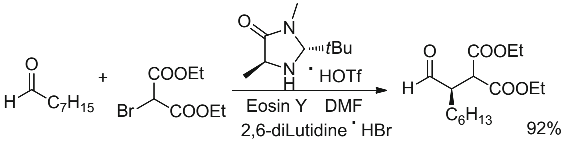


Scheme 12.7 Improved synthesis of vitamin D_3. Tachysterol is formed in equilibrium with provitamin D_3 in the photochemical microreactor (λ 313–578 nm) and conversion to vitamin D_3 is achieved in a further thermal/photochemical microreactor (λ 360 nm, 100 °C). Reprinted with permission from [19]

12.5 Scaling Up a Photochemical Reaction

Green chemistry is not only an academic discipline but one that elaborates syntheses that can be applied under viable conditions, including financially. Thus, it is particularly interesting to devise easily scalable methods, whereas this point is completely disregarded in most of the photochemical literature. Reactions developed on industrial scale are mainly pointed on some classes of reactions, not the most studied in university laboratories, such as chlorination, oxychlorination, sulfochlorination, and nitrosylation of alkanes, as well as more “organic” reactions, such as isomerization for vitamin A precursors and derivatives and cyclization and isomerization for vitamin D and related compounds [21]. Braun has provided details on the practical applications of such reactions [21–23]. A few examples that suggest future development are summarized in Chap. 8 and a list of reactions that have been studied at a concentration >10 g with attention at the preparative result are gathered in Table 12.1. Certainly, large-scale reactions require an appropriate engineering of the irradiation process, a point that has not been explored as

Table 12.1 Exemplificative reactions carried out at >10-g scale

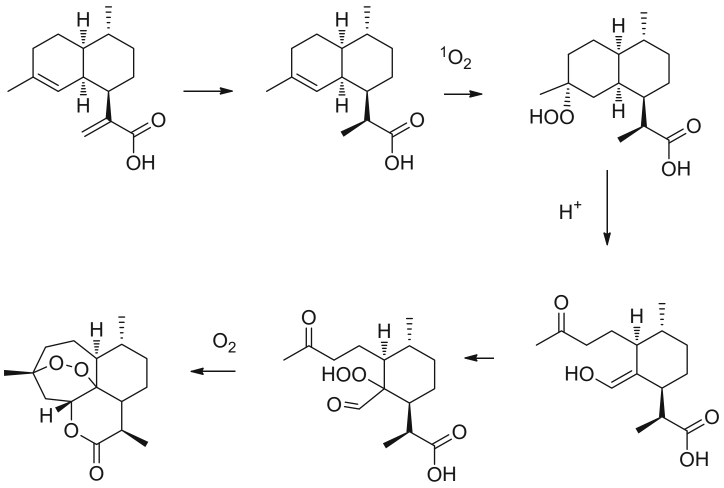
Reaction	Light source, year of publication
	23-W fluorescent bulb or laboratory lighting, 2008 [22, 23]
	14-W fluorescent bulb, 2009 [24]
	XeCl excimer lamp, 2003 [25]
	2000-W Hg arc, medium pressure, 2003 [26]
	Natural sunlight, 2010 [13]
	Natural sunlight, 2009 [27]
	Medium concentrated sunlight, 2006 [28]
	Flow reactor, 23-W fluorescent bulb, 2012 [29]

From [30]

thoroughly as it should for the moment, although the interest for the topic is increasing.

Oxygenation reactions lend themselves to scaling up studies. As an example, in the oxygenation of α-pinene via singlet oxygen, it has been found that the key factors for optimization are reactor miniaturization, the intensity and the spectral distribution of light, and a high oxygen pressure. In a nutshell, one has always to take into account that as much as possible of the light impinging must gives the desired excited state, in this case it is absorbed by the sensitizers and the oxygen concentration is high enough to fully quench the short-lived excited sensitizer [31].

An example where attention has been given to the various aspects is the synthesis of artemisinin, a peroxide highly effective against malaria. This has been prepared from dihydroartemisic acid, in turn prepared either by hydrogenation or by fermentation with a genetically modified enzyme from a much cheaper product, artemisic acid. The reaction involves addition of singlet oxygen (ene reaction), acid catalyzed fragmentation, and addition of ground state oxygen (Scheme 12.8) [32]. Application of the synthesis in a polyfluoroethylene reactor of 26-mL total volume gave 200 g of artemisinin per day (Fig. 12.2).



Scheme 12.8 Flow photochemical synthesis of artemisinin

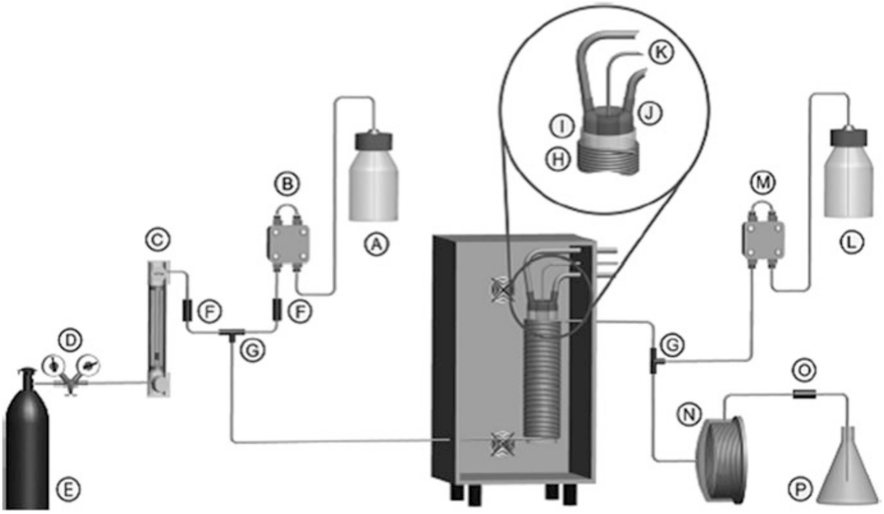


Fig. 12.2 Apparatus for the photooxygenation in flow. (A) Reservoir for the solution of dihydroartemisic acid and the sensitizer (tetraphenylporphyrin) in dichloromethane, (B) HPLC pump, (C) mass-flow controller to control the oxygen flow, (D) manometer, (E) oxygen tank. (F) Check valve, (G) ethylene-tetrafluoroethylene T mixer, (H) fluorinated ethylenepropylene copolymer tubing, (I) quartz immersion well connected to a cooling system, (J) Pyrex filter, (K) connection to the medium-pressure mercury arc (450 W), (L) reservoir for the trifluoroacetic acid solution, (M) acid-resistant HPLC pump, (N) polytetrafluoroethylene thermal reactor, (O) back pressure regulator, (P) collection flask. The two solutions are mixed at a flow rate of 2.5 mL min^{-1} with a stream of oxygen gas (7.5 mL min^{-1}). The residence time in the reactor is ca. 2 min. Reprinted with permission from [32]

12.6 Destructive Green Photochemistry

Many pollutants are not mineralized in the environment and cause many problems, such as accumulation of micro plastics (particles of plastics of dimension below 5 mm). These, along with additives for polymers, pesticides, veterinary and human drugs, halogenated compounds from cleaning, and heavy metals form the large group of persistent pollutants. Their accumulation and persistence often cause serious damage to the environment, from ingestion by sea animals, to inhibiting the normal life course of algae, to the growth of different stems of drug-resistant bacteria when they are exposed to a high concentration of such drugs. In order to eliminate such a menace, it would be necessary to fully destroy the structure of the molecules and mineralize them. Quite often, however, such artificial substances are not fully mineralized in the environment but only partially metabolized. As an example, aromatics, heterocycles, and amines undergo easy (mainly oxidative) degradation of side chain, but the core remains unaltered. Treatment by aggressive chemicals obviously is ill advised because it increases pollution. A solution that has been widely accepted is photocatalysis by using semiconductor powders or suspension. The process has demonstrated to be quite efficient and is suitable for eliminating the last traces of contaminants after pretreatment with hydrogen peroxide or ozone. Research in the field has greatly expanded, resulting now in what is now the most investigated single area in photochemistry. Inexpensive and nontoxic materials such as ZnO and TiO_2 are largely used and are active against low-density polyethylene plastics, phenol, catechol, and organophosphorus pesticides. Hydrogen peroxide and peroxydisulfate enhance the TiO_2 catalyzed photomineralization rate, while the effect of anions is various and difficult to predict. Such photocatalysis combine the effect of adsorption on the surface of the particles with the strong oxidizing/reducing power of the hole/electron pair photochemically generated at the surface of the material [33, 34]. Important is the engineering of the photocatalytic system, both in capturing as much as possible of the impingent flow and in governing the appropriate absorption in the reactor. A more elaborated reactor, as an example a cylindrical multicolumn photocatalytic reactor, may work with an electric energy consumption for photocatalytic degradation of aromatic pollutants in the order of $2–7 \times 10^4$ KWh m^{-3}, less than 1000 times than that known for simple photoreactors. Starting from a charge of 5 mg L^{-1} and with a flow rate (15 mL min^{-1}) under acidic conditions (pH 3), the optimal results were obtained [35]. The orientation toward the sun was also important [36].

A further direction to which research is pointing is the effective use of solar light, which would give an actual “green” application. The absorption of solar light by titania is small. Hence, one of the most active fields of research is extending to the red the absorbance of the photocatalyst, which is most often achieved by doping with a semiconductor, e.g., in the case of titania by nitrogen and boron [37, 38]. Other metals, e.g., titania–iron(III) nanoparticles or nanomaterials with a metal@titania core–shell structure, may have an important effect and extend the active spectrum toward solar light [39]. Magnetic materials are quite useful, since these are easily recovered [39].

The implementation of advanced oxidation procedures based on photocatalysis has to take into account also many organic pesticides that were banned a few decades ago, although they are currently in use in many parts of the world, and that accumulate in organisms [40, 41].

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