Sustainable Solvents

Perspectives from Research, Business and International Policy

Green Chemistry Series

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Preface

Solvents are ubiquitous substances, used widely in cleaning applications, formulation science, and the synthesis and preparation of other materials and chemicals. There has therefore been a lot of interest in solvents, old and new, and how to minimise their impact. It has long been recognised that solvents pose a significant risk to worker safety, public health, and the environment. In response, the development of greener solvents has become an active area of research.

There is an enthusiasm worldwide to overcome the social-economic disparities and environmental consequences of modern society. In 2015, world leaders met at a United Nations summit and agreed on 17 Sustainable Development Goals (SDGs) to be achieved by 2030. Global standards of environmental protection, safe chemical management, and economic productivity through innovation are amongst the many targets incorporated within the seventeen SDGs. As society seeks sustainable practices, solvents and the use of solvents must be similarly evaluated in terms of the SDGs or equivalent indicators. The number of jobs in the global solvent industry and those industries directly dependent on solvents runs into millions, and industrial and consumer products made with or containing solvents are helpful to the majority of the world's population. How to reconcile the clear advantages of solvents with the need to avoid negative impacts caused by their toxicity and flammability, and the risks to the environment caused by volatile organic compounds (VOCs), is the motivation behind current efforts in solvent selection and organic solvent reduction. It is not a question of eliminating solvent use altogether, as regulation might seem to point towards, because of the sheer number of jobs and industries built on solvent based products and processes.

The writing of this book was motivated by the belief that solvents can be made, used, and recovered in a sustainable manner. To be able to use

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solvents satisfactorily in a sustainable way, it is necessary to identify or design solvents that do not demonstrate the hazards that regulation forbids, and successfully apply them in order to provide longevity to jobs and protect the environment. This book is not a handbook of solvent properties, nor does it provide a description of any particular type of solvent and the typical properties and applications associated with it. These types of book are already available, and have served the scientific community well up to this point. Instead, this book addresses the sustainability of solvents, drawing on published technoeconomic and life cycle analyses which have been set in the context of present day regulatory controls, and environmental health and safety challenges. We (the authors) saw a need to encourage the current level of understanding surrounding 'green' solvents towards a more comprehensive understanding of what constitutes sustainable use of solvents. This book is for professional solvent users looking to rationalise their solvent selection procedures, academics interested in the impact of solvents, and students of chemistry, chemical engineering, and environmental science and policy who are looking for information relating to the consequences of solvent use and the role of regulation in determining this.

Solvent sectors are explained in this book (Chapter 2) to provide a context for the scale of solvent use and therefore its potential impact, particularly on the environment. Some applications warranted more attention than others, depending on the size of the industry and the availability of other resources. Readers interested in a specific application of solvents, especially formulations where the relationship between the solvent and the other ingredients is complex, are advised to also read a specialised text to learn more about the role of the solvent in these systems. What you will find in this book is information regarding the sustainability of the solvents used in different applications, and how solvent use is evolving towards sustainable chemistry practices. Readers will find an explanation behind the meaning of sustainable chemistry in Chapter 1. Other topics include life cycle analysis and other solvent evaluation methods (Chapter 3), alternative solvents (Chapter 4) and solvent selection (Chapter 5). A final chapter provides solvent data to help readers complete their own sustainability assessments (Chapter 6). This resource is an asset to solvent substitution experts who are looking to develop their practices beyond superficial arguments and justify replacement solvents on a robust quantitative basis.

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CHAPTER 1

Introduction to Solvents and Sustainable Chemistry

1.1 Sustainable Solutions

As with all products, it is a matter of urgency that the necessary feedstocks, manufacturing processes and habits of end-users become sustainable. Solvents are an important type of chemical product, with a multi-million tonne annual market. The reputation of solvents is strongly linked to their association with volatile organic compound (VOC) emissions. This book offers an insight into the sustainable use of solvents, through discussion of relevant sustainability issues, and by providing data for many different solvents that the reader can take forward into their own sustainability assessments. Case studies illustrate sustainable solvent developments and applications, and methods of solvent selection are also described to help explain a way to introduce sustainable solvents and motivate users to embrace these products.

This book explains how sustainability is applied to solvents (Chapter 3), and how the philosophy of green chemistry can help manage solvent use in a sustainable manner (Chapter 5). Chapter 6 provides extensive data to satisfy sustainability criteria for bio-based solvents and neoteric solvents, which are described in Chapter 4. Trends in solvent use are explained in Chapter 2. A general introduction to solvents and sustainability is provided in this chapter for those readers less familiar with these topics.

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1.2 Solvents

1.2.1 Definition

The term solvent is applied to a vast number of different substances. They are unified by their role as inert fluids with the purpose of dissolving another substance (the solute). Solvents may be reactive under certain conditions, which must be avoided when applying the substance as a solvent. There are several alternative descriptions available, some of which are summarised below (Table 1.1). In this discussion it is also helpful to pinpoint the conditions that define a liquid as separate from other fluids (gases and supercritical fluids) and different from solids. Definitions of solvents usually specify that they are a liquid. Gases are not solvents because they do not have intermolecular bonds, but supercritical fluids are considered to be solvents. A supercritical fluid is a state of matter achieved when the temperature and pressure both equal or exceed a critical point, where the liquid and vapour phases reach the same density and become a single (supercritical) phase. The substance then has properties intermediate of a liquid and a gas, with intermolecular forces, which is why it is capable of acting as a weak solvent.

The United Nations (UN) Globally Harmonized System of Classification and Labelling of Chemicals (GHS),[1] and the subsequent European Regulation 1272/2008 for the Classification, Labelling and Packaging (CLP) of substances,[2] state that a liquid is a substance with a melting point (meaning the initial melting point if relevant) of no more than 20 °C at standard pressure. Also, a liquid is not completely gaseous at 20 °C, and at 50 °C a liquid has a

Table 1.1 Definitions of solutions and solvents.

Definition	Source
Solvent: "*Substances that are liquid under the conditions of application and in which other substances can dissolve, and from which they can be recovered unchanged on removal of the solvent*"	*The Properties of Solvents*, by Y. Marcus[103]
Organic solvent: "*Any volatile organic compound (VOC) which is used for any of the following: alone or in combination with other agents, and without undergoing a chemical change, to dissolve raw materials, products or waste materials; as a cleaning agent to dissolve contaminants; as a dissolver; as a dispersion medium; as a viscosity adjuster; as a surface tension adjuster; as a plasticiser; as a preservative*"	EU Industrial Emissions Directive (2010/75/EU)[104]
Solvent: "*A substance that dissolves other material(s) to form* [a] *solution. Common solvents are liquid at room temperature but can be solid (ionic solvents) or gas (carbon dioxide). Solvents are differentiated from plasticizers by limiting their boiling point to a maximum of 250 °C. To differentiate solvents from monomers and other reactive materials, a solvent is considered to be non-reactive*"	*Handbook of Solvents*, edited by G. Wypych[105]
Solution: "*A liquid or solid phase containing more than one substance, when for convenience one (or more) substance, which is called the solvent, is treated differently from the other substances, which are called solutes*"	IUPAC definition[106]

vapour pressure of 300 kPa (3 bar) or less. Clearly this links to the definition of a gas, which is completely gaseous at 20 °C and at 50 °C has a vapour pressure above 300 kPa. For completeness, a solid is a substance that does not meet the criteria for either a liquid or a gas.

The definition offered by Marcus,[103] relies on our understanding of the liquid state as was previously discussed (Table 1.1). The more specific definition within the EU Industrial Emissions Directive 2010/75/EU,[104] uses applications to establish what an organic solvent is. Although the inertness of the solvent is maintained, some of the applications listed do not require that the solvent is actually dissolving anything. We are also required to appreciate the meaning of VOC, which is also defined in the Industrial Emissions Directive as "*any organic compound ... having at 20 °C a vapour pressure of 0.01 kPa or more, or having a corresponding volatility under the particular conditions of use*". Wypych differentiates between solvents and plasticisers in his definition,[105] while the Industrial Emissions Directive includes plasticisers as an application of solvents. Several of the solvents that will be discussed in this book have boiling points in excess of 250 °C (a plasticiser according to Wypych) and so it is more advantageous to follow the definitions of Marcus and the Industrial Emissions Directive. Also note that other formal definitions of a plasticiser exist without reference to boiling point, which only consider the context in which the substance is used (as a plasticiser).[3] Wypych also suggests that certain solids and gases are solvents, and in doing so stretches the meaning of a solvent beyond what is useful.

The International Union of Pure and Applied Chemistry (IUPAC) decide upon the authoritative nomenclature and descriptions of chemicals and chemical phenomena. The definition of a solution offered by IUPAC alludes to the meaning of the term solvent, but it is not clearly stated.[106] Instead, IUPAC defines different types of solvent separately. For instance, according to IUPAC a dipolar aprotic solvent is "*a solvent with a comparatively high relative permittivity (or dielectric constant), greater than ca. 15, and a sizable permanent dipole moment, that cannot donate suitably labile hydrogen atoms to form strong hydrogen bonds*",[4] and an amphiprotic solvent is a "*self-ionizing solvent possessing both characteristics of Brønsted acids and bases*".[5]

1.2.2 Types of Solvent and Their Origins

The history of solvents is nicely described by Estévez.[6] Before the advent of the petrochemical industry, solvents were limited to water, naturally occurring oils and substances that could be easily fermented or distilled from biomass. By contrast the number of solvents available now is quite overwhelming. In order to provide satisfactory performance in the variety of processes, formulations, and cleaning applications that solvents are needed for, many different types of solvent are required. Large differences in boiling point, polarity, viscosity and several other physical properties can be found between solvents, and are documented in specialised texts.[7] Fundamentally the solvent must dissolve the relevant substrates, sometimes selectively, and not react or decompose within the system. Hence many different chemical functionalities are found in both historically important solvents and contemporary examples. Protic solvents (in a hydrogen bonding sense) include water, alcohols, primary and secondary amines, acids, and multi-functional solvents containing any of these chemical groups. Glycol ethers would be one example. Aprotic solvents are more diverse, including aliphatic, olefinic, and aromatic hydrocarbons, halogenated hydrocarbons, ethers, esters, ketones, carbonates, nitriles, tertiary amines, nitrohydrocarbons, organophosphates, amides and sulphur containing compounds.

All the above solvents (with the exception of water) are routinely made from the major chemical building blocks of the petrochemical industry. These are syngas, ethylene, propylene, the butenes, butadiene, benzene, toluene, and xylenes, as produced from crude oil and natural gas (Figure 1.1). These base chemicals are transformed into functionalised solvents through the processes of oxidation, hydrogenation, dehydrogenation, hydration, dehydration, dimerisation, and esterification.[8]

Before the essential base chemicals can be obtained, the crude oil must be processed accordingly. Firstly desalting occurs, and then the crude oil is subjected to fractional distillation.[9] The naphtha cut is composed of short-chain aliphatic hydrocarbons. *n*-Hexane and *n*-heptane can be separated from processed naphtha with molecular sieves, for example.[10] Naphtha is also suited to downstream chemical production, and through steam cracking is the main source of petrochemical olefins.[11] Shale gas is another economically attractive source of olefins and syngas.[102]

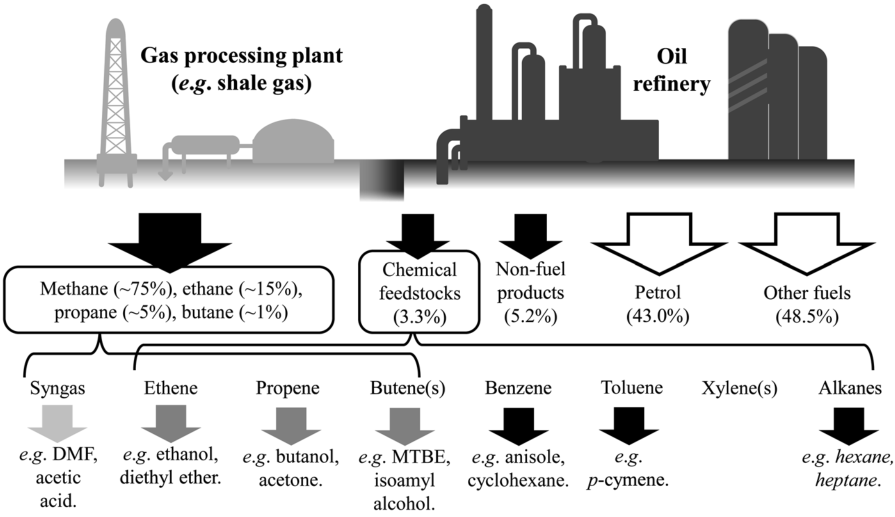

Figure 1.1 Conventional solvent production in the context of the fossil feedstock energy industries, from raw materials to refined feedstocks, onto intermediates and finally solvents.[101,102]

Aromatics solvents (benzene, toluene, xylene(s), collectively known as BTX in oil refinery terms) are produced by the catalytic reforming of crude oil.[12] The aromatics must be separated from their azeotropic mixtures with aliphatic hydrocarbons, and to do this an additional extraction solvent is required. Several processes exist, but the Shell sulpholane process is the most established.[13] More than 90% of BTX separation processes use either this technology, the Udex diethylene glycol process (which the Shell sulpholane process is superseding), or the Lurgi Arosolvan process.[14] The latter uses *N*-methyl pyrrolidinone (NMP) as the primary solvent, and is being introduced as new plants are built.[15] All use a certain amount of water as an anti-solvent.[16]

Biorefineries with the capacity to produce appreciable amounts of renewable solvents are now operational. Bio-ethanol is produced primarily for fuel, but is also a common solvent. Other fermentation products also have applications as solvents (*e.g.* acetone, 1-butanol, lactic acid, and their derivatives). Chemical processes and extractions of natural products can also be applied to produce solvents or their precursors from renewable feedstocks. Chapter 4 will discuss the production of bio-based solvents in greater detail.

Typical properties characteristic of the different classes of solvent have been helpfully tabulated by Wypych.[17] Data for individual solvents can be found in Smallwood's 'Handbook of Organic Solvent Properties'.[7] This book is concerned with the sustainability of solvents, not their physical properties as such, so please refer to the suggested texts for complete descriptions. Chapter 6 presents data relevant for determining the environmental impact and health and safety implications of both bio-based solvents and speciality petrochemical solvents.

1.2.3 Solvent Markets

Accessible data regarding the quantities of solvent used or purchased across large geographical regions is usually outdated. Statistics for western Europe were last published by the European Solvent Industry Group (ESIG) in 1993,[18,19] even predating the European VOC Directive 1999/13/EC.[20] The United States Environmental Protection Agency (EPA) monitors chemical releases and wastes, and compiles the data annually.[21] This data is categorised by substance and industry. Solvents must be identified while recognising that many solvents have other uses, so the data can significantly overestimate industrial solvent use. At the same time, reuse of solvents and the fact that solvents can be contained in final products also influences the accuracy of the dataset.

It is important to regard certain datasets as representative of past solvent use where appropriate, and also bear in mind modern trends, which have reacted to new environmental regulations and are steered by the implementation of greener, more effective technologies. Nevertheless, the information presented in Figure 1.2 is useful as a historical marker, indicating the large volumes of solvent that were used in paints and coatings especially, and

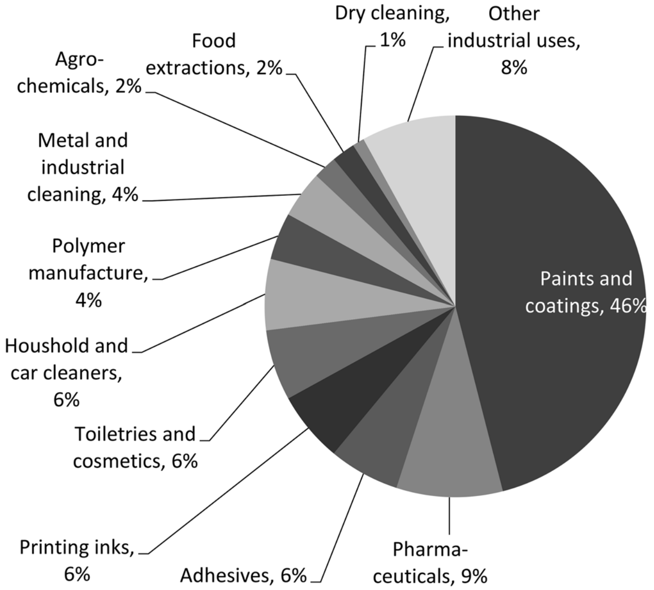

Figure 1.2 Sector data for solvent use in western Europe from 1993.

a reminder of how widespread and diverse solvent use is. Modern data is reviewed subsequently.

Furthermore, US data for the year 1995 was collated by George Wypych in his impressively comprehensive, sector by sector analysis.[22] American industry solvent releases in 1995 were dominated by methanol (Figure 1.3). The most transferred solvent (as waste) was the much less volatile ethylene glycol. Methanol, toluene and xylene, all possessing health hazards, together constitute over half of all solvent releases and transfers. Other solvents in the top ten combined releases and transfers are, in order of significance, methyl ethyl ketone (MEK), carbon disulphide, dichloromethane (DCM), *n*-hexane, methyl isobutyl ketone (MIBK) and *t*-butanol. Although non-solvent uses are included in the data, because solvents are regularly used as high volume auxiliaries in manufacturing, they are more prone to being released or otherwise eventually becoming waste. That said, the use of carbon disulphide as a solvent is minimal, but its continued use as a reactant in rayon manufacture is very significant in terms of volume, and its volatility is contributing to the release data shown (Figure 1.3).[23]

Sector data from the same time shows that the manufacture of polymers, plastics, and organic chemicals contributes highly to solvent emissions (releases and disposal) and waste transfers (Figure 1.4). Together they account for 50% of the reported figures (Figure 1.5). Metal fabrication, the paper and pulp industry and the motor vehicle manufacturing sector are also large contributors, although the paper and pulp industry is overwhelmingly releasing and transferring methanol, which is not a solvent in this instance

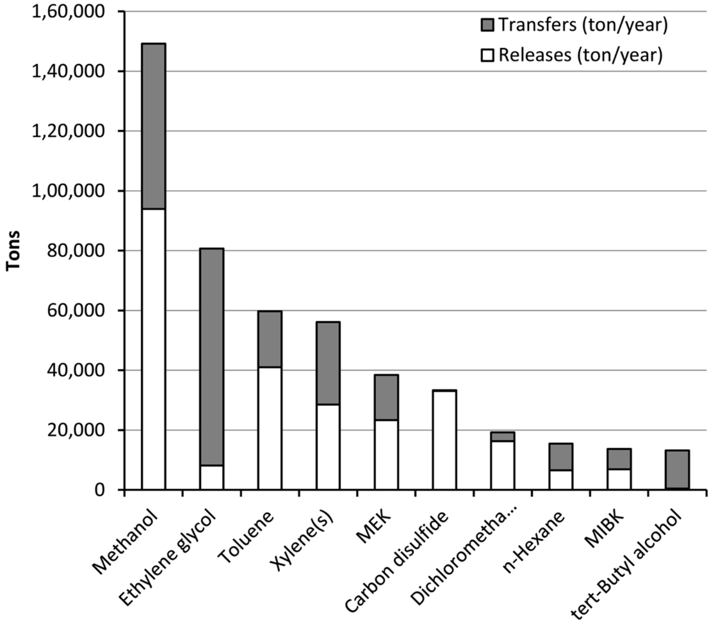

Figure 1.3 Data for the top ten combined US solvent transfers and releases in the mid-nineties (1995).

but a by-product of the Kraft pulping process.[24] Some of the plastic and fiber industry emissions and waste will also be attributed to wastes, *e.g.* from condensation polymerisations, as well as volatile monomers and other reactants. Otherwise, cleaning solvents will make up a significant proportion of the data shown in Figure 1.4.

The Swedish Chemicals Agency (KEMI) has published more recent data for solvent use specifically in Sweden, up to the year 2010.[25] The categorisation of industrial sectors is different to the ESIG data in Figure 1.2, but clear similarities and differences can be seen (Figure 1.6). Total industrial solvent use in Sweden was 228 thousand metric tonnes in 2010. We shall assume Sweden is representative of western Europe to enable comparison with the 1993 data shown previously in Figure 1.2, but obvious market demand differences will be highlighted in the following description. The printing industry is now the major user of solvents, with the paints and coatings sector shrinking relative to the ESIG 1993 data, as water-based paints have started to take a larger market share. Nevertheless, paints and coatings are still significant, and global estimates for the proportion of solvent use in this sector are higher still.[26,27] The pharmaceutical industry was the second largest consumer of solvents in Europe in 1993, but is not represented specifically in the Sweden data. However, there are a number of pharmaceutical companies active in Sweden, and so this sector must be represented within the "manufacture of other chemicals" group (accounting for 6% of the total Swedish industrial solvent use).

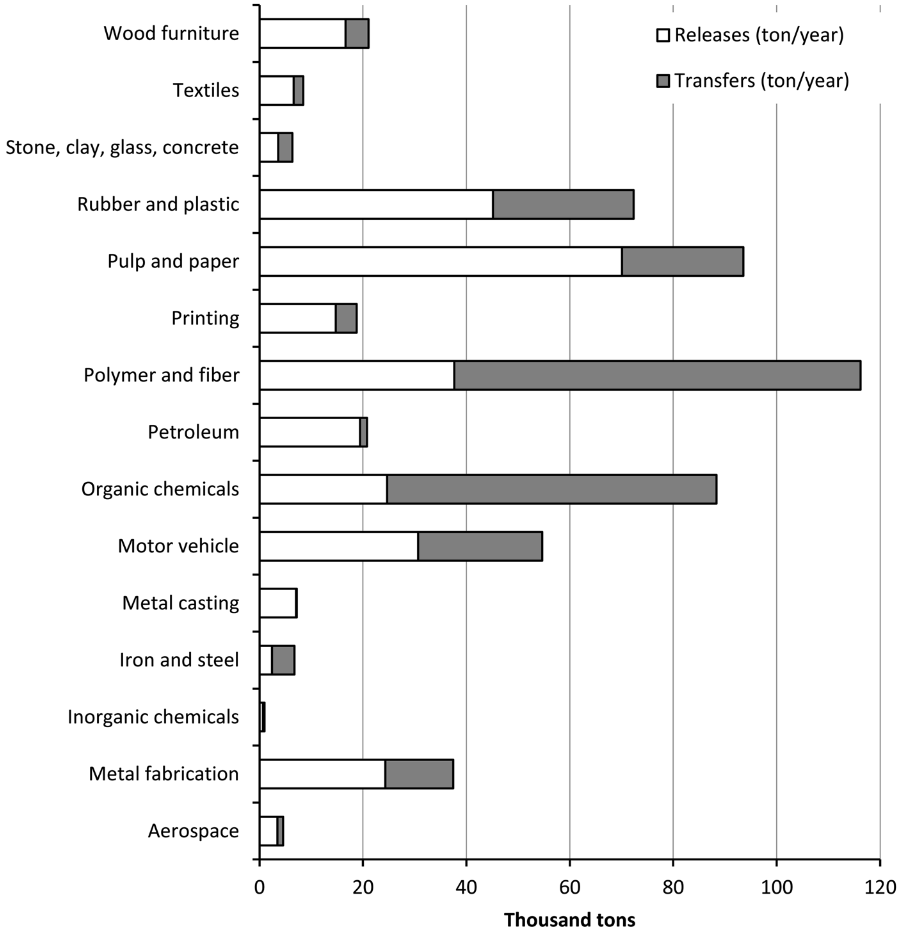

Figure 1.4 Absolute data for US solvent transfers and releases by sector in 1995.

Organic solvent use in Swedish consumer products equalled 50 thousand metric tonnes in 2010, about 80% of the quantity required by the paints and coatings industry (Figure 1.7). The data shown in Figure 1.7 considers consumer products for the general public, and also technical products for industry. Paints accounted for 9% of the consumer solvent use, behind antifreeze and windscreen washing fluids. The market share of antifreeze in Sweden is understandably higher than in warmer climates, and so the size of this contribution to total consumer solvent use is bound to vary considerably from nation to nation. Antifreeze is based on a glycol solvent, ethylene glycol or propylene glycol in applications where the toxicity of the former is an issue. Windscreen washing fluids are aqueous alcohol solutions, that may contain methanol, or again for toxicity reasons preferably ethanol or isopropanol. Most of the other consumer products are based on hydrocarbon solvents.

It follows that the composition of contemporary solvent use in Sweden is dominated by alcohols and hydrocarbons (Figure 1.8). Mixtures of aliphatic and

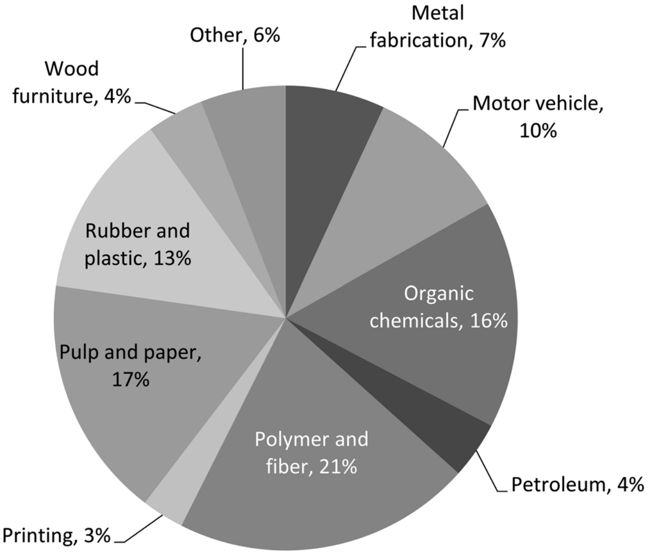

Figure 1.5 Relative US solvent transfers and releases (combined) by sector in 1995.

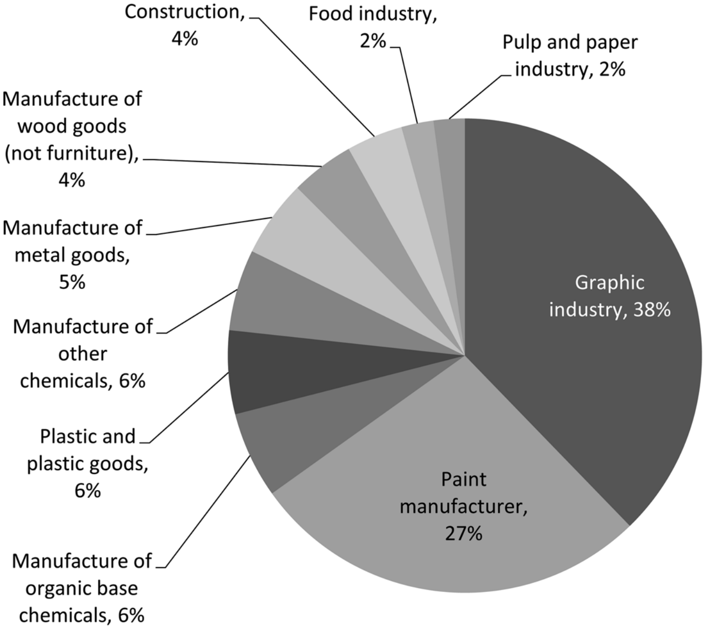

Figure 1.6 Swedish industrial solvent use in 2010.

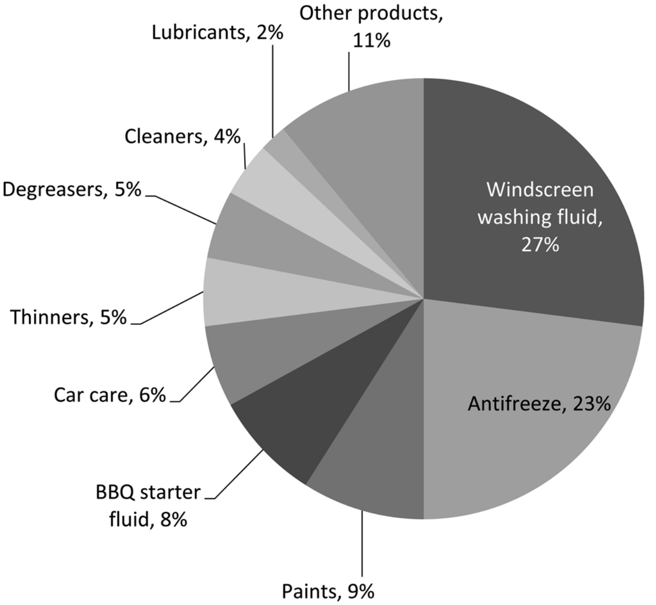

Figure 1.7 Swedish consumer solvent use in 2010.

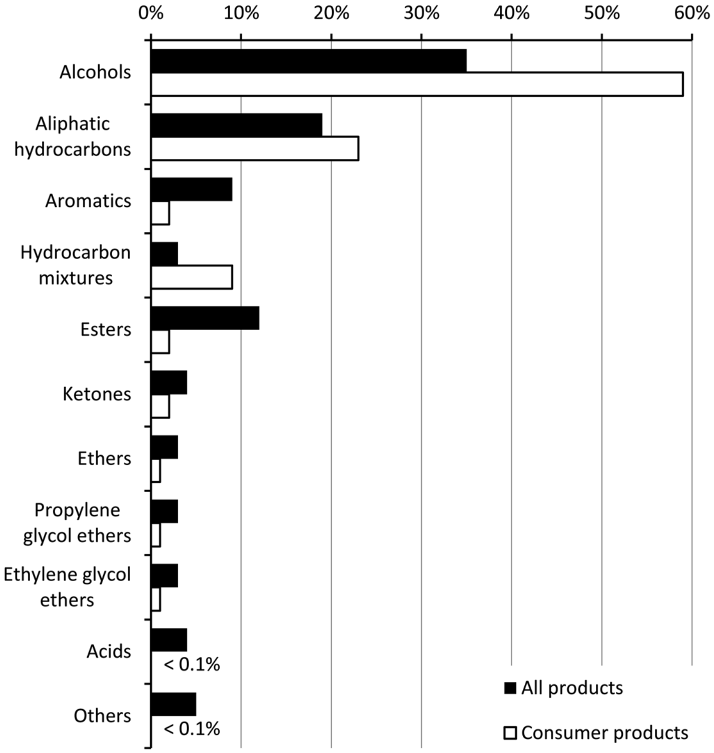

Figure 1.8 Relative solvent use (Sweden 2010, by type).

aromatic solvents are categorised separately. The types of solvent used in industry are more diverse, but still a preference for alcohols and aliphatic hydrocarbons emerges. Esters are the third most common class of organic solvent, but are underrepresented in consumer products. Of course, water is the most popular solvent found in final products, and is used an order of magnitude more frequently than all the organic solvents combined. Note that fuel and chemical intermediates have been removed from this dataset.[25]

It is notable from the types of solvent used (in any appreciable amount at least) that the most infamously toxic and environmentally damaging solvents are absent. The use of chlorinated solvents in Sweden was massively reduced in the 1990's through national legislation.[28] Later, between 2004 and 2010, the demand for chloroform, dichloromethane (DCM), and perchloroethylene stabilised, as is true of total solvent use according to the KEMI dataset. 1,1,1-Trichloroethane was phased out by the Montreal Protocol.[29] Of the remaining options, cumulatively about 500 tonnes of chlorinated solvent is used each year in Sweden (0.2% of total solvent use). Perchloroethylene is still used in dry cleaning, while DCM and chloroform can be used for cleaning if the operator has been issued with a permit. Specialised use in fine chemical manufacture continues. Data from GlaxoSmithKline (GSK), although not a Swedish company, suggests that although DCM use is decreasing, at least relatively, it is still one of their top ten solvents.[30] Solvent use in the pharmaceutical industry is discussed in Chapter 2.

We have arrived at a point where the remaining uses of chlorinated solvents, in Europe and North America especially, have reduced to only "essential" practices, for which an obvious and cost effective substitution is unknown, but the value of the product or process warrants exception. There is a mechanism within the European REACH regulation 1907/2006,[31] that allows companies authorisation to use hazardous substances including solvents.[32] We can expect a low level of chlorinated solvent use to continue, with strict controls over human exposure.

To update Wypych's analysis, data for US solvent wastes and emissions for 2014 has been processed (Figures 1.9 and 1.10). Sector specific information is found in Chapter 2. Only the most used solvents have been included from the United States Environmental Protection Agency (US EPA) Toxics Release Inventory (TRI) databank,[21] and waste transfer databank,[33] for 2014. This was taken to mean more than 1000 tons of waste or emissions for the year. The data has been spread over two charts. Chemicals that are not solvents were removed from the original US EPA TRI data, but substances with uses in addition to acting as a solvent (*e.g.* ethylene glycol as a monomer) are included in Figures 1.9 and 1.10. Figure 1.9 shows the seven highest volume solvents. Figure 1.10 contains the remaining solvents, but because the scale of the axis representing tonnage is magnified compared to Figure 1.9, dichloromethane (DCM) is included in both charts to act as a reference point between the figures. Four end-of-life options are represented. Solvent recycling and incineration are managed end-of-life practices that allow material or energy recovery. Other waste transfers are primarily specialist hazardous substance treatments or discharge into municipal sewage treatment plants (*via* sewage pipes or shipment).

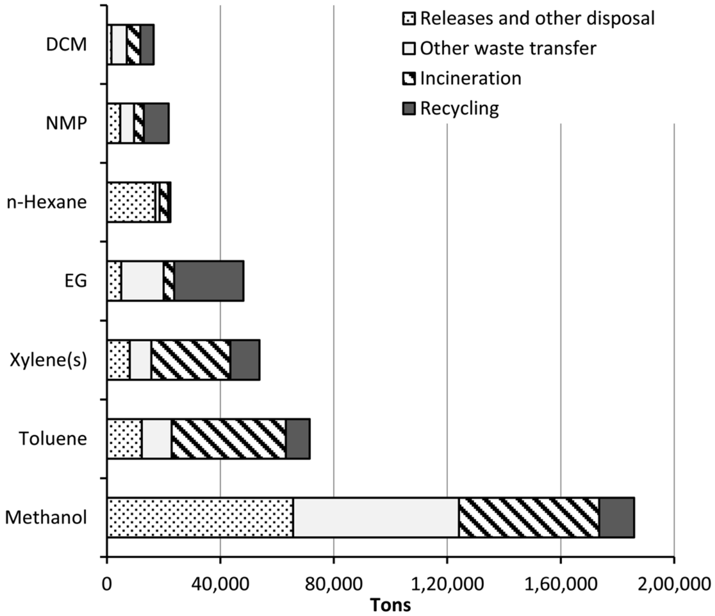

Figure 1.9 Data for the highest volume solvent end-of-life practices (USA, 2014). Ethylene glycol is abbreviated to EG.

It is interesting to observe that the waste treatments being applied are mixed, and in most cases there is not a clear favourite. Toluene and xylene(s) are most frequently incinerated because of their high energy content, but not exclusively. The more volatile *n*-hexane is mostly lost through air emissions. Even though *N*,*N*-dimethyl formamide (DMF) and *N*-methyl pyrrolidinone (NMP) are quite similar, DMF is the only solvent in either Figure 1.9 or Figure 1.10 that is mostly sent to municipal sewage treatment plants once used. By contrast, NMP is mostly recycled. Both solvents are water miscible, making recovery challenging. However, the higher price of NMP is enough to encourage recovery and reuse. This is an example of an economic incentive being the driver behind improving material use. Virtually all 1,1,2-trichloroethane (a carcinogen) is sent for specialist disposal with hardly any lost to emissions.

Trends in worldwide solvent use (are for the time being) different to the localised European data and North American data we have seen thus far. These established markets are experiencing slow growth, a balance controlled by contemporary levels of modest economic growth and the appearance of more aqueous and solvent-free technologies and products. Meanwhile, the largest market, Asia, has an annual solvent demand of over 8 million metric tonnes, which is growing at a rate of 5% per year.[34] Solvent users in Asia have a greater reliance on solvents that are more tightly regulated (and therefore disfavoured) in North America and Europe. For instance, *N*,*N*-dimethylformamide (DMF) is a reprotoxic solvent, and it is manufactured primarily in China where 72% of global DMF usage occurs (2013 data).[35]

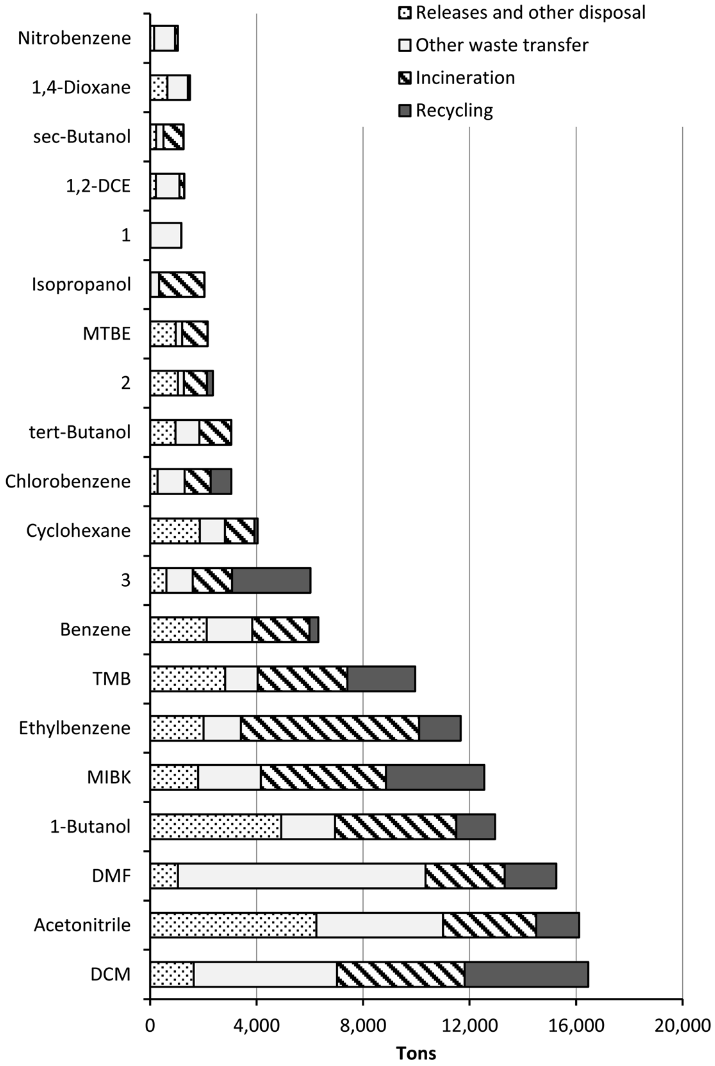

Figure 1.10 Data for other high volume solvent end-of-life practices, repeating the DCM entry of Figure 1.9 (USA, 2014). Key: 1, 1,1,2-trichloroethane; 2, trichloroethylene; 3, tetrachloroethylene; 1,2-DCE, 1,2-dichloroethane; MTBE, methyl *tert*-butyl ether; TMB, 1,2,4-trimethylbenzene; MIBK, methyl isobutyl ketone; DMF, *N*,*N*-dimethyl formamide; DCM, dichloromethane.

Total solvent use globally is 20–30 million tonnes per annum.[102] Paints and coatings are still regarded as the primary use of solvents worldwide; 40% in 2012 is one estimate,[27] which is still in keeping with older data for Europe in 1993 (Figure 1.2). Consequently, significant volatile organic compound (VOC) emissions still come from solvent use. In the UK, 35% of VOC emissions are solvents.[36]

Higher values of 42% are reported by the European Environmental Agency for the European Economic Area,[37] but these are disputed by ESIG who say that this figure is overestimated by about a third.[38] Detailed sector-by-sector solvent VOC emissions data has been published for Germany.[39] Not all solvents are VOCs. Acetone as well as dichloromethane (DCM) are exempt from VOC status in the USA.[40] The reason given is that their photochemical reactivity is insignificant. In Europe the definition is derived from volatility without exception.[41]

Global studies have estimated that ethanol, toluene, ethyl acetate and acetone are the most prevalently used solvents worldwide, while methanol, DMF, isopropanol and methyl ethyl ketone (MEK) are also common.[34] There are obvious differences in the different datasets discussed, but the broad implication is that the fast growing solvent markets in Asia, Africa, and South America are broadly similar to Europe and North America, but with increased reliance on DMF amongst other less desirable solvents.

The overall impression gained from this discussion is that a few particular solvents, used on a considerable scale, need to be considered for immediate replacement (*e.g.* DMF). In Europe, regulation is increasing the pressure to substitute certain chemicals. Although they are used in relatively small amounts, their impact on human health or the environment is profound. More generally, solvents have a disproportionate effect on air quality compared to other types of chemical products, even damaging the atmosphere in the case of ozone depleting solvents. This being the case, there is an argument in support of developing technologies and products that completely reverse our reliance on intentionally releasing volatile organic solvents into the environment as part of their function.

The solvent market is of considerable size, but it is a much smaller sector than plastics, for example, and therefore it could be argued that the upstream issues of resource availability and sustainability are less urgent. This position is supported at the time of writing (that being early 2016) by the oversupply of crude oil from the Middle East, and cheap shale gas used and exported by North America.[102] Nevertheless, fossil fuels are an inherently unsustainable source of chemicals, and falling oil prices are indicative of an unnerving price volatility, not long-term economic sustainability. It remains crucial to consider renewable, non-depleting feedstocks for non-toxic solvents in order to free the industry from the oil refinery, meanwhile also negating solvent emissions and pollution for a sustainable solvent market.

1.3 The Concept of Sustainability

1.3.1 Overarching Definitions

Increasingly, sustainability is being placed at the forefront of considerations regarding manufacturing in the chemical industry and the energy sector.[42,43] Both the terms “sustainable” and “solvent” are intuitively understood by scientists working on these research topics, but whereas the definition(s) of the term solvent are often unnecessarily complicated, and are therefore often best left arbitrary and unspecific, the meaning of sustainability must be objective and tied down to specifics. This is for the sake of people and the planet. "*To be sustainable, a practice, relationship, or institution must maintain the health of the natural environment*", and furthermore "*it must foster a culture of adaptive learning so that its rate and scale of change can be well managed*".[44] "Sustainability" must not be used subjectively as the term "green" is, for example. "Green" can remain a relative description, indicative of incremental improvements to environmental health and safety (EHS), but "sustainability" must be understood according to scientific terms (quantitative if possible) with criteria and thresholds that decide conclusively between sustainable and unsustainable. Misuse of the term "sustainability" will prevent the realisation of the goals of sustainable development in its true meaning.

When defining sustainability, the most frequently cited source is the Brundtland Commission report 'Our Common Future' of 1987, which states "*Sustainable development is development that meets the needs of the present without compromising the ability of future generations to meet their own needs. It contains within it two key concepts: the concept of 'needs', in particular the essential needs of the world's poor, to which overriding priority should be given; and the idea of limitations imposed by the state of technology and social organization on the environment's ability to meet present and future needs.*"[45] The ambition of sustainable development is well explained, with inherent sustainability being the ultimate goal. Sustainable development establishes "*a framework for change rather than a list of prescriptions to achieve it*",[46] and it is that measurement of sustainability, against comprehensive benchmarked indicators, that is crucial. The "triple bottom line" is another means of thinking about sustainability, this time clearly dividing the issue into social, economic, and environmental aspects.[47] All three of the so-called pillars of sustainability must be considered, and the relationships between them understood for this approach to work.[48]

The term sustainability, for all its history of unquestionable purpose and promise,[49] is prone to abuse and misuse. The contrarian environmentalist David Owen said that sustainability is "*one of the least meaningful and most overused words in the English language*".[50] At the most basic level the word "sustainable" comes from the Latin word *sustinere* meaning to "hold up".[51] In fact, this is not quite the right meaning, for society does not gain from sustaining the practices that have adverse effects on people, the economy, or the environment. Sustainable development must instead accelerate change towards more ideal conditions.

Although environmental sustainability is the most obvious concern for the average citizen of a developed nation (compared to the economic sustainability or social sustainability pillars), businesses must firstly prioritise economic viability. For this, the sustainability of the business model must be assured. This does not mean that economic sustainability is in some way superior to environmental sustainability or social rights, or that sustainability assessments can be unfairly biased towards economic gain.[52,53] The opponents of large companies who are perceived as large polluters or as otherwise damaging the environment will claim the only objective of these organisations is short-term profit, but equally "*only competitive and profitable enterprises are able to make a long-term contribution to sustainable development*".[54] Any industry or institution that tries to challenge the *status quo* of "business as usual" will make no impact unless they are financially able to continue to operate.

The same large organisations that are most liable through the scale of their operations to adversely impact the environment are also best placed to preserve it, and at the same time provide jobs and community investment. Managed use of natural resources such as biomass can be the foundation of a successful way to secure the prosperity and long-term future of valuable ecosystems and the economy. Each pillar of the triple bottom line has a role to play in the sustainability of business practices, from push (compliance with environmental regulation) to pull (more rewarding and diverse business relationships increasing the exchange of products and services). Short term interests are often fulfilled through unsustainable actions, but longer term ambitions and the success they bring certainly require sustainable practices.

The idea of sustainability is commonly regarded in the same way as the adjectives "green" or "eco-friendly". However, this is not advantageous. The political theorist Leslie Paul Thiele recognises that "*when sustainability gets defined … in terms of general values and abstract concepts without any specific means of implementation … it ceases to be a force for positive change*".[51] This is as true for general government policies as it is specific sustainability assessments, but even more so in the case of the latter. Instead, quantitative indicators of sustainable objectives must be used to initiate comparisons, gauge progress, and achieve products, processes, relationships and institutions that do not undermine the environmental, social, and economic conditions of their own existence.[55]

At the highest (and therefore most generic) level, international sustainable development goals (SDGs) have been set by the United Nations.[56] The '2030 Agenda for Sustainable Development' (of September 2015) contains 17 goals, divided into 169 targets.[57] The strong emphasis on social sustainability is a stark contrast to the understanding of sustainability commonly held by (green) chemists and other solvent users who think primarily in terms of process safety and environmental (pollution) issues (Table 1.2). The role of the chemical sciences is pronounced when taken to include many of the most

Table 1.2 Sustainable development goals proposed by the United Nations.

Goal	Pillar	Role of chemistry
1. End poverty in all its forms everywhere	Social	Indirect
2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture	Social	Agrochemicals, considerate land use for non-food biomass production
3. Ensure healthy lives and promote well-being for all at all ages	Social	Medicines
4. Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all	Social	Indirect

5. Achieve gender equality and empower all women and girls	Social	Indirect[a]
6. Ensure availability and sustainable management of water and sanitation for all	Social	Contribution to wastewater purification technology, and cleaner processes that do not pollute water
7. Ensure access to affordable, reliable, sustainable and modern energy for all	Social	Materials for energy capture and storage
8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all	Social and economic	The chemical industries are an important sector worldwide for jobs and societal wellbeing
9. Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation	Economic	Renewable chemical production is a key area of innovation and growth in the manufacturing sector
10. Reduce inequality within and among countries	Social and economic	Indirect
11. Make cities and human settlements inclusive, safe, resilient and sustainable	Social	Indirect
12. Ensure sustainable consumption and production patterns	Economic	Renewable chemical production
13. Take urgent action to combat climate change and its impacts	Environmental	Reduction of VOCs by replacing solvents, non-polluting renewable energy
14. Conserve and sustainably use the oceans, seas and marine resources for sustainable development	Environmental	Biodegradable, bio-based substances
15. Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss	Environmental	Working with sustainable biomass to create sustainable products
16. Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels	Social	Indirect
17. Strengthen the means of implementation and revitalize the Global Partnership for Sustainable Development	Social and economic environmental	Indirect

[a] Note the use of reprotoxic chemicals creates otherwise avoidable gender imbalances in the chemical sector. The use of *N*-methyl pyrrolidinone (NMP) in coating formulations means some facility's risk assessments state they are only to be operated by males.[107]

important manufacturing industries (*e.g.* plastics), chemical and material water purification technologies, pharmaceuticals, and agrochemicals.[58] Note that all of these sectors are solvent users in one way or another.

How to actually measure sustainability by meeting targets (criteria), as set by the United Nations for example, has been discussed frequently in the literature, not least by Moldan *et al.*[47] Defining the indicators of sustainability is often considered as a more difficult challenge than obtaining the data to prove the chosen indicators. One approach is to establish acceptable conditions relative to baseline conditions. The most famous example is that global temperatures should not exceed 2 °C above pre-industrial levels. Such targets are set by policymakers, and this particular indicator was adopted by the 'UN Framework Convention on Climate Change' (UNFCCC) and reaffirmed at the '21st Conference of Parties' (COP 21) in December 2015.[59] Qualitative (soft) indicators are often set, especially for social sustainability targets, as is true for the United Nations '2030 Agenda for Sustainable Development'. Here, debate and consensus is required rather than creating arbitrary but legally binding targets. Whereas the 2 °C climate change indicator is a "bottom-up" approach designed to limit environmental damage, a "top-down" approach defines what sustainability looks like and then implements targets to reach this state. Bottom-up impact assessments seek to minimise (but ideally eliminate) adverse effects. By meeting the targets, the result is an outcome that is not less sustainable than the starting conditions. Objective-led (top-down) sustainability assessments define aspirational targets with indicators that must be maximised, but still these conditions are not necessarily indicative of an absolute state of sustainability, but relatively speaking only more sustainable if chosen correctly.[53] It can be helpful to think of indicators as only needing to define target conditions where the degradation of the environment or social conditions is slow enough to allow for improvements to technology and infrastructure to later rectify remaining issues, and meanwhile conditions are "consistently tolerable".[47,60] Ultimately something is sustainable or it is not, it is not actually a relative term even if it is convenient to express it as such. We cannot conclusively understand the point at which something becomes indefinitely sustainable, but it is appropriate to say that by achieving the goals of a sustainability assessment, conditions are improved within the defined framework of sustainability (Figure 1.11).[53] A sustainability assessment may be restricted to an isolated process or region, or only focus on one of the pillars of sustainability. The assessment will also be limited in its temporal focus.[61] Retrospective assessments monitor progress. Descriptive assessments analyse the present day scenario, and may (in part) be derived from a life cycle assessment (LCA), for example. Prospective assessments help decide on what action to take, ideally at the process/product design phase, typified by cost-benefit analyses and technoeconomic assessments.

To put these approaches into the context of chemical processes or product (*e.g.* solvent) design, the top-down approach lends itself to LCA, now a common method of determining environmental impact. As a means of

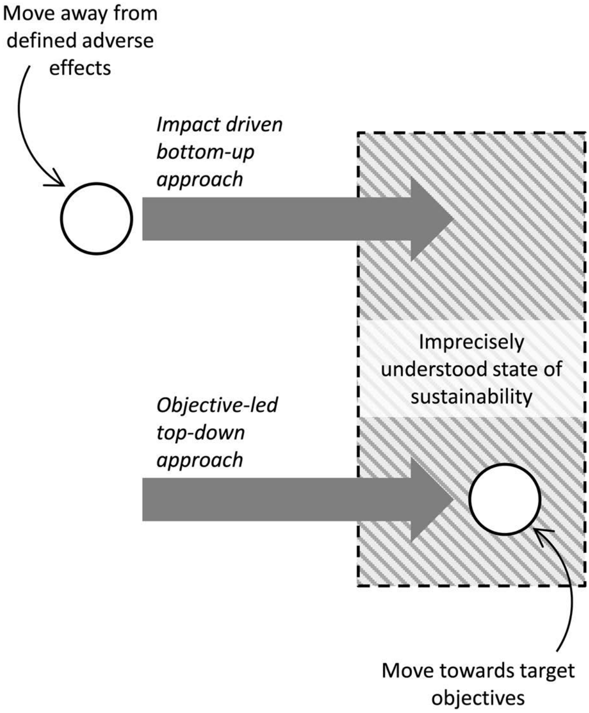

Figure 1.11 Approaches for sustainability assessment.

interpreting data, the results of an LCA can be taken forward into a sustainability assessment. A bottom-up approach will embrace broader issues, although admittedly it is more frequently applied to overarching government policies, such as emissions targets,[62] rather than to products. Nevertheless, many sustainability schemes of the sort used to certify biomass as sustainable do use some indicators based on bottom-up environmental impacts. Measures to protect highly biodiverse ecosystems would be an example. Several sustainable biomass certification schemes are formally recognised as compliant with the European Renewable Energy Directive (2009/28/EC) requirements for sustainable biofuels,[63] but some are also applicable to the feedstocks of bio-based products. For example, the Roundtable on Sustainable Biomaterials (RSB) offer a standard for the certification of bio-based products (see Chapter 3).[64] Most of the objectives in sustainable biomass certification schemes may be demonstrated with top-down indicators, especially those concerning economic management and social rights.

Lapkin's discussion of sustainability indicators for the chemical industry, the means that offer the proof that certain criteria have been fulfilled, is important for chemists to appreciate.[65] Usually the only calculation of interest to a bench chemist is product yield, but increasingly, green chemistry metrics and LCA style indicators are being used to evaluate processes at all

Table 1.3 Environmental issues defined as sustainability indicators.

Product level	Company level	Government level	Societal level
Reaction mass efficiency (RME)[108]	Production efficiency	Material intensity per unit service	Global warming potential
Atom economy[109]	Water use	Sustainable process index (SPI)[110]	Ozone depletion
Use of renewables	Energy use		Water depletion
Solvent use	Product toxicity		Resource depletion

operational scales (bench to manufacturing).[66] Table 1.3 provides some useful environmental indicators, which take the form of numerical calculations, including solvent use. More discussion of sustainable chemistry is present in Section 1.3.2.

George has attempted to develop measurable criteria based on international sustainable development targets.[67,68] His criteria form a checklist of requirements, mostly based on fairness under the terms of social sustainability (Table 1.4).[68] The definitive "yes" or "no" answers that are needed stimulate a thought provoking exercise. Although thresholds for quantification are not directly included, the environmental criteria allude to measurements that would demonstrate compliance. The implementation of these criteria is geared towards the evaluation of government sponsored developments in "industrial countries".[67] However it is not unreasonable to expect that many of the criteria will already have to be followed to obtain permits for the construction of chemical plants in most countries. By completing the checklist, commercial chemical processes stand a better chance of longevity in a world with increasing social, economic and environmental pressures.

1.3.2 Sustainable Chemistry

Sustainability is of special relevance to chemistry and its associated disciplines because of the connection between climate altering emissions such as CO_2 and other environmental pollutants and the industries producing chemical products. Sustainable chemistry is not simply the use of only abundant metals, or renewable raw materials, and is not to be confused with low toxicity products, good environmental health and safety (EHS) practices, or other "green" initiatives. The sustainability of a chemical process or product is subject to the same rigours of environmental, social, and economic sustainability assessment as any other commodity or activity. Green chemistry metrics can contribute to sustainability assessments (Table 1.3), but only incompletely.

Sustainable Chemistry was defined in an Organisation for Economic Co-operation and Development (OECD) workshop in 1998 dedicated to the topic: "*Within the broad framework of Sustainable Development, we should strive to maximise resource efficiency through activities such as energy and non-renewable resource conservation, risk minimisation, pollution prevention, minimisation*

Table 1.4 Criteria for sustainable development appraisals.

Principles	Criteria
Local and regional intra-generational equity	Have all social groups within the planning area been identified, and have the social, economic and environmental impacts on each group been assessed separately where they are likely to be different, including different impacts on men and women? Will the planning documents and the sustainability appraisal be published and made readily available to all members of the public? Will all members of the public have the opportunity to comment on the planning documents and the sustainability appraisal, and will their views be taken into account before plans or planning guidance are adopted? Have suitable provisions been made for the participation of disadvantaged minorities in the decision-making process?
National intra-generational equity	Has all relevant national planning guidance been complied with?
Transnational intra-generational equity	Have significant transboundary impacts been identified and properly assessed, are relevant international agreements complied with, and will affected parties be consulted before final decisions are made?
Global intra-generational equity	Have all potential global impacts been identified and properly assessed, and are relevant global agreements complied with?
Preliminary inter-generational equity	Have any potentially critical ecosystem factors that may be affected been identified? Has the risk of serious or irreversible damage arising from any such impact been satisfactorily assessed, with suitable systems for monitoring and impact avoidance where needed, and using risk assessment techniques where appropriate?
Strong inter-generational equity	If the risk of serious or irreversible damage is significant, or if a risk that is already significant may be increased, will the impact be fully mitigated, in kind, such that there will be zero adverse residual impact?
Weak inter-generational equity	Has the natural capital that may be converted into other forms of capital been identified? Is it satisfactorily demonstrated that total capital will be conserved?
Global biodiversity	Is any loss of natural habitat quantified, where it is important for species conservation? Is it demonstrated that the rate of loss will not exceed the equilibrium regeneration rate?
Global climate change	Is an appropriate contribution to reducing greenhouse gas emissions shown to be made, which is in accordance with the Kyoto agreement?

of waste at all stages of a product life-cycle, and the development of products that are durable and can be reused and recycled. Sustainable Chemistry strives to accomplish these ends through the design, manufacture and use of efficient and effective, more environmentally benign chemical products and processes."[69] This description is akin to the objectives of green chemistry and fails to provide targets or a method of actually measuring sustainability. In 2004, an article by Steinhäuser *et al.* recognised the limitations of, and the confusion created by, the unsystematic use of the phrase "sustainability" within chemistry.[70] The unwillingness of those responsible for chemical plant design and the chemical products themselves to establish criteria to measure (and hence improve) sustainability at that time was also highlighted by Steinhäuser *et al.* In the decade since, gradual improvements have been made towards the quantifiable practice of sustainable chemistry, but no consensus has been reached. One area that has seen great improvement is the application of life cycle assessment (LCA), which has become reasonably widespread. An LCA is not a sustainability assessment in itself, but the results can be interpreted in the context of environmental sustainability (provided thresholds are introduced to mark the point at which a sustainable level of emissions and resource depletion is reached). Life cycle assessment is explained subsequently in Chapter 3. Social and economic considerations then also need to be addressed by other means, for neither is within the scope of an LCA. When combined, social, economic, and environmental impacts can be evaluated in the framework of a complete sustainability assessment. The different but interlinked roles of the principles of green chemistry for environmentally benign deliberative product and process design,[71] and LCA as a method for quantifying impact, are represented pictorially in Figure 1.12.[72]

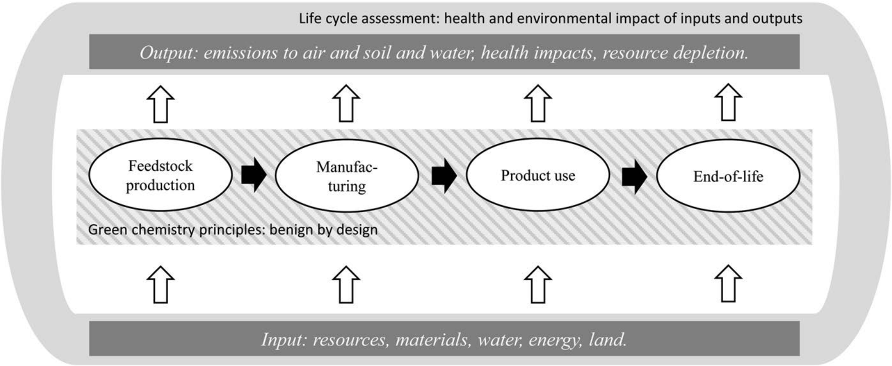

Figure 1.12 The stages of a cradle-to-grave life cycle (white ovals) are dependent on inputs, and result in outputs (dark grey boxes). The remit of green chemistry encapsulates the design of products and processes, and the monitoring and reduction of hazards (striped region), while a life cycle assessment quantifies the consequences outside of the direct product value chain (light grey region).

The lack of differentiation generally made by chemists between green chemistry, LCA results (and other types of environmental assessments), and sustainability is a persistent problem, and all three are often used interchangeably in discussion, to the detriment of establishing truly sustainable chemistry.[73,74] Calls to educate students and create a widespread awareness of how broad the concept of sustainability actually is have not been acted on to a sufficient extent.[75] A common feature of green chemistry and sustainable chemistry is the requirement to plan and design appropriately. The fragmented, reductionist manner in which products and processes are designed is not conducive to creating sustainable practices, and it will take time to rectify this.[76] But whereas green chemistry is a practical philosophy of science that seeks to improve the design of processes to be less wasteful and more energy efficient, and for the products to be non-toxic, sustainability when applied to chemistry quantitatively analyses the effect on the communities and ecosystems exposed to any waste, the impact of land use (direct and indirect) and other wide ranging problems such as biodiversity and water scarcity that lie beyond the immediate influence of green chemistry. The 12 principles of green chemistry are qualitative, and do not come together to form an absolute definition of what is green and what is not.[77] Green chemistry clarifies progress and provides a means of comparison. Meanwhile, environmental sustainability assessments only make sense if indicators of progress are used. Economic and social factors are not covered by green chemistry. While economic sustainability is proven mathematically and through business plans and economic uncertainty analyses, social sustainability assessments may require criteria to be fulfilled with qualitative indicators.[78] Nevertheless all types of sustainability thresholds are defined and proven with falsifiable indicators.

Hutzinger offers clarification of the different meanings of green chemistry and sustainable chemistry,[79] stating that "*sustainable chemistry is the maintenance and continuation of an ecologically sound development whereas green chemistry focuses on the design, manufacture, and use of chemicals and chemical processes that have little or no pollution potential or environmental risk and are both economically and technologically feasible … the terms cannot easily be exchanged*."

The following table notes some differences between the approach and focus of green chemistry and sustainable chemistry. In Table 1.5 the 12 principles of green chemistry and a selection of sustainability criteria are listed as they would be used to help with the design of a chemical process, as put into practice by Saavalainen *et al.*[80] It is clear that green chemistry emphasises the consequences of the design of the chemical process, and sustainability criteria measure the resulting impact outside the plant. Forward thinking life cycle assessments can be performed early in the plant development to ensure that the lowest possible impact to the environment occurs.[81–84] Green chemistry, assuming the role of risk assessment, can integrate well with LCA, and although neither constitutes a complete sustainability assessment, the result can help with plant or product design to reduce the environmental impact. Life cycle assessments do not typically incorporate dimensions

Table 1.5 Consequences of applying the 12 principles of green chemistry, contrasted with similar considerations of environmental sustainable chemistry in the context of plant design.

Triple bottom line	Green chemistry design criteria	Sustainable chemistry criteria
Social	Design the process to use and generate only non-toxic substances (can be quantified with the toxicity of each chemical)	Health and safety (calculate the inherent toxicity of chemical substances used)[72]
	The products should be designed for optimal performance and minimal toxicity	Human rights
	Continually monitor and analyse the process to avoid accidents	Employment practices (diversity, equality)
	Reduce the inherent potential for accidents and releases with safe chemicals	Social responsibility
Economic	Choose the most appropriate chemical synthesis for the product (can be quantified with atom economy)	Operating costs, profit, investment, decommissioning and clean-up cost[111]
	Shorten the process by only conducting chemical derivatisation that is evident in the structure of the final product	Market presence and business relationships
	Conduct the process at ambient temperature and pressure	Taxes and cost of environmental liability
Environmental	Design the process to minimise waste (can be quantified by E-factor or similar metrics)	Calculate emissions and their impact on global warming, ozone depletion, and smog (ozone creation)
	Use a renewable feedstock	Calculate water use and the amount of water discharged from the plant
	In order of preference: do not use auxiliary chemicals; use safer, non-toxic auxiliaries; use less materials	Calculate the amount of solid waste produced by the process
	Use catalysis	Measure depletion of biotic and abiotic reserves
	The product should be designed to be biodegradable with innocuous by-products	Calculate energy use
		Calculate emissions and their impact on acidification and eutrophication
		Calculate emissions and their human toxicity and their eco-toxicity

of time or space, or the probability that an emission will actually have the assumed effect.[85] Alternative assessments to an LCA do have dimensions, but this does not replace the risk minimising aspect of green chemistry, or the benefits of the "benign by design" approach.[110] The link between the principles of green chemistry and sustainability criteria are weakest for economic considerations. This is to be expected, and this shortfall is met by technoeconomic assessments, for example.[86] Thus we can think about the relationship between green chemistry and sustainability as follows. Products, and the processes chosen to make them, should be designed with risks considered to reduce EHS impacts. Different options can be compared at the design phase with a LCA to refine the implementation of the principles of green chemistry for the best overall outcome. The data produced by an LCA is then applicable to a sustainability assessment in which the less chemistry centred considerations of social impact and economic viability are introduced in order to establish and maintain a sustainable value chain for products and services.

The feedstock and process selection is important, and many successful attempts to demonstrate the viability of chemical production from biomass have been made in the context of green chemistry.[87] Also site selection is important, but this is not covered by the green chemistry principles. The production site should be accessible to raw materials and markets.[88] The social and economic impact of the site can be understood in terms of, amongst other considerations, the opportunities for regional employment that are created, and conversely the nuisance of increased transportation, noise, and visual impact on the local area. If any of these factors risks the long-term success of the operation, it is not sustainable. Above all these considerations, sustainable land use has attracted the greatest interest of late, due to the gap in quantitative understanding of the impact of indirect land use change (ILUC) especially,[89] and how ILUC is represented in regulations governing sustainable biomass production. When biomass production on agricultural land is dedicated to bio-based products,[90] as is true of the present day bio-fuel industry, the shortfall in food production must be made up by intensification or adoption of new land (including previously biodiverse grassland or forest). Both approaches can have negative environmental impacts, which should be appreciated as a consequence of bio-economy activities. A more ambitious longer term goal is to move non-food biomass production off-shore (*e.g.* as algae). The European Renewable Energy Directive was supplemented in 2015 with a European Directive ((EU) 2015/1513) to minimise the impact of ILUC in achieving renewable energy targets.[91]

It is not only our chemical methods and processes that are subject to change as we seek sustainable development. The business models we use to offer the services of chemical substances need to be rethought, especially with the aim of minimising waste and pollution.[92] Chemical products are generally sold on the basis of mass (or equivalent). Therefore, it is in the interest of the supplier to sell more product with the consequence of unnecessary waste. Add to that the inherently unsustainable nature of fossil-derived products,[93] and it is clear that an improved business model for bio-based products would be environmentally beneficial. If the social benefits of products can continue to be delivered with a new, economically sustainable approach, then an overhaul of current commercial practice can be justified. Chemical leasing is an intriguing concept where the customer pays for the service of a product rather than the amount of product.[70,94] Examples have included painting, waste water treatment and solvent metal cleaning.[95] This involves the producer using less resources, and even taking back the product after its primary use to recover and reuse it. It certainly requires a different business model to grow this approach.

1.3.3 Relevance of Sustainability to Solvents

Sustainability is as relevant to solvents as it is to any other chemical product. Solvents are widely understood to be volatile organic compounds (VOCs), and will have greater impacts on air quality than non-volatile substances. Often solvents are burnt as a fuel after use, and before that, they are reconditioned between uses with energy intensive distillations, and so the global warming potential of solvents can be expected to be more pronounced than that of products with longer lifespans, or those that are mechanically recycled. It is certainly true that the high volume of solvent use in a typical solution phase process means that solvents dominate the emissions and energy demand of such processes.[96] As is true for the general discipline of sustainable chemistry, authors of solvent-related studies are sometimes keen to define the role of a sustainable solvent more specifically. However, claims of sustainability must be appropriate and justified. If a solvent is renewable, it is not automatically sustainable. It may be sustainable for a variety of other reasons, in addition to being derived from a renewable feedstock, but the nature of the raw material alone is not enough of an indication. Life cycle assessment as a contributing tool towards a sustainability assessment is mostly based on emissions, but can also include land use and depletion of resources and biodiversity. An LCA is equally applicable to petrochemical solvents as it is to bio-based solvents, and the former may appear to be superior to the latter in a comparative assessment. Fossil resources such as crude oil and natural gas are not an economically sustainable basis of energy or materials because they are used at a far greater rate than they could ever be replenished. It is unforeseeable that future generations could rely on primary resources of fossil fuels to the same extent as us, or at all based on projected world population growth estimates. Recycled or otherwise reclaimed materials that have a petroleum origin can be considered as suitable feedstocks, as long as their conversion into solvents does not prevent the material from being used again after the solvent becomes waste. The firm stance that primary fossil reserves are inherently unsustainable is adopted in this book, and equally the energy required in any solvent producing process should also be renewable. In an LCA, non-renewable energy use is a typical indicator. In terms of a threshold, zero depletion of non-renewable resources might be the only acceptable indication of sustainability in this respect.

When referring to sustainable solvents, ultimately it is the final, formulated product or process that must be sustainable. The solvent has what might be described as a passive role, for it is certainly not the reactant or the active ingredient. However, the solvent must of course be sustainable, for if it is not, the sustainability of the product or process is jeopardised. The amount of solvent is typically significant, and the solvent actually often makes up the majority of the mass of chemicals used in a process or found in a formulation.

Two review articles from the recent literature address the role of solvents in sustainable chemistry. The earlier of the two (published 2014) was produced by Charles Eckert and Charles Liotta and co-workers, and is entitled 'Solvents for Sustainable Chemical Processes'.[97] The more recent review by Tom Welton, 'Solvents and Sustainable Chemistry' (2015), has a similar title.[98] It is noticeable that the authors all refrain from stating that any solvent is itself sustainable, but it is the characteristics of the solvent that impart sustainability onto the process (neither review describes solution-based products). The solvents described in 'Solvents for Sustainable Chemical Processes' are supercritical fluids, gas-expanded liquids (GXLs), switchable solvents, organic-aqueous tuneable solvents (OATS), and superheated water.[97] These types of neoteric solvent are all waste reducing technologies, and are covered in Chapter 4. Waste is not the only consideration of importance, but if solvent waste is avoided, this will translate to a major material saving in many cases. In turn, less raw materials are needed to replenish the solvent that would have previously been lost, and the emissions from solvent release or incineration are lessened. In support of this mentality, complementary to European ambitions of a circular economy,[92] Horváth has said "*resources including energy should be used at a rate at which they can be replaced naturally and the generation of wastes cannot be faster than the rate of their remediation*" assisted through "*sustainable refurbishing, remanufacturing, and recycling processes and/or technologies*".[99]

Eckert and Liotta explain how the Brundtland commission,[45] in their definition of sustainable development, focuses the objectives of sustainable chemistry: "*What we seek are processes that are not only green, but also economically favorable to promote their implementation by industry*".[97] Despite social impacts being neglected, the importance of economic drivers are correctly realised, stepping beyond the 12 principles of green chemistry. They go on to say "*A green and sustainable solvent can be defined as a solvent that addresses environmental issues, contributes to the optimization of the overall process, and is cost-effective*". Welton's interpretation of a sustainable solvent is similar, but he is rightfully cautious about assigning the term "sustainable" to a solvent, or any chemical or process in fact without the proof needed to do so.[98] The definition of sustainable chemistry is supplemented by Welton with social factors when he says "*the benefits of modern chemistry and chemical products should be made available to all communities*", and economic factors: "*a sustainable chemical product should be supplied at a price that enables it to be accessed by its users while at the same time being commercially viable for its producers*".[98]

One might conclude that the understanding of sustainable chemistry is easier to grasp when in the context of a specific type of chemical (*i.e.* solvents), because the definitions supplied previously in Section 1.3.1 were almost too embracing of worldwide sustainable development objectives to be useful to chemists. Focusing in on solvents, we know that if we want to achieve benign and sustainable processes across the chemical industries, the role of solvents is hugely important. There are acute sustainability issues for many metal catalysts that also warrant our attention,[100] but the solvent regularly contributes to sustainability impacts and environmental health and safety more than anything else. The use and choice of the solvent must be regarded as at least as important as the catalyst and the selected reactants. If non-hazardous solvents become routinely recovered and reused with little impact caused by release or disposal, a great step will be made towards the sustainability of the chemical industry.

In reality it is not nice-sounding aspirational objectives that initiate change, but definite and forceful actions. If a solvent is not acceptable because it is banned through regulation, or creates conditions that breach regulations indirectly, it cannot be considered as sustainable because it cannot be used. Business relationships that rely on products or processes utilising a solvent with an uncertain future with respect to its regulatory control are not the basis of lasting partnerships. In turn, the entire economic viability of using solvents at risk of increased restrictions is questionable. The reasons for the increased controls that several solvents now face are likely to be toxicity or environmental issues, with probable consequences that also impair social sustainability. The exact nature of these regulations is dealt with in Chapter 2, and their implications in Chapter 5 under the umbrella of solvent selection. In the discussion of sustainability found in Chapter 3, it is assumed that regulation is not influencing the sustainability of the solvents, unless spoken of directly. In reality, many regulations relevant to solvents set limits on emissions, or the acceptable toxicology profile in the form of exposure limits of airborne solvent vapour or residual solvent in products, and these thresholds are complementary to the demonstration of some sustainability indicators. The demonstration that a chosen solvent is a sustainable option is thus subject to proof that regulation (now or with reasonable certainty in the future) will not inhibit the market potential of products and processes reliant on that solvent, and that no harm will come to people or the planet because of that choice of solvent. Foremost, the benefits imparted by a product or process must counterbalance the impact of all the solvents and other material and energy inputs required to deliver that product or process.

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CHAPTER 2

Modern Trends in Solvent Use

2.1 Policies, Regulation and Opportunities Influencing Solvent Use

2.1.1 Push: Regulation

Regulation is the most important force in the chemical industry for stimulating change from old habits, requiring operators to reduce emissions or implement solvent substitutes. Half of the greenhouse gas emissions from pharmaceutical manufacturing are still directly related to solvent use.[1] Solvents that used to be popular can become obsolete because of regulation. Regulatory requirements can be specific to different industries and regions, with some of the strictest legislation in terms of solvent use applied to pharmaceuticals and food processing. Summarising these regulations is not completely helpful because they are frequently revised and updated, and will not necessarily apply to your region. Therefore, it is important to read any legislative texts directly if they are relevant to your work. That said, overviews of solvent regulation are available, and can be useful to generate awareness. The European Solvents Industry Group (ESIG) provide an overview of solvent regulation on their website for the European audience.[2] Other books provide a description of international regulations.[3,4]

Long standing international conventions have famously restricted the use of ozone depleting solvents (*i.e.* the Montreal Protocol).[5] In addition, they have defined the permissible levels of residual solvents in pharmaceuticals,[6] and established a unified system of categorising the hazards of substances for the purpose of safe transport and handling (*i.e.* the United Nations (UN) Globally Harmonized System (GHS) of classification and labelling of chemicals).[7] Several prominent regulations and directives applicable to the European Union apply to solvents (Table 2.1). The terminology dictates that a

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Table 2.1 Legislation for solvents in the European Union (2016).

Legislation	Purpose
VOC Solvents Emissions Directive 1999/13/EC[227]	To limit the emissions of volatile organic compounds (VOCs) caused due to the use of organic solvents in industries such as printing, coating, cleaning, and the manufacture of pharmaceuticals
The Paints Directive 2004/42/EC[228]	To prevent the environmental impact caused by VOC emissions from decorative paints and vehicle refinishing products. This directive acts as an amendment to 1999/13/EC
The Industrial Emissions Directive 2010/75/EU[229]	To control pollution caused by the emissions from industrial installations. This directive is the result of a recasting of several emissions and wastes directives, including the original VOC Solvents Emissions Directive (1999/13/EC)
Air Quality Directive 2008/50/EC[230]	To establish air quality objectives, limiting anthropogenic particulate matter, NO_x and SO_x, and maintaining good air quality
National Emission Ceilings Directive 2001/81/EC[231]	To implement upper limits for emissions of pollutants chiefly causing acidification, eutrophication and ground-level ozone, these being VOCs, sulphur dioxide, nitrogen oxide(s) and ammonia. The fugitive evaporation and incineration of solvents is a significant contributor to atmospheric pollution. A revision is planned to extend the scope of this directive until 2030 and also include methane and airborne particulate matter
Waste Framework Directive 2008/98/EC[232]	To define waste management practices that reduce waste and maximise the potential to reuse and recycle. Revisions to this directive will be implemented in the future according to the EC circular economy strategy[233]
Water Framework Directive 2000/60/EC[234]	One of many objectives is the monitoring of chemicals in waterways. Priority substances are subject to concentration limits (solvents come under scrutiny here), and priority hazardous substances must be phased out by given deadlines
Extraction Solvents used in the Production of Foodstuffs and Food Ingredients Directive 2009/32/EC[235]	To define solvents appropriate for the extraction of foodstuffs or food ingredients. Solvents that may be used for any food extractions are butane (gas), carbon dioxide (gas), ethanol, ethyl acetate, nitrous oxide (gas) and propane (gas). Acetone is restricted only in olive pomace oil extractions. Conditions are imposed on other solvents
Cosmetics Regulation 1223/2009[236]	To control the ingredients used in cosmetic products
REACH Regulation 1907/2006[237]	Ultimately to restrict the use of hazardous substances that are either toxic to humans or damaging to the environment. REACH is the Registration, Evaluation, Authorisation and Restriction of Chemicals
CLP Regulation 1272/2008[238]	To communicate the hazards of substances in a universally understood manner. CLP is the Classification, Labelling and Packaging of Substances and Mixtures, based on the UN GHS[7]

European Directive outlines an ambition which individual European member states achieve by their own means (including the implementation or revision of their own national laws). On the other hand, a European Regulation is binding legislation in its own right. Note that in Table 2.1, the European VOC Solvents Emissions Directive of 1999 has now been updated, and two separate directives relating to paints and industrial emissions renew and elaborate the purpose of this legislation.

Arguably the most significant piece of (European) regulation to effect solvent use, and probably the most debated, is REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals), Regulation EC 1907/2006.[237] Its implementation is overseen by the European Chemicals Agency (ECHA). Depending on the volume in which a substance (including solvents) is manufactured or imported into Europe, a number of chemical properties must be registered. These are then evaluated to assess the hazards (if any) posed by the substance. The mechanisms behind the implementation of REACH are numerous and complex. Specialist texts are available for more information,[8] and the online resources available are detailed.[9] Please be aware that a review of REACH is due in 2017, and so updated information should be sought after this date. However, the basic premise, as set out below, will undoubtedly remain more or less unchanged.

If a solvent, for example, is considered to possess significant human toxicity or pose a significant environmental hazard, it is then regarded as a Substance of Very High Concern (SVHC). Any carcinogenic, mutagenic, or reprotoxic (CMR) substances are designated as a SVHCs. So are chemicals that are persistent in the environment, bioaccumulating, and toxic (PBT). Very persistent and very bioaccumulating (vPvB) substances are also recognised as SVHCs.

Every SVHC is eventually subjected to a comprehensive assessment to identify the best approach to minimise the risks associated with it. This process is very much still ongoing, with more than 150 SVHCs at the end of 2016 identified but yet to be fully evaluated (some are solvents, such as *N*,*N*-dimethyl formamide, DMF).[10] After evaluation, a substance may then be subject to authorisation.[11] This means that after a specific date, companies must be granted authorisation to be permitted to continue to use the chemical in question. To justify authorisation, a comprehensive justification must be supplied to the ECHA. This takes the form of a so-called "socio-economic assessment", which proves that the benefits generated from the use of the SVHC outweigh the risks.

Alternatively, a restriction may be placed on the SVHC.[12] Any solvent subject to a restriction can only be used within Europe under the terms defined by REACH. Often the restriction is in the form of a maximum permitted concentration in certain products, or perhaps the airborne concentration of its vapour during use in an industrial setting is limited. For end-users and the public, the ECHA also provides simple infocards for registered substances.[13] These short summary sheets provide an overview of any prominent hazards, as well as general information about production/import volumes and relevant uses of the substance.

The impact of REACH on solvents has already begun. In particular, aromatic solvents, chlorinated hydrocarbons, and certain ethers and amides are vulnerable because of their chronic toxicity. As of 2016, there are just over 30 substances that are part of the REACH authorisation procedure. Two are solvents, with chromium salts, arsenic compounds, and phthalate plasticisers making up most of the list. One of the solvents in question is *bis*(2-methoxyethyl) ether, a reprotoxin for which the period of full authorisation will commence in August 2017. The carcinogenic trichloroethylene is the other solvent in the list of REACH authorised substances. Its authorisation period started in April 2016. Companies that have been granted authorisation can continue to use trichloroethylene,[14] but otherwise its sale and use is now prohibited in the European Union. Although several applications have been submitted, thus far only one European company has secured authorisation to use trichloroethylene. Permission was obtained to operate two processes using trichloroethylene, both for resin recovery, one from dyed cloth and another from waste water.[15]

REACH-implemented restrictions may only apply to specific applications.[12] For instance, chloroform is restricted as a substance or mixture (if present at levels above 0.1%) from products either sold to the public, or used for surface and fabric cleaning. Academic and industrial uses remain possible. Medicines and cosmetics are covered by their own specific sector regulations, as noted in the REACH regulation itself.[237] Restrictions are also in place for flammable liquids and substances responsible for chronic toxicity. These restrictions apply to various types of products made for the general public. Restrictions on common solvents and substances that could be used as solvents under REACH apply to the following (as of 2016):

- Benzene
- 2-(2-Butoxyethoxy)ethanol
- Chloroform
- Cyclohexane
- 1,4-Dichlorobenzene
- 1,1-Dichloroethane
- Dichloromethane (DCM)
- 2-(2-Methoxyethoxy)ethanol
- Pentachloroethane
- 1,1,1,2-Tetrachloroethane
- 1,1,2,2-Tetrachloroethane
- Toluene
- 1,2,4-Trichlorobenzene
- 1,1,2-Trichloroethane

There are a number of additional solvents in earlier stages of the REACH process pipeline, which have already been recognised as SVHCs,[10] but are yet to see restrictions or authorisation put in place. For most, European restrictions can be expected in the future. Several amide, chlorinated, and ether solvents are featured in this SVHC list due to their carcinogenicity (chlorinated solvents) or reprotoxicity (amides and ethers):

- 1-Bromopropane
- 1,2-Dichloroethane
- 1,2-Diethoxyethane
- 1,2-Dimethoxyethane
- *N*,*N*-Dimethyl acetamide (DMAc)
- *N*,*N*-Dimethyl formamide (DMF)
- 2-Ethoxyethanol
- 2-Ethoxyethyl acetate
- Formamide
- 2-Methoxyethanol
- 1,2-*bis*(2-Methoxyethoxy)ethane (triglyme)
- *bis*(2-Methoxyethyl)ether (diglyme)
- *N*-Methyl acetamide
- *N*-Methyl pyrrolidinone (NMP)
- Nitrobenzene

These lists should not be considered as exhaustive. Many other substances are now formally designated as SVHCs or are already restricted in Europe. At the less stern end of the regulatory spectrum, solvents not subject to REACH authorisation or restriction must still comply with general labelling requirements to communicate the hazards associated with the substance. The UN GHS created a framework adopted by the European Union for regulation (European Regulation 1272/2008).[238] Hazard Statements and their associated pictograms clearly communicate environmental health and safety (EHS) issues in a systematic way. Some of the most relevant hazards for solvents are related to flammability, toxicity and ecotoxicity. The most pertinent Hazard Statements for selected solvents are documented in Chapter 6.

2.1.2 Pull: Green Solvents

Clearly a great burden is placed on solvent producers and users to adhere to legislation. Regulation has made the use of certain solvents near impossible in some disciplines, and in other instances it is tightly controlled. One way to avoid or lessen the responsibility to observe regulations is to only use substances that pose no hazard, or at least less severe hazards. Similarly, the solvent market is also changing to reflect greater user demand for safer chemical substances. Green and bio-based solvents are increasing in market share in response to legal limitations on the VOC content in paints, labelling and certification pressures, and regulated residual solvent limits in products (amongst the many important considerations that affect solvent use today). A market study (Technavio, 2016) places the growth of green and bio-based solvents at 8%, returning billion dollar revenues annually.[16] The use of solvents with environmental benefits (as reported by Technavio, although this term is

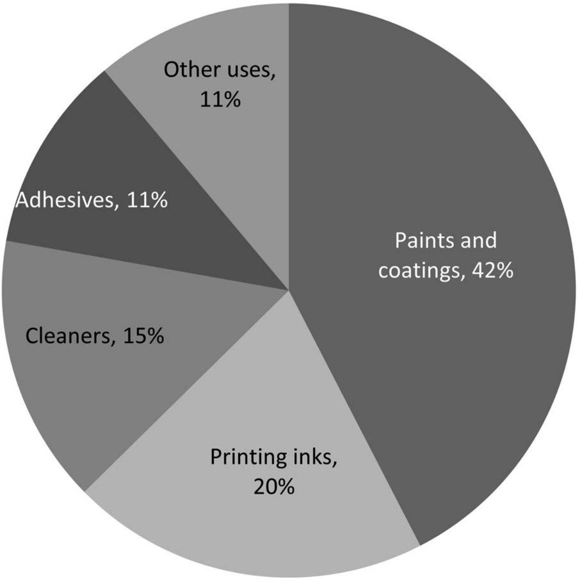


Figure 2.1 A projection of green and bio-based solvent use by 2020.[16]

not defined) seems to correlate well with total solvent use patterns globally. Paints and then printing inks dominate the green solvent sectors. Cleaning formulations and adhesives are the other major sectors most interested in green solvents (Figure 2.1). The impact of solvents extends far beyond these industries, and so the remainder of this chapter is dedicated to a discussion of the sectors that are most dependent on solvents, and what they must achieve in terms of solvent substitution to continue to operate successfully. The case studies presented are a mixture of large solvent users, including pharmaceuticals, and growing applications, *e.g.* graphene production. Green solvents are only a first step towards a sustainable, solution-based chemical industry, and there is a lot still to be achieved before that goal is realised.

2.2 Pharmaceuticals

The pharmaceutical industry is regarded as Europe's second largest user of solvents.[17] Multi-step reactions and extensive purification processes (recrystallisation, chromatography) escalate the solvent demand above that of the commodity chemical sector. Estimates from GSK place solvent use at 80–90% of the total material use (excluding water).[18] This has consequences for the energy use and emissions associated with the manufacturing of high value, fine chemicals.[1] However the scale of research and development in this industry means that small scale chemistries collectively also use considerable quantities of solvent. The greater freedom to work when at smaller scales and the expectation of reproducible and high yields, along with high throughput, means that undesirable solvents are frequently used, usually following literature precedents. An evaluation of solvent use in early stages of pharmaceutical research, through to pilot plant optimisation and finally manufacturing is worthwhile to harmonise efforts towards greener and more sustainable solvent use. Currently the design of large scale processes is hampered, because it requires the substitution of solvents used at smaller scales to avoid conflict with regulations. To its advantage, the current model does not impede drug discovery labs by imposing solvent restrictions, and this permits drug candidates to reach scale-up as quickly as possible.

The importance of correct solvent selection means different things to different people, depending on the scale they work at. Discovery chemists use colour-coded solvent selection guides to steer them away from the most hazardous solvents. Process development teams need to go a step further because of the harsher restrictions imposed on them. For example, simple LCA-type tools may be used to optimise solvent selection.[19,20] Environmental, health and safety regulations determine what solvents can be used in the manufacturing of an active pharmaceutical ingredient (API), as do the best available manufacturing techniques for the handling and recovery of solvents. Regulatory approval is especially stringent in the pharmaceutical industry.[21] The registration of an API defines the residual solvents and morphology, which means that changing a solvent in a manufacturing process is extremely difficult without having to also re-register the drug (Section 2.2.7). Thus it is important to optimise solvent selection as soon as possible.

Life cycle assessment (LCA) is now considered a vital tool for the pharmaceutical industry, and is gaining wider recognition.[22] Details of the principles behind LCA are found in Chapter 3, but the results of published LCA studies are of interest here. In one example, solvent recycling was identified as important to reduce the environmental impact of the synthesis of the anti-convulsant drug Rufinamide.[23] It was found that the majority of the environmental impact comes from the reactants, but waste treatments (including the needed to deal with the solvent) were also significant. Streamlining the synthesis with multi-step reactors and solvent-less reactions was shown to reduce the environmental impact, chiefly through reduced solvent use. With so much solvent required by this sector, the increasing use of LCA and an underlying interest in the telescoping of reactions, flow chemistry, and other solvent-saving practices will increasingly direct the pharmaceutical industry towards using less solvent, and of course different types of solvent in response to regulations.[24]

2.2.1 Reaction Overview and Solvent Use in the Pharmaceutical Sector

The pharmaceutical industry is known to be the sector using the most varied types of solvents, and the most solvent compared to the amount of product created.[25] For this reason, solvents are prominent in the efforts of pharmaceutical companies to reduce their environmental footprint, even down to the smallest scale chemistry.[26] Data published in 2001 indicates that alcohols and aromatic solvents are the most common solvents within the pharmaceutical

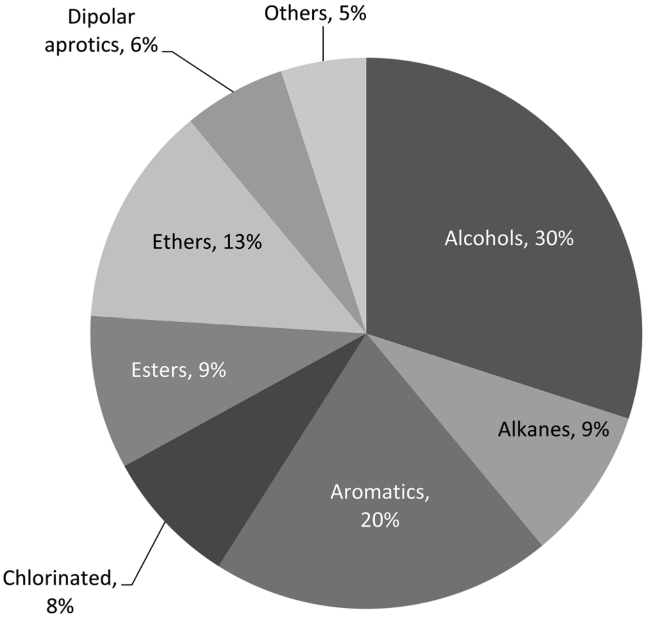


Figure 2.2 A pie chart indicating solvent use in the pharmaceutical industry (GSK data).[27]

industry (Figure 2.2).[27] An interesting comparison to the data in Figure 2.2 can be provided by reviewing the data for pharmaceutical industry solvents that are not recovered (and therefore incinerated or released). Numbers from 2010 indicate that over 43 thousand tonnes of solvent were incinerated or released by the USA-based pharmaceutical industry.[28] Methanol and toluene are the most significant (Figure 2.3), which are, of course, alcoholic and aromatic solvents. Worryingly, the amount of dichloromethane (DCM) and DMF released or incinerated is also high.

Data is available in the published literature that describes the typical reactions used by the pharmaceutical industry, and goes some way to explaining why they use the solvents they do. Each reaction to create a drug prototype, intermediate or final API will typically require a solvent for that transformation. Table 2.2 contains information on reactions involved in at least 1% of practices in drug discovery (GSK),[29] process development at AstraZeneca, GSK, and Pfizer,[30] and manufacturing processes at Pfizer.[31] Reactions used in less than 1% of all instances have been excluded to prioritise the more common transformations. This data has been annotated with notes on solvent use, collated from the examples found in Kleemann and Engel's 'Encyclopaedia of Pharmaceutical Substances',[32] for the top 200 pharmaceutical products.[33] Christian Reichardt's book 'Solvents and Solvent Effects in Organic Chemistry' was also used as a source,[34] as was 'Greene's Protective Groups in Organic Synthesis'.[35] The way each source has collated its reaction data means

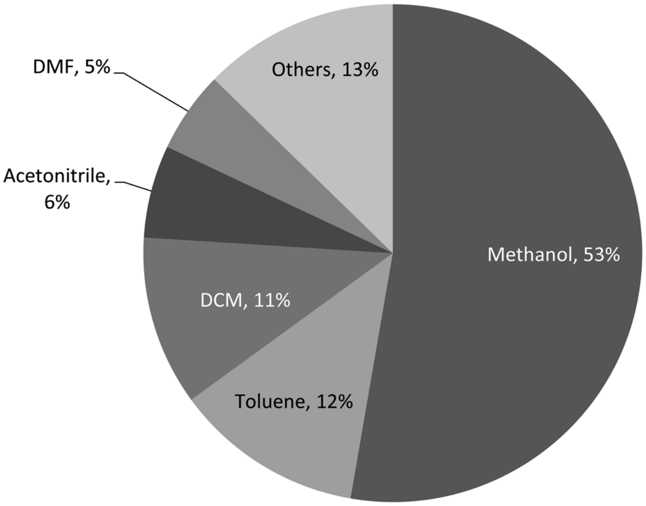


Figure 2.3 The relative proportions of solvent released or incinerated by the pharmaceutical industry in 2010 (USA national data).[28] Note that the data capture does not cover all solvents.

that comparison between datasets is difficult. For example, 17% of discovery chemistry reactions are condensations, but it is not clear how many refer to carbon–carbon bond formation and how many are esterifications or other bond formations with heteroatoms. Therefore, they could not be included specifically within the summary presented in Table 2.2. The blank entries in Table 2.2 do not necessarily signify an absence of reactions, only that the data could not be interpreted. Each general type of reaction is sub-divided into specific classes of reaction (shown in italics). The percentages quoted in Table 2.2 are based on all the reactions performed at that level of chemistry.

The analysis in Table 2.2 shows a reliance on a few specific chemistries that are worth considering in more detail, especially those where the favoured solvents are toxic. Each of the subsequent reaction case studies (acylation, alkylation, cross-coupling, heterocycle synthesis, peptide synthesis) have been subject to evaluations in the literature to uncover the exact mechanistic role of the solvent and what alternative solvents can maintain performance with improved environmental health and safety characteristics. Also note that catalysis is prevalent in the manufacture of pharmaceuticals, and the synergy between solvent and catalyst is important to consider.[36,37]

2.2.2 Acylation of Alcohols and Amines

The formation of esters and amides is very important in drug discovery (medicinal chemistry) through to manufacturing. The optimisation of solvent use in the manufacture of sildenafil citrate (the active ingredient in

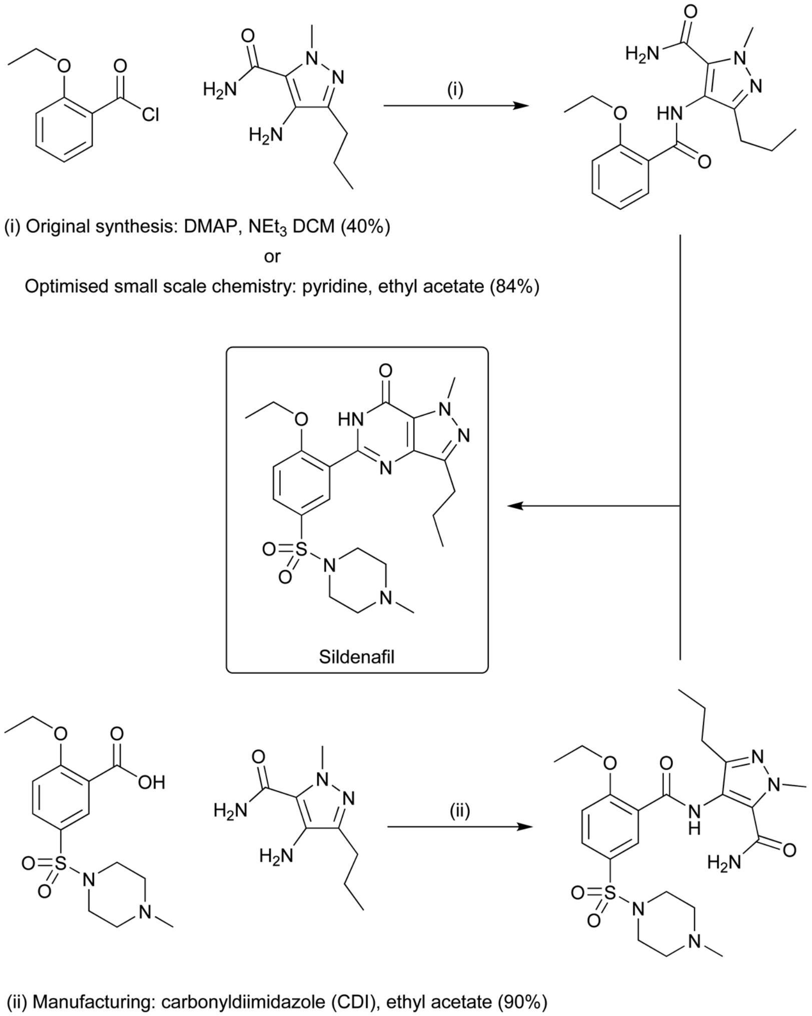
Table 2.2 The solvent requirements for solvents in the pharmaceutical industry at the drug discovery (A),[29] process development (B),[30] and manufacturing (C) level.[31]

Reaction type	A	B	C	Ideal solvents
Acylation	~	12%	26%	
N-Acylation to amide	~	8%	10%	Non-hydrogen bonding solvents (entropic control)
O-Acylation to ester	~	~	5%	Non-hydrogen bonding solvents (entropic control)
N-Sulphonation to sulphonamide	~	1%	~	Rapid reaction, polar solvents used for solubility reasons
Aromatic heterocycle formation	5%	5%	3%	Broad area of synthesis. Solvent depends on the reactions required
Heteroatom alkylation	17%	19%	~	Strongly dipolar solvents (enthalpic control)
N-Substitution	~	11%	3%	
O-Substitution	~	5%	2%	
S-Substitution	~	2%	~	
S_NAr (N-Arylation)	~	~	2%	
Functional group addition	~	3%	~	Often dipolar solvents, typically chlorinated solvents are required
Halogenation	5%	2%	~	
Nitration	~	1%	~	
C–C bond formation	~	11%	14%	
Aldol condensation	~	~	2%	Varied instances of solvent use
Claisen condensation	~	1%	2%	A base is formed from an alcohol, therefore any excess acts as solvent
Enolate alkylation	~	~	2%	Tetrahydrofuran (THF) and DCM
Friedel–Crafts	~	~	1%	Typically chlorinated solvents
Michael addition	~	~	1%	Toluene and DCM
Organometallic	~	1%	2%	Ethers used to stabilise organometallic reactants
S_NAr (Ullmann etc.)	~	~	1%	Dipolar aprotic solvents
Cross-coupling (palladium)	17%	2%	2%	Typically, dipolar aprotic solvents are used. Sometimes aqueous alcohols are suitable (*e.g.* Suzuki cross coupling)
Functional group interconversion	~	10%	~	
Alcohol to halide	~	2%	~	Dipolar solvents used to stabilise the activated complex
Acid to acid chloride	~	1%	~	Aromatic and chlorinated solvents. DMF is helpful to accelerate procedures with thionyl chloride
Amide to imidoyl chloride	~	1%	~	Aromatic and chlorinated solvents. Low boiling point solvents help control the reaction
Oxidation	4%	4%	3%	Fully oxidised solvents such as acetone, and chlorinated solvents
Oxidation of sulphur	~	1%	~	
Oxidation of alcohol	~	~	~	
Oxidation of nitrogen	~	~	~	

Reduction	5%	9%	12%	Alcohols are common solvents especially for hydrogenations. THF, aromatic solvents, and chlorinated solvents are also popular for reductions
Acid derivative reduction to amine	~	~	1%	
Alkene to alkane	~	1%	~	
Hydride reduction	~	~	2%	
Imine/nitrile to amine	~	1%	3%	
Nitrate to amine	~	2%	~	
Reductive amination	~	1%	3%	
Protection	12%	6%	~	Dichloromethane is often used as a useful polar and volatile solvent. Acetonitrile, THF and dipolar aprotic solvents are also used depending on the exact reaction
Amine	~	2%	~	
Carboxylic acid	~	2%	~	
Alcohol	~	2%	~	
Deprotection	~	15%	~	Similar to protection reactions, with water featuring as a solvent in hydrolytic procedures
Amine	~	7%	~	
Carboxylic acid	~	4%	~	
Alcohol	~	2%	~	

Viagra™) includes a key amide formation to converge two syntheses.[38] Originally, a *N*,*N*-dimethylaminopyridine (DMAP) catalysed reaction between an amine and an acyl chloride was used, but this reaction used dichloromethane (DCM) as a solvent, and also required a chromatographic separation to give just 40% yield. Pfizer optimised the medicinal chemistry route to provide much improved yields in ethyl acetate. This alleviated the need for solvent intensive chromatography, and replaced a toxic solvent with a reasonably benign substitute by comparison. The commercial route differs because the order of the synthesis of sildenafil citrate was rearranged, but still an amide bond must be formed. In its final revision, a yield of 90% was achieved with ethyl acetate as the solvent (Scheme 2.1). Over the course of refining the synthesis, the initial 1300 litres of solvent per kilogram of sildenafil citrate needed in medicinal chemistry was optimised to 100 L kg^{-1}, with the manufacturing process needing only 22 L kg^{-1} of solvent.[38] The use of DCM is no longer necessary, and solvent recovery means that now, just 7 litres of solvent waste are associated with each kilogram of product. This waste includes *t*-butanol, ethyl acetate, methyl ethyl ketone and toluene.

In the example of sildenafil citrate, ethyl acetate was found to be a satisfactory replacement for DCM in the amidation reaction. It is not always obvious whether this sort of solvent substitution is possible, and when it can be successfully implemented. Understanding why certain solvents are suitable in given applications, and how to select or design solvents for certain tasks, requires an appreciation of the role of the solvent. The pharmaceutical industry, with its rich and diverse use of organic chemical reactions, is an ideal area to explore solvent effects. Solvents such as DCM, toluene, and other aromatic and halogenated solvents are often used in amidations. If you take away the coupling agents and catalysts, and investigate only the thermally activated amidation, the role of the solvent becomes apparent.

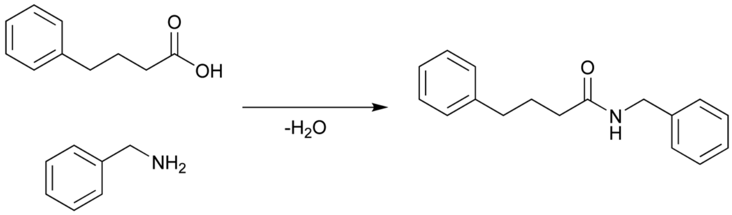


(i) Original synthesis: DMAP, NEt_3 DCM (40%)
or
Optimised small scale chemistry: pyridine, ethyl acetate (84%)

(ii) Manufacturing: carbonyldiimidazole (CDI), ethyl acetate (90%)

Scheme 2.1 Amidation options to produce sildenafil.

Performing a direct reaction between an amine and a carboxylic acid is often not feasible due to salt formation. However, a few examples can produce the desired amide product.[39] Combining 4-phenylbutyric acid and benzylamine with a solvent in a reaction at 100 °C will form the amide product (Scheme 2.2). In hydrocarbon solvents, the product will precipitate, an important benefit that is worth prioritising in solvent selection. It was found by Clark *et al.* that solvents without the capacity to hydrogen bond accelerate this model reaction.[40] This was reported to be due to an entropic effect. Whereas hydrogen bonding with the solvent is beneficial to the activated complex through



Scheme 2.2 The direct synthesis of *N*-benzyl-4-phenylbutanamide.

a reduced enthalpy of activation, the penalty of ordering the solvent molecules is greater. This justifies the frequent use of chlorinated and aromatic solvents, especially for smaller scale reactions in drug discovery where DCM and toluene are frequently “go-to” solvents.

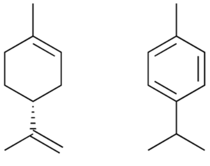
The use of kinetic studies to understand solvent effects is hugely beneficial, although in the case of amidation of carboxylic acids this is not the whole story. Thermal amidation,[41] and even catalytic methods,[42] are rare. This is because the success of coupling agents in amide synthesis means that the majority of chemists have no need for alternative, less wasteful procedures. Although coupling agents such as carbonyldiimidazole (CDI) and the carbodiimides allow room temperature reactions to rapidly proceed to completion, they generate a large mass of by-product in the form of the spent (hydrated) coupling agent. The same types of solvent are effective for the coupling of carboxylic acids and amines as for thermal amidations, because carbonyl addition is still the key reaction step. With the rapid reaction conditions permitted by coupling agents, the solvent effect is less crucial to the yield, and amidations are also selective and high yielding in less hazardous ester and alcohol solvents.[43] Dipolar aprotic solvents can be used under these conditions to improve the solubility if needed. In a study by MacMillan *et al.* the high productivity of amidation reactions in ethyl acetate (as seen previously in the sildenafil citrate synthesis example) was matched by dimethyl carbonate and 2-methyltetrahydrofuran (2-MeTHF).[43] The yields compared well with procedures conducted in either dichloromethane (DCM) or *N*,*N*-dimethyl formamide (DMF).

Alternatively, the carboxylic acid can be converted into an acyl chloride, and then reacted with an amine. This activates the acid and avoids salt formation. The procedures typically used to form the acyl chloride (thionyl chloride, phosphorus oxychloride) exclude some of the greener solvents now proven to work with coupling agents for reactivity reasons. Another way around the obstacle of amidation without coupling agents is to react an amine with a carboxylic ester. This base catalysed chemistry can work with isopropyl alcohol as the solvent, but the yields are not always quantitative depending on the substrate.[44] On balance, considering that the majority of the mass in the reaction will be the solvent, the use of greener coupling agents would seem the superior option to many,[45] in turn allowing for greener solvents to be used. This shows that the choice of reaction chemistry should be considered in conjunction with solvent selection, and both optimised in tandem.

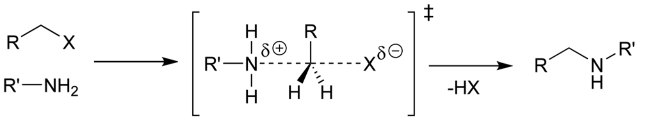
Fischer esterification to give the esters of carboxylic acids and alcohols follows many of the same principles described for amide synthesis. Once again this is a common transformation in the pharmaceutical industry, and the solvent effect means that the reaction benefits from the use of non-hydrogen bonding solvents. One difference compared to amidation is that catalysis is common for direct esterifications.[46] However research has shown that regardless of whether a traditional acid catalysed Fischer esterification is used, or an uncatalysed reaction with activated acyl groups is preferred, the solvent effect is the same.[40,47,48] This is also true in enzymatic esterifications, although the solvent effect is influenced by additional factors in this instance.[49,50] Limonene, extracted as the major component of the essential oil of citrus fruits, is capable of acting as a solvent in both esterifications and amidations.[40] However, it is a reactive compound due to a pair of double bonds. Alternatively, *p*-cymene is an aromatic solvent that can be synthesised from limonene,[51] and performs comparably to toluene in carbonyl addition reactions (namely amidation and esterification) (Scheme 2.3). Limonene and *p*-cymene have also been shown to enhance the yields in the synthesis of phospholipid pharmaceutical products.[52] However, they have some stability issues and may be oxidised under certain conditions. Nevertheless, this is a demonstration that solvents can be selected on the basis of more than just high reaction yields, thinking about renewability also, for example.

2.2.3 Heteroatom Alkylation

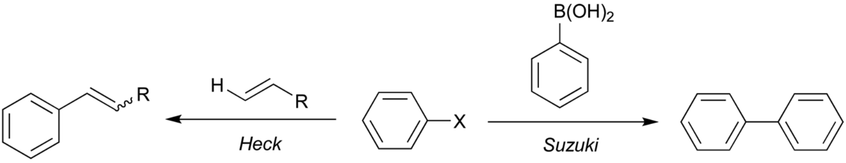
N-Alkylation is the most frequently occurring reaction in pharmaceutical chemistry at the process development scale. Here, the use of highly dipolar solvents is favoured to accelerate the rate of reaction. The activated complex of an S_N2 reaction features a charge separation, which can be stabilised by dipolar solvents (Scheme 2.4). Here, solvent selection requires sustainable options to replace some prominent dipolar aprotic solvents that are recognised as reprotoxic. The typical dipolar aprotic solvents are amides, including *N*,*N*-dimethyl formamide (DMF), *N*,*N*-dimethyl acetamide (DMAc), and *N*-methyl pyrrolidinone (NMP). All pose a reprotoxic hazard. Dimethyl



Scheme 2.3 Limonene (left) and *p*-cymene (right).



Scheme 2.4 A representative S_N2 reaction between a primary amine and a haloalkane with an activated complex involving a charge separation stabilised by dipolar or polarisable solvents.



Scheme 2.5 The two most common types of cross-coupling reaction in pharmaceutical process research and development,[30] generalised for aryl–aryl or aryl–allyl couplings where X indicates a halogen atom.

sulphoxide (DMSO) can be used in place of amide solvents to afford high reaction rates in S_N2 heteroatom alkylations.[53] Unfortunately DMSO poses its own problems, including limited stability, odour, and high skin permeability. Sulpholane is also an option with its own advantages (lower skin permeability) and disadvantages (toxicity).[54]

2.2.4 Cross-Coupling Reactions

Palladium catalysed cross-coupling reactions to give carbon–carbon bonds (Scheme 2.5) are routinely used in medicinal chemistry, but less so at larger scales. The habit of applying homogeneous palladium catalysis to sub-gram scale reactions is convenient, but for manufacturing practices the costs involved make alternative methods more attractive where available (including heterogeneous catalysis). It is also true that cross-coupling allows drug templates to be quickly assembled, allowing many different functional groups to be tested rapidly and later fine-tuned, confirming the position of cross-coupling as an indispensable tool for drug discovery.[55]

Regardless of the frequency with which they are used in manufacturing processes, because cross-coupling is important to generate the original drug candidates, solvent selection remains an important issue to address given the significant cumulative solvent use in small scale chemistry across many labs. As for S_N2 heteroatom alkylations, dipolar aprotic solvents are the most commonly used solvents for cross-coupling. Sometimes toluene is preferred, and for Suzuki cross-coupling, water,[56] alcohols,[57] and aqueous solvent mixtures are also viable solvents.[58] However, the Suzuki reaction is the most tolerant of water amongst the popular cross-coupling protocols, with the Heck cross-coupling reaction and others more difficult to achieve in aqueous solution.[59]

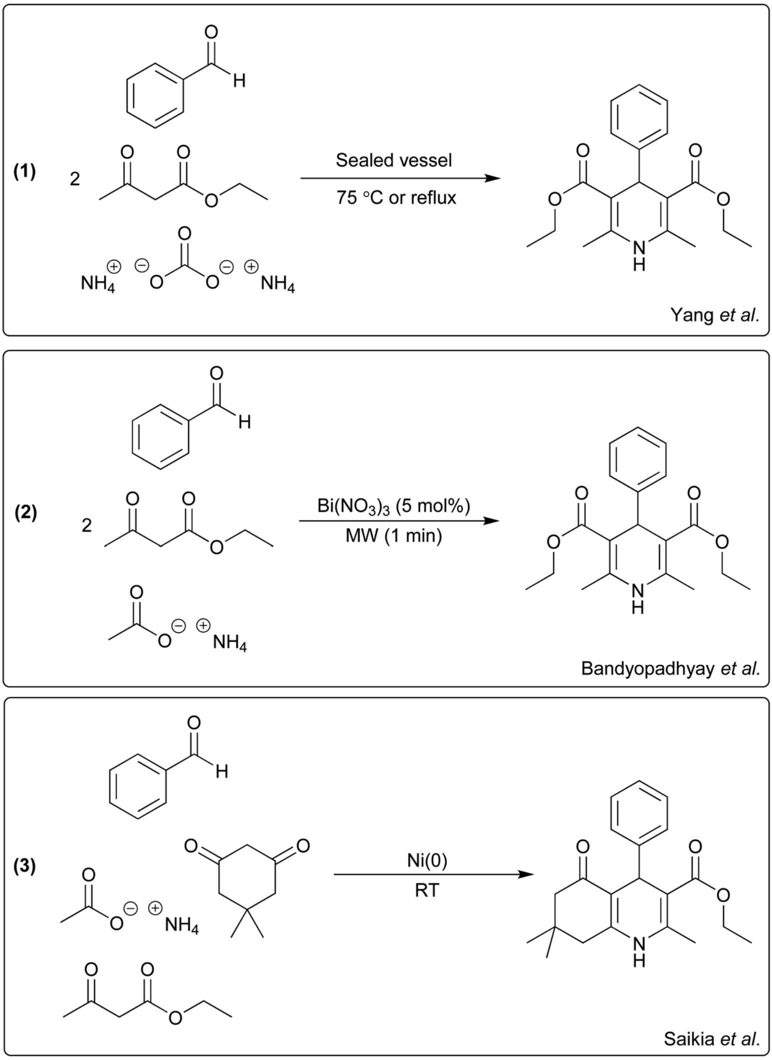
Early developments towards new dipolar aprotic solvents for cross-coupling reactions and other applications since the formal recognition of their chronic toxicity were not very meaningful. For example, *N*-ethyl pyrrolidinone (NEP) has been employed as a substitute for NMP.[60] This is convenient to avoid any association with popular solvents that draw attention as chronic toxicants, as the most widespread solvents are the first targets for SVHC listing. Almost inevitably, evidence has been gathered that shows that the reprotoxicity of NMP is not eliminated by replacing the methyl group with an ethyl group.[61] Exposure to NEP can be controlled to minimise the health hazard,[62] but to completely avoid the issues regularly posed by the amide functionality, completely different solvents must be identified that can operate in the same types of applications. *N*-Alkylations and cross-coupling reactions have been shown to work successfully in a series of speciality polar solvents, including 2-methyltetrahydrofuran (2-MeTHF),[63] γ-valerolactone,[64] ethylene carbonate and propylene carbonate,[65] and dihydrolevoglucosenone (Cyrene™).[66] All of these solvents only contain carbon, hydrogen, and oxygen, and none are suspected of possessing any chronic toxicity. However, γ-valerolactone[67] and Cyrene[68] have not been fully tested to demonstrate that no chronic health concerns exist (including carcinogenicity, mutagenicity, reprotoxicity, and chronic organ damage). Finally, as an exception to prove the rule, there is an amide solvent for S_N2 and cross-coupling reactions that has undergone satisfactory toxicity testing.[69] *N*-Butyl pyrrolidinone is harmful if swallowed and an irritant,[70] but this level of hazard is manageable and very much preferable to the threat of chronic toxicity posed by other amides.

2.2.5 Heterocycle Synthesis

Non-peptide drugs are very often based on a molecular template (as is well-known), which forms the core of the molecule to which the various functional group appendages are bonded. This is usually a heterocycle. Heterocycle synthesis is underrepresented in the Table 2.2 dataset, with the majority of early stage pharmaceutical chemists purchasing the basic heterocyclic reagents, or producing the heterocycle infrequently in-house in large batches that provide all of the material for medicinal chemistry studies on that particular template. The types of heterocycle most often used are pyridines, although other nitrogen containing heterocycles are common.[30]

Heterocycle synthesis lends itself to achieving greater sustainability in chemical manufacturing, due to the fact that it is suited to multicomponent reactions.[71] This means that multiple reactions occur between 3 or more reactants, ending when a stable (heterocyclic) molecule is produced. An obvious and beneficial outcome of this is a reduction in the volume of solvent required, which will be somewhat proportional to the number of separate reaction steps eliminated. In addition, the crystalline nature common to many heterocycles helps with the precipitation of the product from solution, reducing the demand for work-up solvents. Preferable solvents for heterocycle synthesis continue to be a significant area of research.[72]

The Hantzsch pyridine synthesis is a classic example of a multicomponent heterocycle synthesis. The actual product is a dihydropyridine (Scheme 2.6), but mild oxidative conditions in a subsequent reaction will produce the pyridine analogue.[73,74] Three examples of the Hantzsch synthesis can help us appreciate the role of the solvent. Yang *et al.*,[75] and Bandyopadhyay *et al.*,[76] have performed a typical reaction between benzaldehyde, ethyl acetoacetate,



Scheme 2.6 Three examples of the Hantzsch synthesis of dihydropyridines.[75–77]

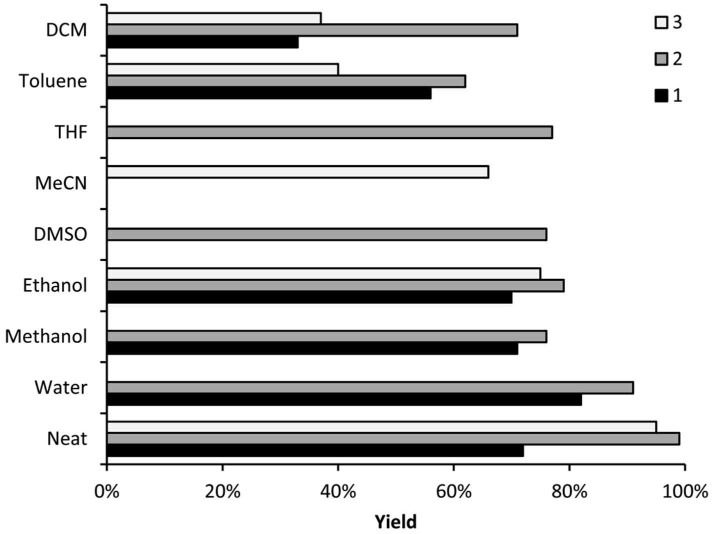


Figure 2.4 Yields of multicomponent Hantzsch dihydropyridine reactions (following the numbering of Scheme 2.6) in different solvents, where DMSO is dimethyl sulphoxide, MeCN is acetonitrile, THF is tetrahydrofuran, and DCM is dichloromethane.[75–77]

and an ammonium salt in different solvents. Saikia *et al.* have modified the procedure to produce an unsymmetrical bicyclic heterocycle.[77]

Examining the different conditions and different substrates covered in Scheme 2.6 leads to the conclusion that water is the ideal reaction medium, or no reaction solvent at all (Figure 2.4). The solvents tested vary between the examples, but there is likely to be a common solvent effect where protic solvents are better suited to the demands of the reaction than aprotic solvents. The weak hydrogen bond donors (toluene, dichloromethane) gave the lowest yields.

From this evidence (Figure 2.4) it is hard to argue against using solvent-less conditions. In fact, despite the straightforward appearance of the reaction, it can yield a mixture of dihydropyridines and oxidised pyridine isomers as products. It was found that solvent-less conditions (and when using acetic acid as a solvent) favour a 2-aryl pyridine product, so both the constitution and oxidisation state of the product are unexpected (Figure 2.5).[74] This result reminds us to be careful when performing multicomponent reactions because a large number of potential products can be formed, but it also emphasises the role of the solvent (or no solvent) in reaction selectivity. It was actually DMSO that provided the highest proportion of the expected product, but obviously for medicinal chemistry it could be another isomer that is actually of interest from a biological activity point of view.

A related multicomponent reaction is the Biginelli synthesis of dihydropyrimidinones.[78,79] Here the ammonium salt is replaced by urea (or equivalent) and only one equivalent of the dicarbonyl reactant is required (Scheme 2.7). The usual choice of solvent is ethanol, but acetic acid is also popular in the

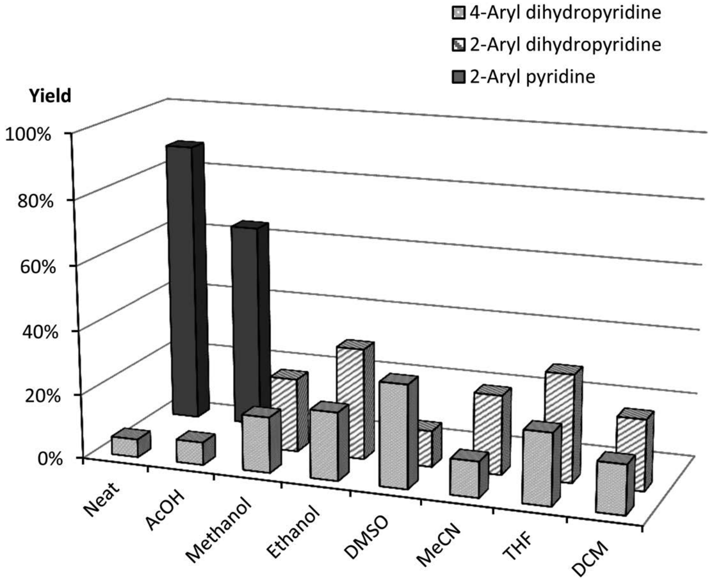
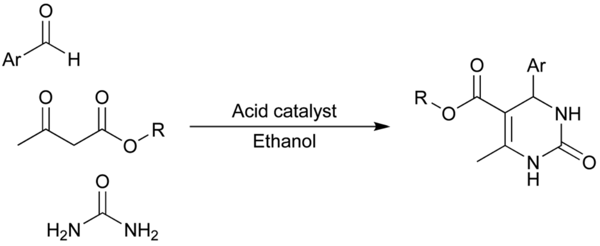


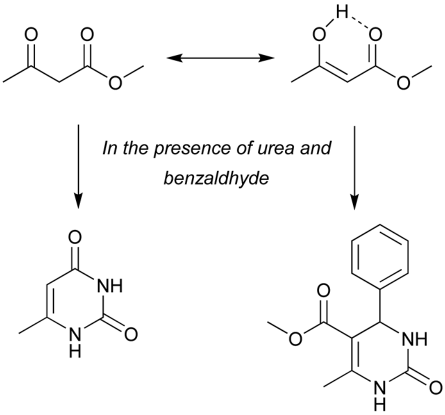
Figure 2.5 Reaction selectivities for Hantzsch (dihydro)pyridine synthesis using benzaldehyde, ethyl acetoacetate and ammonium acetate in different solvents, where AcOH denotes acetic acid.[74]



Scheme 2.7 A general example of the Biginelli reaction.

older literature.[78] The benefit of ethanol over acetic acid is that precipitation of the product can often be achieved.

If was found by Clark *et al.* that the productivity of the reaction is highly dependent on the tautomerisation of the 1,3-dicarbonyl reactant,[80] and this is solvent dependant. Solvents that are highly polar suit the diketo tautomer of methyl acetoacetate. In non-polar solvents, the enol tautomer is preferred by establishing a stabilising intramolecular hydrogen bond. Carboxylic acid solvents (*e.g.* acetic acid) interfere with the self-stabilising hydrogen bond of the enol, reducing its prevalence in the solution. It is the enol tautomer that proceeds through the reaction to make the final dihydropyrimidinone product. An abundance of the diketo tautomer should be avoided, as it is reactive with urea and forms an undesirable uracil by-product (Scheme 2.8).[81]



Scheme 2.8 The different reactivity of methyl acetoacetate tautomers with urea and benzaldehyde.

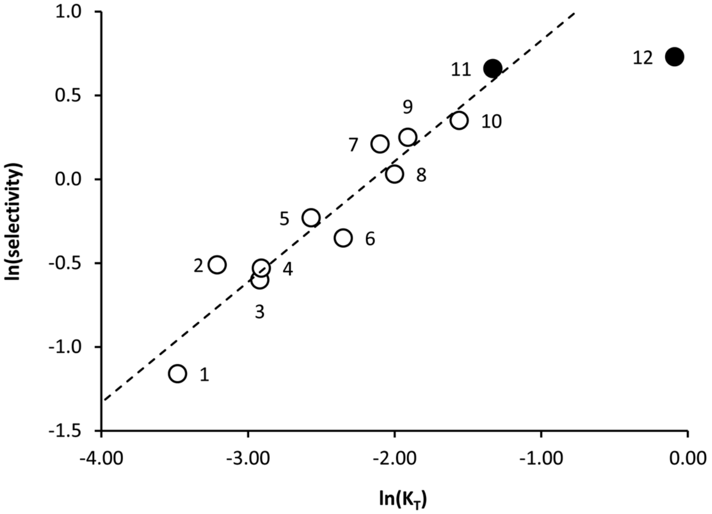


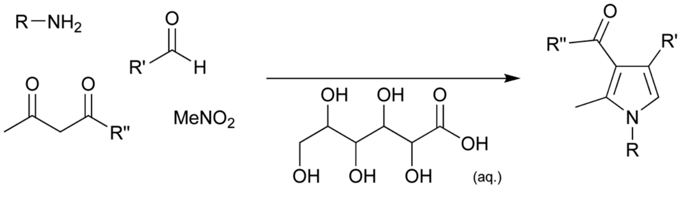
Figure 2.6 The relationship between enol-diketo tautomerisation and the resultant product distribution.[80] Key: 1, lactic acid; 2, ethylene glycol; 3, acetic acid; 4, *N*,*N*-dimethyl formamide (DMF); 5, 1,2-dichloroethane (DCE); 6, propanoic acid; 7, *t*-butanol; 8, ethyl acetate; 9, ethanol; 10, toluene; 11, *p*-cymene; 12, cyclohexane.

A clear relationship can be seen between the tautomerisation equilibrium (K_T) and the proportion of product isolated compared to side products (Figure 2.6). The conditions of this reaction are three hours of stirring at 75 °C in the presence of 10 mol% HCl. Upon cooling, the product precipitates unless the solvent is DMF or acetic acid. Recrystallisation in ethanol can be used for product purification. The data trend established with a set of 10 solvents (white data points, Figure 2.6) shows that toluene (59% yield) provides a slightly better reaction medium than ethanol (56% yield) because of the greater proportion of methyl acetoacetate enol existing in the solution. Based on this information, *p*-cymene and cyclohexane were chosen as new solvents for the Biginelli reaction (black data points, Figure 2.6), resulting in 66% and 68% yield, respectively.[80] Cyclohexane is believed to deviate from the trend established in Figure 2.6 because of the poor solubility of the reaction components, but provided the highest yield regardless. The Biginelli reaction can also be optimised to proceed in glycerol,[82] or without solvent for example,[83] but for producing libraries of dihydropyrimidinones, hydrocarbon solvents are ideal for use in unoptimised reaction conditions to modify acyclic 1,3-dicarbonyl compounds. For the Biginelli reaction using cyclic dicarbonyl compounds, the enol-stabilising intramolecular hydrogen bond does not exist, and solvents that provide that hydrogen bond, including water, are superior.[80] In summary, the solvato-catalytic effects of the Biginelli reaction are well understood, and continue to fuel a productive area of research.[84]

Pyrroles are another valuable nitrogen containing heterocycle with a rich array of synthetic methods available by which to synthesise them.[85] The use of solvents is diverse. One interesting development is the use of an aqueous solution of gluconic acid as the reaction medium.[86] Under conditions where organic solvents, water, and ionic liquids did not facilitate the reaction, a 50 wt% gluconic acid solution was efficient, without the need for a catalyst, and tolerating a broad substrate scope (Scheme 2.9).

2.2.6 Peptide Synthesis

Not covered in the discussion thus far (and excluded from the data in Table 2.2) are peptide drug molecules. Protein therapeutics already account for a significant number of drug sales, and offer great potential for future pharmaceutical developments as well.[87,88] Solid phase peptide synthesis is the most worthwhile approach to achieve the synthesis of peptides.[89] It is common to use dichloromethane (DCM) and *N*,*N*-dimethyl formamide (DMF) as solvents. However, it has now been shown that 2-methyltetrahydrofuran (2-MeTHF), cyclopentyl methyl ether (CPME) and ethyl acetate are viable alternatives.[90,91] This is a complicated case study for improving the choice of the solvent, requiring high reaction efficiencies due to the sequential, linear nature in



Scheme 2.9 The synthesis of substituted pyrroles in gluconic acid solution.

which the peptides are created, one amino acid at a time. The amino acids are protected to control the reaction, and therefore a quantitative deprotection step is needed as well. The solubility of amide coupling agents and the ability of the solvent to swell the resin onto which the peptide is tethered during the process are also important. At this stage of development, alternative solvents look promising, but much more work to prove their robustness is needed to convince scientists to commit to changing the solvent system in their automatic peptide synthesisers.

2.2.7 Purity of Solvents and Products

This summary of some key reactions required by the pharmaceutical industry demonstrates the need for different solvents, but it is not the most significant use of solvents. Small scale exploratory chemistry in particular often requires purification by column chromatography. The reward of a pure product is worth the large amounts of silica waste and mixtures of spent solvent requiring disposal. The solvents most commonly used are ethyl acetate, DCM, methanol, and a hydrocarbon (petroleum spirit or cyclohexane, for example). Greener solvent options are available,[92,93] but the only way to circumvent the large amounts of mixed solvent waste created in column chromatography is to look for alternative techniques.[94] At larger scales, column chromatography becomes unwieldy anyway, and makes way to purification by crystallisation and aqueous-organic extractions. When designing a sustainable process, it is important to prioritise the easy to overlook areas such as the work-up and cleaning solvent for improvement. Presently, it is true that reaction solvents are a more popular topic of investigation than the more voluminous work-up and cleaning solvents, at least according to the number of academic publications found in the literature. An argument to justify this focus of attention is that a work-up solvent or cleaning solvent tends to be less toxic than the reaction solvents, and if not its substitution has a lower impact on the product and process. Often a simple oxygenated solvent that would likely be reactive under typical reaction conditions (*e.g.* an ester such as ethyl acetate) is stable enough for extractions and separations. Cleaning of vessels in the pharmaceutical industry can be achieved with biodegradable surfactants instead of organic solvents in some cases.[95,96]

A further consideration for the manufacturers and formulators of pharmaceuticals is the purity of the solvents used, the composition of the impurities (stabilisers, decomposition products, left-over reactants), and how that might impact adherence to regulations with respect to residual solvents in the final product. As well as having an impact on safety, the crystal structure of the active pharmaceutical ingredient can be influenced by the solvent and its impurities. Drugs molecules are registered with a defined crystal structure. Traces of different solvents can change the pattern of crystal growth and therefore create a conflict between the registered product and the actual product. To what degree the solvent influences the registration of pharmaceuticals is related to when it is used in the synthesis. The solvents used in the latter stages of manufacturing are the most important to consider. This level of scrutiny means that solvents can only be recovered and reused if they match the specification of the virgin solvent. This means that, in practice, the recovered solvent is only reused in the same process in a closed loop. Still, the impurities would be measured and included on a specification sheet to prevent a negative impact on the process. For the interested reader, this topic of discussion is presented in much greater detail in George Wypych's 'Handbook of Solvents'.[97] The implication for sustainable solvents and sustainable processes is that new solvents designed for lower environmental impact are not included in the scope of regulations defining acceptable solvents. They will also be limited in availability at first, making the use of specialist solvents difficult to justify in large scale processes with strong quality controls in place.[6]

2.3 Process Research and Development for Fine Chemicals

Process research and development is a crucial stage of product commercialisation, where considerations relating to solvent selection are no longer entirely focused on reaction yield, but more on engineering factors (pumping of solutions, heat sink function) and regulated emission limits. The literature survey of Ashcroft *et al.* provides a detailed summary of current trends of solvent use in this field.[98] Some of the key findings relate to the prevalence of undesirable solvents. Of 388 publications considered, most at the 1–100 kg scale, dichloromethane is used in nearly half, a trend that has held steady with time between 1997 and 2012. The use of dipolar aprotics is mainly concentrated on acetonitrile, which poses less of a health hazard than *N*,*N*-dimethyl formamide (DMF) or *N*-methyl pyrrolidinone (NMP). Dimethyl sulphoxide (DMSO) is the third most common option, after DMF, and before NMP, which is the fourth most common. Although proportionally DMF use was consistent between 1997 and 2012, the application of NMP has been increasing over time. A positive changing trend in solvent use is the increasing preference for 2-methyltetrahydrofuran (2-MeTHF), which is displacing non-renewable ethers and occasionally chlorinated solvents in process development studies. The prevalence of 2-MeTHF is now at 14% of the papers surveyed.[98] No evidence of neoteric solvents being applied at scale (ionic liquids, supercritical fluids, *etc.*) was found.

2.4 Polymers

Polymers are ubiquitous, both in nature and in synthetic products, and plastics are undoubtedly a defining material of the 20th century. The global plastic market dwarfs the solvent market by an order of magnitude or more.[99] This is consistent with the fact that the most common plastics are mostly produced in the absence of solvent. However, many polymer precursors are manufactured from liquid phase processes, and some polymer processing procedures also require a solvent. European data places solvent use in polymer manufacturing at 4% of the regional total.

The USA plastics and rubber sector is also a significant contributor to national solvent release and disposal figures (equating somewhat to the potential for environmental impact). Releases are categorised to include fugitive air emissions (leaks, spills and surface evaporation), point source air emissions (purposely released), and surface water discharge (from outflow pipes, for example).[100] Disposal includes underground injection and landfill. Not included is spent solvent transferred to waste management facilities, which will be reviewed separately. Data from the United States Environmental Protection Agency (US EPA) Toxics Release Inventory (TRI) program for the year 2014 list the hazardous chemical output from this industry.[101] Note that not all substances are captured in the US EPA TRI, and smaller facilities do not have to submit reports.[100] Styrene is the most highly released substance, with release figures more than double those of carbon sulphide in second place, but styrene is obviously used mostly as a monomer, and not primarily as a solvent if at all. The use of carbon disulphide is highly specialised to the production of rayon, which is a regenerated cellulose fiber,[102] produced on a very large scale. At first glance, its role might be considered as that of a solvent,[103] but in fact carbon disulphide reacts with cellulose and sodium hydroxide to form sodium cellulose xanthate, an intermediate of the process.[104] Where carbon disulphide was previously used as a solvent, for oil extractions,[105,106] and analytical test methods,[107] solvent substitutes have been implemented. Historically, evidence shows that frequent exposure to carbon disulphide results in acute psychosis in the short term, and chronic health issues in the long term.[108,109] It is also flammable,[110] and reprotoxic.[111] In third placed is zinc and its compounds (from the rubber industry).

An evaluation of the US EPA TRI data, excluding chemicals not used as solvents such as those ruled out in the previous paragraph, is provided as Table 2.3. The rank given relates to statistics including other substances as well as solvents, and hence the number sequence is not complete. Bear in mind that non-solvent uses will also be included in the reported annual release and disposal figures, which may artificially elevate a substance in the ranking provided. It is possible that non-solvent uses, as a reactant perhaps, is the major application. It is not known specifically what the solvent uses are, and some may be primarily cleaning solvents. Information on typical uses of each solvent relevant to the plastics industry has been obtained from the TOXNET Hazardous Substances Data Bank (HSDB).[112]

Of the 20 entries given in Table 2.3, in terms of releases and disposal the highest ranked is toluene (4th), but as noted in Table 2.3 its uses are not limited to only as a solvent. Next are the xylenes (5th), with half the releases and disposal of toluene. Xylene is the precursor to terephthalic acid, a monomer used to make polyethylene terephthalate (PET), which should explain most of the xylene tonnage needed by the polymer industry. Methanol, the sixth highest releases and disposal entry of all recorded substances, is also used in PET production, because dimethyl terephthalate is often the actual monomer used in its reaction with ethylene glycol (which is also found in Table 2.3).

Table 2.3 Disposal and release data and waste transfer data for the USA plastics and rubber industry in 2014, solvents only.[101,112]

Solvent	Applications	Annual release and disposal/ton	Rank	Annual waste transfers/ton	Rank
Acetonitrile	Solvent for butadiene extraction, and wet spinning of fibers. Produced as a by-product of acrylonitrile manufacture, which generates enough acetonitrile to fulfil the solvent market	1	69	32	38
Benzene	Solvent for resins and natural rubber. Releases probably due to its use in styrene production	0.2	89	0	n/a
1-Butanol	Solvent for resins. Also an intermediate	22	37	106	28
Cyclohexane	Solvent for resins, cellulose ethers and rubber. The vast majority of all cyclohexane is intended for nylon synthesis	108	22	40	35
1,2-Dichloroethylene	Degreasing agent, and solvent for resins	0.01	99	0	n/a
DCM	A foam blowing agent, a solvent for metal degreasing and production of cellulose acetate films	143	19	6	61
DMF	Solvent for polyacrylonitrile when making fibers, polyurethanes, and coatings on leather. Also used to make polyamide coatings	53	29	8304	1
1,4-Dioxane	Solvent for resins, cellulose acetate and polyvinyl polymers	0.04	94	1	74
Ethyl benzene	Solvent for resins. Releases probably due to its use in styrene production	84	24	192	18
Ethylene glycol	Blended into solvent mixtures for cellophane. Releases probably due to its use in polyester synthesis as a monomer reactant	315	10	497	13
n-Hexane	Degreasing agent. Medium for addition polymerisations[239]	200	17	31	42
Methanol	Occasional solvent use for polymers. Releases probably due to its use in methyl methacrylate and dimethyl terephthalate production	473	7	637	11
2-Methoxyethanol	Solvent for resins and cellulose acetate	0.1	91	11	58
MIBK	Solvent for resins	125	20	135	22
NMP	Solvent for resins (acrylics and epoxy resins) and polyurethanes, and the reaction medium for polyethersulfones and polyamideimides	181	18	1473	4
Tetrachloroethylene	Solvent for silicones, and a degreaser	3	59	0	n/a
Toluene	Solvent for resins, and a medium for addition polymerisations. Releases may be due in part to its use in making the precursors of polyurethanes	1114	4	925	6
Trichloroethylene	Degreasing agent, and used to recover resins from waste water and cloth[15]	363	9	25	45
Xylene(s)	Occasional solvent use for polymers, and as a degreaser. Releases probably due to its use in making the precursors of polyesters	587	5	849	7
Hazardous glycol ethers	Formulations of paints, coatings, and inks	237	15	249	16

A solvent is used in the PET production chain, which is acetic acid. Acetic acid is the solvent for the oxidation of *p*-xylene to terephthalic acid,[113,114] and only the production of polyvinyl acetate is a larger user of acetic acid globally.[115] Despite this, acetic acid is not found in Table 2.3. Like ethanol, acetone, and tetrahydrofuran, the impact of these solvents is not sufficient to warrant the data collection exercise for the US EPA TRI.[116]

Substances used exclusively as solvents for polymer manufacture and casting, that are released or disposed with environmental exposure consequences on a considerable scale in the USA, include trichloroethylene, *n*-hexane, *N*-methyl pyrrolidinone (NMP), dichloromethane (DCM), and methyl isobutyl ketone (MIBK). Below these, with less than 100 tons of annual released and disposed material, are solvents such as *N*,*N*-dimethyl formamide (DMF) and tetrachloroethylene. It is worth thinking of these values in the context of overall solvent releases and disposal, across all industries. In Figure 2.7 the

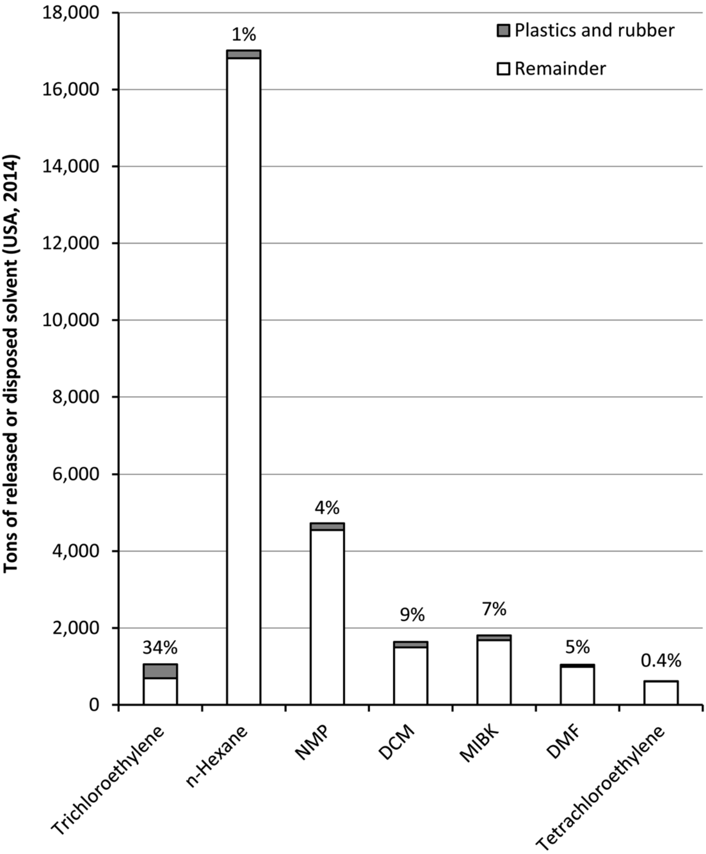


Figure 2.7 Solvent disposal and releases (combined figures) for the USA (2014) for solvents of significance to the plastics manufacturing sector compared to their total use.

proportion of solvent use in the American plastics and rubber industry is compared to their applications outside of the polymer industries. Within this select dataset, *n*-hexane is overall the most widely used solvent (all sectors), but applications in the polymer industry are comparatively small. Nine percent of DCM releases and disposal originate from the plastics and rubber sector (although the absolute value is lower than *n*-hexane) making it a notable contribution to total DCM releases for a solvent that has broad uses across many sectors.

However, the solvent with the largest contribution to releases and disposal from the USA polymer industry is trichloroethylene (34%). Methanol, toluene and xylene(s) have higher releases and disposals but also find use as reagents, and so it is not clear what proportion of these chemicals are put into solvent applications. Overall the majority of trichloroethylene is used as a chemical intermediate for refrigerants within closed systems,[117] but that means it is consumed and not strongly reflected in that regard by the data provided here, which is based on releases and disposal. In terms of use in the plastics industry, we know trichloroethylene is used to recover resins from dyed cloth and waste water, as it is for these two applications that a European authorisation to use trichloroethylene exists.[15]

The continued use of the carcinogenic trichloroethylene is a recognised health issue.[118] Historical data shows that trichloroethylene use (inferred from wastes and emissions) was actually significantly higher in 2001–2003, falling to less than half of the 2002 levels by 2005 (Figure 2.8). The high

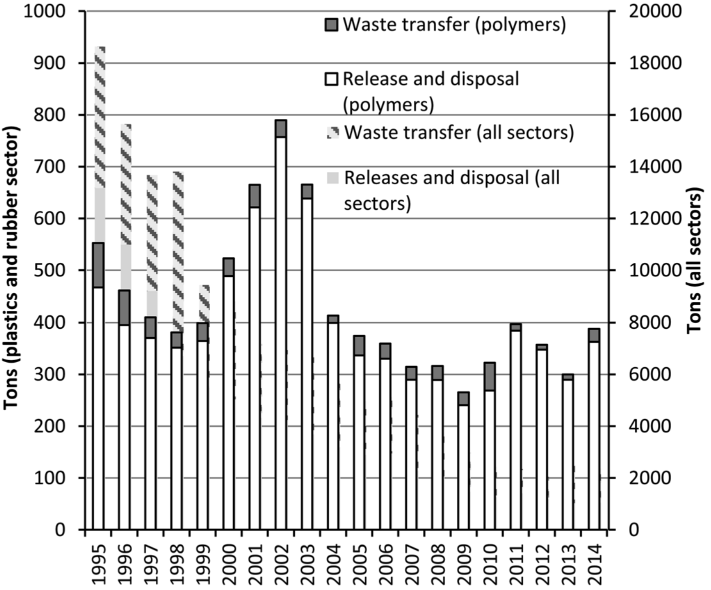


Figure 2.8 Use of trichloroethylene in the USA plastics and rubber industry from 1995–2014, compared to total USA reported use as gauged through waste and emissions data.

demand period for trichloroethylene in the USA polymer industry was set against continued reductions in trichloroethylene releases and waste transfers in other sectors. The global economic crisis caused the use of trichloroethylene in the polymer industry to fall to its lowest level in the past 20 years, but recently wastes and emissions have risen again, showing no significant improvement (*i.e.* reduction) since the major 2004 drop. Data for Sweden shows that trichloroethylene use also experienced similar reductions on the same sort of scale, but began a decade earlier.[119] The reason was because of legal restrictions. In Sweden, permits were introduced that discouraged industrial users, but not without a period of controversy.[120] Today trichloroethylene use in Sweden is very low after sustained reductions in chlorinated solvent use were achieved. In the USA, attempts to restrict the use of trichloroethylene were also controversial. In 2001 the US EPA attempted to introduce regulations to prevent unnecessary exposure to trichloroethylene, but this move was met by huge opposition from other federal agencies in particular.[121] Their motivation was partly to protect themselves from paying for soil remediation activities after decades of using trichlorethylene as a metal degreaser to clean the engines of aircraft and rockets, for example. The result was that the legislative process stalled. Nevertheless, users of trichloroethylene, including the polymer industry, scaled back their trichloroethylene releases and disposal, which presumably means substitute solvents were successfully implemented. Only recently, under a revamped Toxic Substances Control Act (TSCA),[122] has it been possible to reignite efforts to limit American trichloroethylene use. Now any new significant uses of trichloroethylene will need to be vetted by the US EPA before they can commence.[123]

The data in Figure 2.8 shows that while formal waste management is not a significant approach for the plastics and rubber industry when it comes to dealing with trichloroethylene (fugitive air emissions are the main contributor to releases), this is not the case for all solvents. The waste transfer data in Table 2.3 indicates that *N*,*N*-dimethyl formamide (DMF) and *N*-methyl pyrrolidinone (NMP) waste is mostly transferred (Figure 2.9). Consistent with data for all sectors found in Chapter 1 (Section 1.2.3), specifically DMF is mostly discharged in waste water to municipal sewage treatment plants (83% of total waste transfers), and the more expensive NMP is mostly recycled (67%) according to US EPA data for 2014.[124] *N*,*N*-Dimethyl formamide use is extremely high, which was not apparent from the releases and disposal data alone (Figure 2.7). As a low volatility, water miscible solvent used to dissolve polymers to make coatings, DMF emissions to the air are less significant than the potential to end up in waste water.

Whereas trichloroethylene use was shown not to be concentrated in the polymer industry (refer to the scales of the axes in Figure 2.8), DMF is very much so, with recent expansion in capacity leading to over half of American DMF use being attributed to the plastics sector (Figure 2.10). Overall use of DMF (as inferred from releases and wastes) is also generally increasing in the USA, despite its well-known reprotoxicity health hazard. An anomalous data spike in 2004 is attributed to waste transfers to an unspecified "other off-site

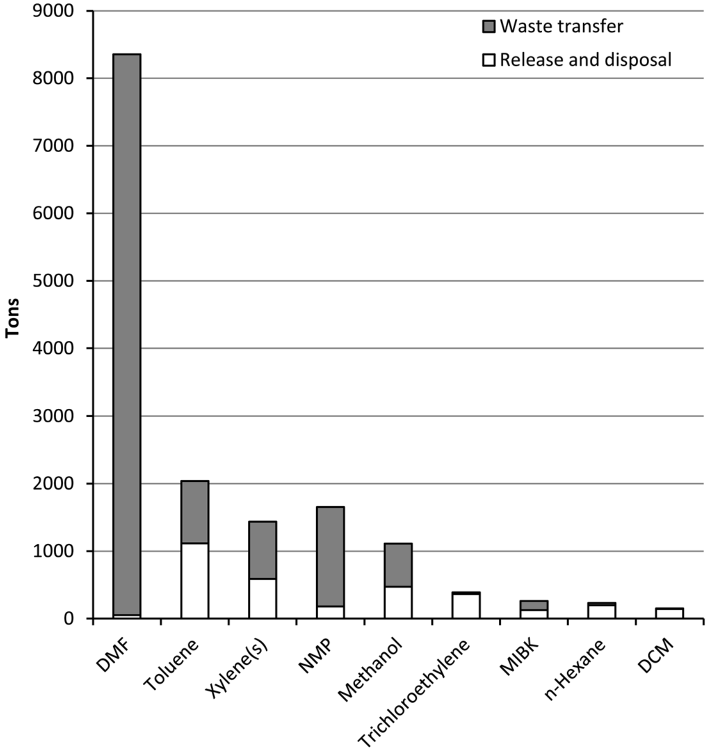


Figure 2.9 Comparison of the nine most significant hazardous chemical releases and waste transfers originating in the USA polymer industries for substances with solvent applications.

location",[125] in this case attributed to a single paint company who presumably needed to get rid of their DMF stock for one reason or another.[126] Worldwide, most DMF consumption is in China, who also house about half of the world's DMF production capacity.[127] In Europe, DMF is listed as a substance of very high concern (SVHC).[10] A plan has been proposed for a restriction on the use of DMF,[128] under the European REACH regulation 1907/2006.[237] This has not been implemented, but looks likely to apply to DMF where present at a level of 0.3% or higher, setting inhalation exposure limits for workers. As a reprotoxic substance, DMF is already restricted in the European Union to professional users only.

Solvent use patterns always have the potential to change, and substitutions should be actively sought to achieve a reduction in the use of hazardous solvents. Change can be slow to commence, but thankfully rapid once begun as the case study of trichloroethylene shows. The reason why a given solvent might be used is partly historical, but is increasingly influenced by regulatory permissions. Replacing one solvent for another in a large scale process might require a new storage licence or environmental permit, or

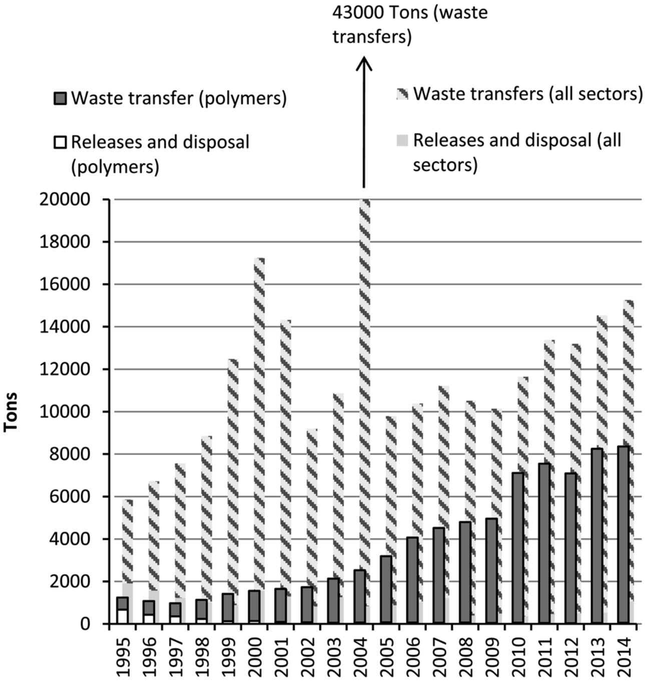
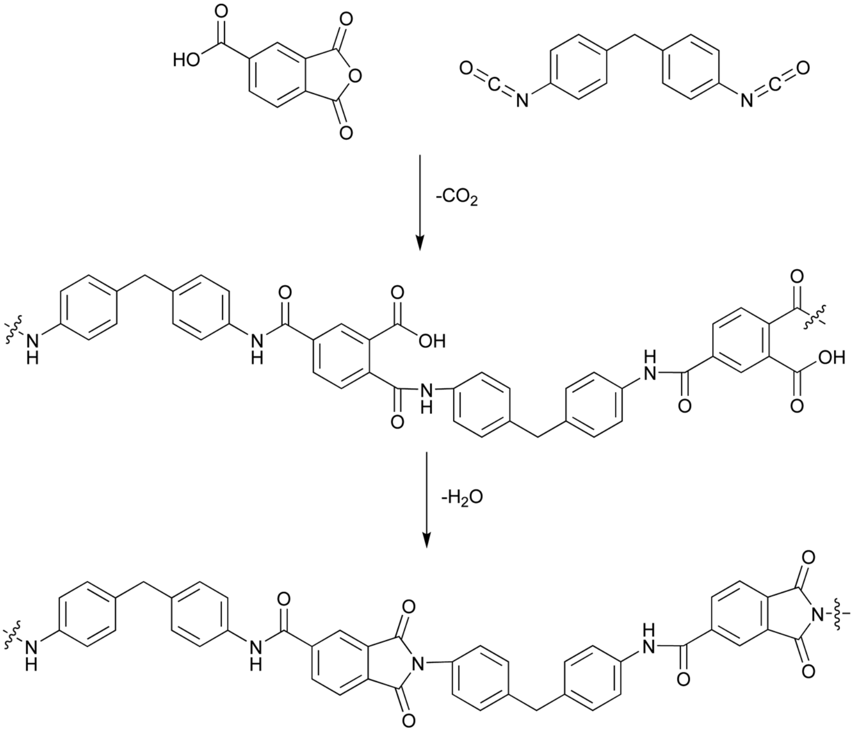


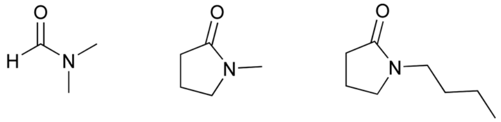
Figure 2.10 Use of DMF in the USA plastics and rubber industry from 1995–2014, compared to total USA reported use as gauged through waste and emissions data.

require modifications to the plant infrastructure. Due to the costs involved, it may need to be revisions to regulation that force these measures. That is not to say we cannot investigate alternative solvents without the push of regulation. It helps to be prepared when an opportunity arises to substitute a solvent. Taking a more protectionist approach, the chemical industry can also benefit from a lack of proven alternatives, as this will limit how far the impact of legislation can go while still preserving the economic benefits of a strong chemical manufacturing sector. To elaborate, *N*-methyl pyrrolidinone (NMP) has a notable use in wire enamel production. Like DMF, it too is a reprotoxic amide functionalised solvent.[129] Wire enamel is an insulating coating made of a polyamideimide (Scheme 2.10), with quite specific solubility and performance requirements. In Scheme 2.10, trimellitic anhydride and 4,4′-methylenebis(phenyl isocyanate) condense to form a polyamide by liberating carbon dioxide. The fully imidised polyamideimide is achieved by the reaction of the free acid with its neighbouring amide functionality.

The polymerisation reaction to form a polyamideimide is conducted in NMP, up to temperatures of 140 °C.[130] The viscosity of the polymer solution can be modified with other solvents (*e.g.* xylene(s)) if needed. Copper wires are coated in the polymer solution, and then a strong heat treatment is applied to evaporate the solvent(s) and afford the finished product. In the REACH restriction proposal for NMP, the performance of possible substitute solvents for wire insulation enamels has provided crucial evidence.[131] Dimethyl sulphoxide (DMSO) was chosen as a comparison, but it was found that the heat stability of DMSO was not sufficient for wire enamel production. Ultimately, the proposed (but not yet enforced) restriction on NMP is similar to that proposed for DMF, that being strict exposure limits for professional workers. Meanwhile, it has been shown by Vandeputte *et al.* that some amide solvents are not reprotoxic, and of those, *N*-butyl pyrrolidinone (Scheme 2.11) can be used to produce wire enamels with equivalent performance and longevity to those made with NMP.[130] Therefore, there is an alternative to NMP that



Scheme 2.10 The polymerisation of trimellitic anhydride (top left) and 4,4′-methylenebis(phenyl isocyanate) (top right).



Scheme 2.11 The chemical structures of three amide solvents: *N*,*N*-dimethyl formamide (DMF, left), *N*-methyl pyrrolidinone (NMP, centre), and *N*-butyl pyrrolidinone (right).

can be used to improve one of the health risks associated with the polymer industry. If substitutes had been considered more thoroughly, the proposed controls on NMP use in Europe may have been much stricter.

The manufacture of some other resin precursors also requires NMP as a polymerisation solvent. These are produced and sold as monomers for polyimides or polybenzoxazoles, which are thermally cured by the end-user for specific applications in the electronics sector. An attempt to substitute NMP can been published making use of a life cycle assessment to justify the conclusions (Figure 2.11).[132] The recycling of NMP, DMSO and sulpholane was additionally studied, which requires the removal of water by distillation to dry the organic solvent. The vast majority of emissions were carbon dioxide, a consequence of the energy demands of the process.

What we learn from the results of the LCA in Figure 2.11 is the strong contribution of the solvent manufacture itself to the environmental impact of downstream processes. Intuitively it follows that recycling should be prioritised. Recycling NMP reduces emissions by 44%, with recycling energy requirements now dominating emissions. A 95% recovery rate was assumed in this study.[132] Dimethyl sulphoxide (DMSO) and sulpholane help reduce emissions significantly if no solvent recovery is performed, but the benefit is

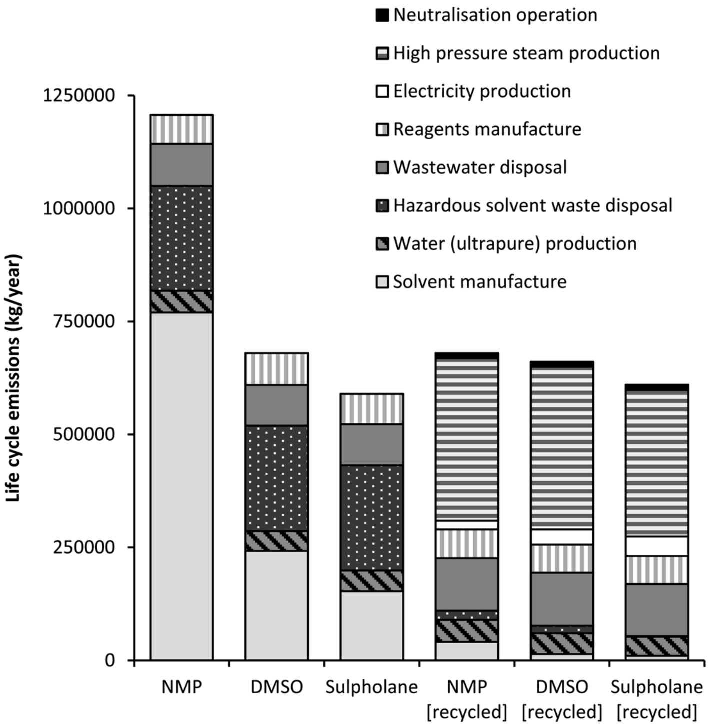


Figure 2.11 The life cycle emissions associated with different versions of a resin precursor manufacturing process.

marginal compared to a NMP recycling scenario, and no benefit is seen comparing the recycling of the sulphur-based solvents to a scenario when they are not recycled. This is because the benefit of DMSO and sulpholane comes from their own lower manufacturing emissions (compared to NMP). When the solvent is recycled as a matter of course with high recoveries, the impact of the original solvent manufacturing is supressed to negligible levels, and given that performance and recovery is not compromised, this means the choice of solvent is of little consequence to the life cycle emissions. When the impact of solvent manufacture is low, emissions are comparable to recovery processes. What is not conveyed in this life cycle study are the impacts of solvent selection and solvent recycling beyond (carbon dioxide) emissions. Resource depletion, health risks (to workers and the public) and acidification as a consequence of sulphur containing solvent use and release are obvious considerations that ideally should also be made. What this study does reveal is that seemingly reasonable assumptions about the benefit of solvent substitution and recycling are not always found to be true.

Polymer membranes for nanofiltration are gaining traction in the separation and purification sectors as a potentially low energy technology. Fabrication of membranes requires a solvent to dissolve the polymer. Unfortunately, tetrahydrofuran (THF) and reprotoxic amides (DMF, DMAc and NMP) are favoured for this purpose.[133] A detailed comparison of membrane fabrication methods has identified how wasteful the use of solvents is, concluding that poly(ether ether ketone) membranes are preferable to the more popular polyimide membranes used for organic solvent nanofiltration, because of solvent use in the production phase.[134] Recent advances include the application of the plasticiser acetyl tributyl citrate as a solvent for polyvinylidene difluoride hollow fiber membrane production,[135] and ionic liquids for cellulose acetate membrane fabrication.[136]

Other academic developments towards solvent substitution to improve environmental, health and safety impacts in the production of polymers include solubility studies to justify greener alternatives. In one example, mixtures of butyl acetate and aromatic solvents used to form nitrocellulose lacquers were taken as a case study.[137] It was found that glycerol-derived solvents, particularly 1,2-diacetin, could be designed to fulfil the identified solvent characteristics that are beneficial in this role. The Hansen solubility parameters of solvent and solute were important to direct the study, rather than relying on experimental trial and error. Duereh *et al.* used the Kamlet–Abboud–Taft solvatochromic parameters instead in their attempt to find mixtures of benign solvents for polyamic acid.[138] Dipolar aprotic solvents are the conventional option. The following mixtures were successful solvents for the polymer precursors pyromellitic dianhydride and 4,4′-oxidianiline, and polyamic acid, with equivalent performance to NMP: γ-valerolactone and ethanol; γ-valerolactone and water; γ-butyrolactone and water. In other work, d-limonene has been used as a polymerisation solvent, making use of its alkene functionality,[139] and chirality,[140] to influence process performance and the properties of the resulting polymer.

2.5 Paints and Coatings

Paints and coatings is the largest solvent sector in terms of the annual volumes used. The difference between a protective coating and a paint is that the latter contains pigment with the purpose of decoration. The typical organic solvents required in paint and coating formulations are hydrocarbons, glycol ethers and acetate esters, but sometimes also alcohols and ketones.[141] The role of the solvent is vital to create a homogeneous dispersion of pigments, binders and other additives. The exact formulation and its intended purpose determine the choice of solvent(s), which then have a role in ensuring the smooth and uniform application of the coating, and finally the drying of the paint.[142] Because the solvent is so intrinsically linked to the formulation as a whole, books dedicated to the topic of paints and coatings have already covered all the relevant aspects of solvent use in this industry. Interested readers are recommended to read the following for detailed information: ‘The Chemistry and Physics of Coatings’, edited by Alastair Marrion,[143] and ‘Paints, Coatings, and Solvents’, edited by Stoye and Freitag.[144]

The performance of the solvent system in a paint formulation is gauged by the finish achieved, requiring a smooth and even deposition of pigment. For this the evaporation of the solvent is necessary, which will often be directly to the air, and this is certainly the case for consumer products. The rate of evaporation must be tuned with the use of solvent mixtures so that the drying rate is not longer than customer expectations, but not too rapid as to rupture the coating. The VOC content of consumer paints has been reduced over time through legislative measures,[145,146,228] meaning that waterborne paints are now the norm. The major paint producing companies and industry associations all have sustainability strategies to direct their business along a path of low solvent use and low environmental impact.[147–149]

Solventborne paints are still needed for particular (large scale) industrial uses, including vehicle coatings.[150] Solventborne paints typically have a high solids content, minimising the quantity of solvent required.[151] This can be as high as 85% solids content.[152] The medium is usually a blend of solvents, needed to tune the solubility, viscosity, and evaporation rate.[153]

To take an example of a solventborne coating technology, metal coil coating refers to a process of cleaning, painting, oven curing, and rolling of large metal sheets for transportation before fabrication into end-products.[154,155] The coil coat is a high solids formulation, although that can mean up to 40% solvent. Alongside hydrocarbons, propylene glycol monomethyl ether and its acetate ester have been suggested as common solvents.[156] The investment already made in existing metal coil coating lines means changing to solvent-less coating technology can only be expected when a major refurbishment is required anyway. The solvent is evaporated during the process at the curing phase, and collected for incineration. This has made some authors question the need to replace the current solvent systems on the basis that emissions are low.[157] It is true that modern systems have very low fugitive solvent emissions,[158] but given that 0.1 million tonnes of solvent is used in coil coating processes (higher estimate, 2007), solvent reduction would have obvious benefits.[159] In Europe, only 7 out of 158 coil coating operations currently use solvent-free powder coatings, and less than 1% of pre-fabricated metal products use waterborne coatings.[159] We can expect the coil coating industry to continue its gradual move away from organic solvents in much the same way as consumer paints and other coatings have, without any major revolutionary steps.

2.6 Construction Materials

Solvent use is generally low in the production of commodities such as metals, wood products, minerals, and the finished articles and building materials made from them. However, the large size of these industries can mean that the modest use of solvents for cleaning equipment and finishing products can accumulate into major annual volumes of solvents. Wood products require varnishes and pre-fabricated metal sheets are treated with solvent-based coatings, both of which are significant in their contribution to total solvent demand in the construction industry.

Fabricated metal products are cut, shaped, assembled and coated, originally from molten metal. Metal refining does not require solvent until the final finishing stages, before fabrication into a final product. Oil, grease and oxides are removed with hydrocarbon solvents, but also methyl ethyl ketone (MEK) and trichloroethylene have been reported as being used by the iron and steel industry.[160] Recycled metal is also degreased.[161] Metal casted (moulded) parts do not require solvents directly for their production, but the construction and cleaning of the moulds uses solvent and lubricants. Aside from the usual cleaning of equipment, and the cutting and forming operations, the paints that are used can of course be solvent-based.

Alongside steel and other metal products, inorganic mineral products are a common basis for construction materials. This includes glass, and concrete, stone and clay. Solvents are required for finishing products, especially the more specialised composite articles. Wypych has previously reported some changing trends in solvent use,[162] but not to the benefit of the environment or sustainability objectives. These include a degreaser for glass made from *n*-propyl bromide,[163] a reprotoxin,[164] NMP, DMF or *N*,*N*-dimethyl acetamide (DMAc) (all reprotoxic) for clay dispersions to make thin films for solar cells,[165] and anti-smudge fluorosilane coatings for glass components in electronics, for which the solvent needed is the ecotoxic ethyl nonafluorobutyl ether.[166]

2.7 Materials for Energy Applications

Energy materials are becoming more elaborate and sophisticated, and increasingly moving towards organic molecules. The development of solar cells demonstrates this trend (Section 2.7.2). This transition means that solvents are increasingly important for the synthesis and fabrication of organic electronics and other materials for energy applications. Even down to the molecular level, solvents are important for the action of molecular motors.[167]

2.7.1 Lithium Ion Batteries

Carbonate solvents are attracting interest as solvents for reaction chemistry,[168] but they have a more vital function as the electrolyte in lithium ion batteries.[169] It is also possible to recover the electrolyte (dimethyl carbonate–diethyl carbonate–ethylene carbonate ternary mixtures) from used batteries.[170] Another role of solvents in battery manufacture is in the production of electrodes. A life cycle analysis (LCA) study has demonstrated that the use of NMP to make a slurry for the casting of lithium-ion battery electrodes is not favourable compared to water as an alternative, environmentally benign solvent.[171] Making printed electrodes requires a solvent to produce an 'ink', and again NMP is favoured for solubility reasons, although other dipolar aprotic solvents can be used.[172]

2.7.2 Solar Cells and Organic Electronic Devices

In anticipation of large scale production of perovskite photovoltaic cells for solar panels, a new demand for chlorobenzene, DMF, DMSO and γ-butyrolactone solvents will be created.[173] New solvent systems are being investigated meanwhile, including the use of an acetonitrile-methylamine binary system, which is optimised to dissolve the methylammonium iodide and lead diiodide precursors of a perovskite film.[174]

Academic studies are advancing the state-of-the-art in the next phase of photovoltaics based on organic molecules. Not long emerged from its infancy, a reliance on chlorinated solvents in the production of organic photovoltaics is proving hard to shake off.[175] Sometimes aromatic solvents are suitable from a performance perspective,[176,177] and ethers such as 2-methyltetrahydrofuran (2-MeTHF),[178] and phenyl ethers,[179] can be used in some cases. An approach to 'rational solvent selection' is urgently required to correctly identify why chlorinated solvents are so important, and what can be done to find alternatives in a more systematic way. The Hansen solubility parameters provide a means of identifying the correct solvent or solvent blend based on polarity.[180] Machui *et al.* determined the Hansen solubility parameters of the thiophene and fullerene polymers typically used as organic semiconductors in organic photovoltaic devices.[181] This meant that it was possible to screen solvent blends for optimum solubility of the substrates, although the authors decided this information was best used to see how far chlorobenzene could be diluted in acetone and remain a suitable solvent system.[182] With environmental impact currently considered a barrier to large scale commercialisation, further advances in the synthesis of organic semiconductors is needed.[183]

In addition to photovoltaics, there are a great number of electronic components being developed on the basis of organic molecular components. Research into the use of alternative and benign solvents has led to the use of short chain alcohols for the production of field-effect transistors based on organic semiconductors.[184] Limonene has also been proven as a useful solvent for the fabrication of field-effect transistors.[185] Printable sensors also require a solvent in their manufacturing process for the purpose of casting polymer films.[186] In one solvent substitution, *N*,*N*-dimethyl formamide (DMF) can be replaced by 1,3-dioxolane in the production of poly(vinylidene fluoride–trifluoroethylene) films.[187] Also, piezoresistive addition polymer composites made with carbon nanotubes can be printed using cyclopentyl methyl ether (CPME) instead of toluene as the solvent.[188]

2.8 Graphene

The two dimensional material graphene is an iconic material with many potential applications.[189] It can be made from graphite using adhesive tape to peel the carbon layers apart, but obviously this is not appropriate for high volume manufacturing. Instead, graphite exfoliation in a solvent is preferred as a scalable approach to graphene manufacture.[190] The most frequently used solvent for graphene processing is NMP,[191] with 1,2-dichlorobenzene and other polar solvents sometimes used.[192] These solvents permit high concentrations of high quality graphene flakes, as needed for applications in electronics. The requirements of the solvent relate to the need to separate the individual sheets of graphene, and keep them separated as a dispersion without causing oxidation or other defects.

Experience shows that graphite processing into graphene has come to rely on aprotic, polar and high boiling point organic solvents. As well as being toxic, their low volatility leads to problems for the isolation of the graphene. Low boiling solvents would be preferable for low energy deposition of graphene onto surfaces. To this end Coleman and co-workers have proven that isopropanol (flammable, irritant) and chloroform (suspected of causing cancer) are able to perform the exfoliation of graphite and subsequently disperse graphene.[193] The dispersion concentrations are half that of equivalent processes in NMP, but the graphene is of high quality, which is the more important factor for high-end applications.

Hernandez *et al.* have investigated the effect of solvent polarity on the achievable concentration of graphene in dispersion.[194] Not only does the graphene need to be high quality, but for a high volume industry to be realised, graphene production cannot rely on dilute solutions in toxic solvents. The graphene was produced with a short ultrasound treatment of 0.1 mg of graphite per millilitre of solvent, after which the sample was centrifuged to remove any remaining graphitic flakes. Twenty of the forty solvents tested by Hernandez *et al.* are given in Figure 2.12 to illustrate the effect of solvent polarity. The data includes 4 solvents with superior graphene concentrations to NMP. These are cyclopentanone, cyclohexanone, *N*-formyl piperidine and benzonitrile. Other dipolar aprotic solvents, including *N*-ethyl pyrrolidinone (NEP), are less efficient.

The particularly favourable graphene concentration in cyclopentanone is complemented by its reasonably benign hazards (flammable, irritant), making it an excellent substitute for NMP. More caution should be taken with cyclohexanone, which is being investigated with respect to its potential chronic toxicity.[195] The reason behind the excellent performance of the

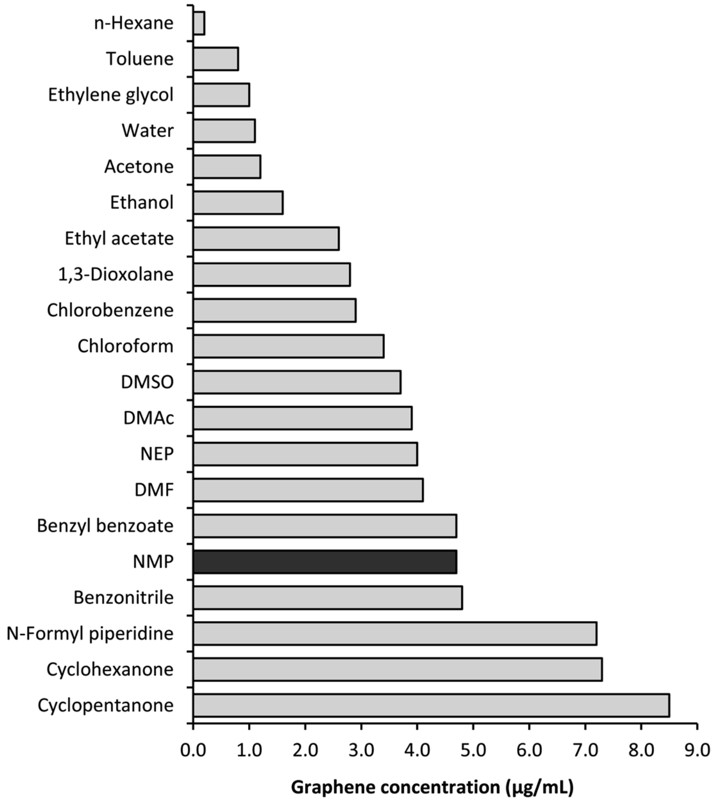


Figure 2.12 Graphene concentrations in different solvents (NMP emphasised).

cyclic ketone solvents is attributed to surface tension and polarity (Hansen solubility parameters). Graphene has Hansen solubility parameters of δ_D = 18.0 MPa$^{1/2}$; δ_P = 9.3 MPa$^{1/2}$; and δ_H = 7.7 MPa$^{1/2}$, relating to dispersion forces, dipolarity, and hydrogen bonding.[194] Solvents with a similar polarity will provide the highest dispersion concentrations. The surface tension of solvents is important for the exfoliation of graphite to graphene. Surface tension is proportional to surface energy. The surface energy of graphene is 68 MJ m^{-2},[190] and it is this force that associates the layers of graphene together in the familiar graphite layered structure. If the solvent has a similar surface energy, it can come between the graphene flakes without any energy penalty, making exfoliation favourable.

2.9 Biomass, Natural Products and Biotechnology

The development of a global bio-based economy relies on efficient means of extracting value in volume from abundant renewable resources. The process technology as well as the feedstock must be sustainable. Solvents will continue to develop as part of the repertoire of biomass processing technologies needed to separate, extract, and react biomass to obtain useful products.[196] Biomass conversion in neoteric solvents is a strongly advancing field of research, in which the new-found solubility of structural biomass components (*e.g.* lignocellulose) in ionic liquids and deep eutectic solvents allows pre-treatment of biomass into useful fractions for downstream processing.[197,198] Solvent pre-treatments can assist cellulosic ethanol production,[199] and lignin extraction.[200,201]

Extraction is a diverse field, and the case of natural product extraction is also faced with the challenge of overcoming the complexity of the original biomass and understanding the composition of the extracts. The recent work of Chemat is comprehensive in this regard, covering the extraction of essential oils,[202,203] and vegetable oils,[204,205] and also the use of essential oils,[206] and vegetable oils,[207] as extraction solvents themselves. Polyhydroxyalkanoate (PHA) biopolymers are extracted from bacteria using chlorinated solvents for use as biodegradable plastics.[208] The Hansen solubility parameters have assisted solvent substitution in favour of a choice of cyclohexanone or anisole instead.[209]

Biocatalysis, the use of enzymes to accelerate reactions, is an extension of biomass pre-treatment and extraction helpful to yield fine chemical products that can be considered ‘natural’. Water is the logical choice of solvent, as in nature. However, organic solvents offer advantages in the form of catalyst stability and space-time yield, and also permit the reaction of hydrophobic reactants.[210,211] The understanding of biocatalysis is now sufficient to design optimised systems for green processes,[212] with bio-based solvents an obvious partner for a bio-based catalyst.[213] Low polarity hydrocarbon solvents are ideal for accelerated enzymatic reactions, the reasons for which are still being examined and debated.[49,50]

2.10 Leather

Leather tanning is a water-based industry, and so organic solvent use is insignificant. Water is safe and non-toxic, and generally abundant and cheap. Leather tanning protects the product from microbial decay. The hazards posed come instead from the use of chromium. While many sectors (especially paints and coatings) seek water-based alternatives to organic solvents, in the leather tanning industry the combination of water as a solvent and toxic heavy metal salts means that, counter to current trends, an organic solvent might actually be more beneficial than an aqueous system.[214] In leather tanning, at best only 70% of the chromium is transferred to the leather, creating an estimated 24 tonnes of chromium salt waste discharged in over 25 billion litres of water every year.[215]

For effective leather tanning, several tests are needed to confirm the performance of the solvent. These include chromium transfer, the resultant stability of the leather in a boiling water test, its appearance, and its resistance against microbial activity. A recent study has performed a solvent selection exercise to identify an organic solvent for leather tanning.[216] From eight

Table 2.4 Leather tanning performance of selected solvents.

Solvent	Chromium transfer	Leather quality	Boiling water test	Microbial resistance
2-Butanol	99%	Flat with uniform colour	No change	One week
Butyl acetate	99%	Wrinkled and patchy	No change	Not tested
Dimethyl carbonate	99%	Flat with uniform colour	No change	Two weeks
Ethanol	99%	Flat with uniform colour	No change	One week
Ethyl acetate	99%	Wrinkled and patchy	No change	Not tested
Ethyl lactate	56%	Wrinkled and patchy	Shrinkage	Not tested
1,2-Propanediol	6%	Untanned	Shrinkage	Not tested
Propylene carbonate	99%	Flat with uniform colour	No change	More than 8 weeks

green organic solvents, it was found that six allow for near quantitative chromium transfer from solution to leather, thereby greatly reducing chromium demand (Table 2.4). Ethyl lactate and 1,2-propanediol were unsuitable, but also butyl acetate and ethyl acetate did not yield a quality product. Of the four remaining solvents, 2-butanol, dimethyl carbonate and ethanol produce leather prone to fungal growth, but propylene carbonate produced resistant leather.[217]

Other work moving towards non-aqueous leather tanning has investigated the pre-processing removal of hair,[218] and fat,[219] using propylene glycol and supercritical carbon dioxide, respectively. For the chrome tanning process, a water–ethanol–ethyl acetate ternary mixture is another viable system,[220] as is a deep eutectic solvent consisting of ethylene glycol (two equivalents) and choline chloride.[221]

2.11 Dry-Cleaning

Our final application case study is dry-cleaning, the history of which is quite interesting in terms of how certain solvents have fallen in, and then out, of favour. Detailed accounts of the history of dry-cleaning have been given by Estévez,[222] and Hasenclever.[223] In short, various hydrocarbon solvents were used in the 1800s until non-flammable chlorinated solvents became available in the following century. Dry cleaning processes finally settled on tetrachloroethylene as their favoured solvent after previously using more toxic types of chlorohydrocarbon solvents. That is not to say that tetrachloroethylene is safe and non-toxic.[224] Tetrachloroethylene is recovered after dry cleaning by distillation with minimal losses.[223] Siloxanes are also used as dry-cleaning solvents,[225] but it is a supercritical carbon dioxide ($scCO_2$) medium that would seem to offer the most promise of realising a sustainable dry-cleaning process. Unfortunately, the high efficiency and low solvent demand of modern day tetrachloroethylene processes means that $scCO_2$ dry-cleaning is not competitive.[226]

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CHAPTER 3

Sustainability Applied to Solvents

3.1 Sustainability Assessment Methods and Approaches

It is clear that sustainability is a broad and difficult subject area. Approaches to dealing with sustainability in terms of chemicals and chemistry are varied. The least helpful are throwaway comments suggesting a product or process is sustainable without comprehensive data across the three pillars of sustainability to back up the claims that are made. The most comprehensive assessments interpret quantitative datasets against benchmarks, establishing requirements that must be met for social, economic, and environmental sustainability. Studies with a narrower scope that only consider energy demand, or volumes of waste, for example, are valuable in their own right, but must be balanced against other available studies and holistic conclusions made.

The focus of this overview of approaches will be environmental sustainability, that being the most frequently studied and most clearly understood attribute of sustainability with respect to chemistry. Life cycle analysis is the primary tool to evaluate the environmental impact of a manufacturing process and/or the use of the resulting product. It is important to remember that LCA is only a means of interpreting data that is relevant to environmental impact. Social and economic sustainability are not addressed. For this, social-LCA and life cycle costing analysis are acceptable tools (Figure 3.1). A LCA will not conclude whether a product or process is sustainable within the boundaries of the assessment. To do that, the data must be aligned with environmental sustainability indicators that are proven by not exceeding a threshold (for example, a maximum tolerable land use or quantity of greenhouse gas emissions).

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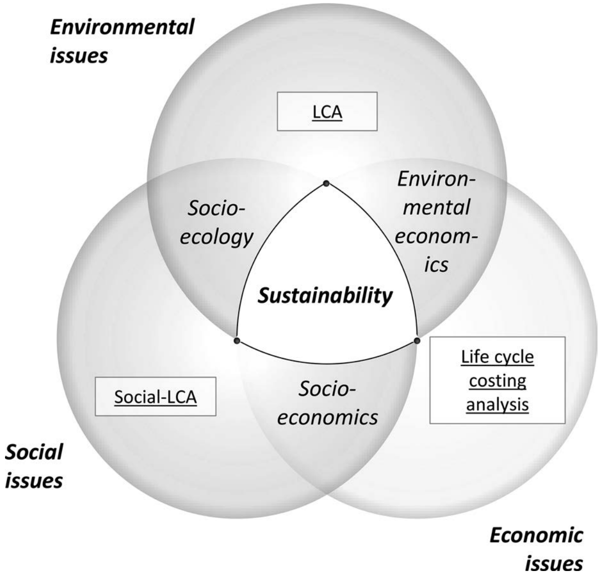


Figure 3.1 The themes of sustainability,[171] and the key tools to evaluate them.[172]

Integration of LCA into environmental sustainability schemes and complete sustainability assessments are briefly addressed here. For a full appreciation of social,[1] and economic,[2] sustainability please refer to specialised texts. Solvent LCA studies have generally addressed the evaluation of end-of-life options (incineration *versus* recovery), with increasing interest now in the production of solvents from biomass. Some of the most prominent studies in the scientific literature are reviewed in this chapter, after the introduction to LCA.

3.1.1 Life Cycle Assessment

A life cycle assessment (LCA) is an "*environment management tool*".[3] It quantifies what is taken (land use, resource depletion) and what is created in its place (emissions and wastes). The output of a LCA is either divided into individual outcomes (*e.g.* land use, amount of water consumption, eutrophication potential), or combined into an overall rating. The former is more informative but the latter easier to compare with other products or processes. The boundary of the life cycle analysis is typically either "cradle-to-gate" or "cradle-to-grave" (Figure 3.2). Transfers between the life cycle stages (indicated as white boxes in Figure 3.2) usually require transportation as a further consideration. Transportation also requires energy and material input resulting in emissions and waste (black boxes in Figure 3.2).

In the context of solvents, a cradle-to-gate LCA would consider raw material and energy inputs for the manufacturing process, and of course the emissions and wastes generated as a result. Cradle-to-grave assessments would also take into account transportation of the final product, the impact of its

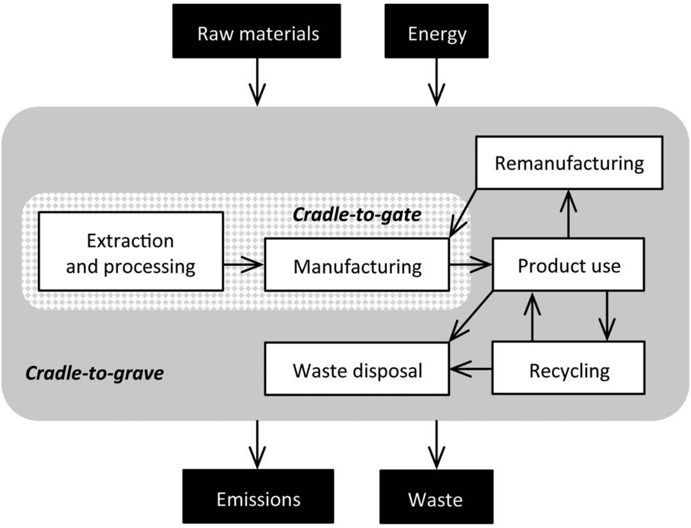


Figure 3.2 Life cycle assessment boundaries, either cradle-to-gate (lighter checked shaded area) or cradle-to-grave (solid grey shaded area).

use, and finally disposal. Particular to solvents are analyses of the different end-of-life options, but these are not necessarily a complete LCA, but a more specific type of assessment found in the literature.[4]

Once the scope is defined (including the LCA boundaries and the functional unit on which comparisons will be based), a life cycle inventory (LCI) is created, establishing all the inputs and outputs of the system (material and energy use, land use, emissions to air, water and soil, solid waste, *etc.*). To be able to complete the LCI, the process within the boundaries of the LCA must be comprehensively understood. Sometimes allocation of the life cycle flows is needed, for instance when multiple products are made from a single integrated process.[5] Waste streams are not permitted to bear any of the environmental burden: all the impact is assigned to products with value. Preferentially, the allocation process is avoided by dividing the process into sub-processes. If that is not possible, allocation on a mass basis is preferred, although the economic value of the products can also be used. The example of vegetable oil transesterification provides a helpful illustration. Biodiesel (fatty acid methyl ester, FAME) is created alongside the co-product glycerol. The glycerol may be considered a waste product, and indeed present day production exceeds demand.[6] In this instance, all emissions, energy use, *etc.* associated with biodiesel production can be attributed to the fatty acid methyl esters. However, glycerol is a valuable chemical, including uses as a solvent and an intermediate for solvent production.[7] The transesterification of a vegetable oil into FAMEs will typically co-produce 9–12% glycerol as an output by mass. The allocation of environmental burdens assigned onto glycerol would then be in the region of 10% and the remainder onto the biodiesel.

However, the surplus of glycerol on the market means the economic ratio between the two products is much more slanted towards the FAMEs, which after all are the primary product. Furthermore, if the vegetable oil feedstock is obtained as a waste product after primary food uses, then no life cycle impact due to biomass production would be allocated to a downstream fuel or solvent product.[8] The isolation and purification of crude glycerin into a marketable solvent for fine chemical applications will regardless have some dedicated environmental impacts due to energy consumption associated with it.

The LCI is followed by the impact assessment. The impact assessment requires that impact categories are set, and the data regarding environmental burdens from the LCI is converted into a result for each category indicator.[9] The impact assessment is arranged into mid-point categories (signifying environmental problems), or an end-point category (quantifying overall damage). Examples are given in Table 3.1.[10] Different LCA methodologies take different approaches, each with their own precise guidelines. Mid-point categories are described in more detail in the 'International Reference Life Cycle Data System' (ILCD) 2011 handbook,[11] which has been produced to be consistent with international standards on LCA.[12,13] Representative of a damage-orientated methodology is 'Eco-Indicator 99'.[14,15] Sometimes the approach combines and unifies mid-point and end-point categories, *e.g.* IMPACT 2002+.[16,17] End-point categories group several mid-point indicators together. This provides a definitive, numerical outcome, but is considered to be susceptible to greater uncertainty,[18] with less transparency, and is harder to understand.[19] Mid-point categories have the advantage of being openly interpreted by decision makers, who have the flexibility to derive an end-point indicator of their own if necessary. The limitation of a collection of mid-point categories is that the relative importance of each remains subjective, and the perception of different stakeholders will influence any decisions based on the result of the LCA.

Table 3.1 Environmental and human health categories found in life cycle assessments.

Environmental burdens	Environmental problems (mid-point categories)	Environmental damage (end-point categories)
Energy use	Abiotic resource depletion	Damage to human health
Material use	Biotic resource depletion	Damage to resources
Emissions (air)	Land use impact	Damage to ecosystems
Emissions (water)	Water consumption	Human environment
Solid waste	Global warming potential	
	Ozone depletion	
	Photochemical ozone creation potential	
	Human toxicity	
	Ecotoxicity	
	Acidification	
	Eutrophication	

The choice of indicators and their implementation are critical to the success of the LCA, and ultimately any sustainability assessments using the results of that LCA. Failing to define and implement LCA categories correctly will result in decisions that do not improve sustainability, to the detriment of the environment.[20] Carbon capture was not included in Table 3.1. It is recognised that bio-based products do capture carbon, but the lack of a time dimension in the LCA methodology[21] makes representing this attribute fraught with difficulty, and from this, discrepancies between LCA approaches have emerged.[22]

The results for each LCA category must be expressed in widely used and accepted normalised units (*e.g.* CO_2-equivalents when reporting global warming potential). Then a simple comparison between the values of each impact assessment category is the basis of an environmental assessment between two or more case studies. Additionally, the framework of a sustainability assessment creates a context for the LCA indicators of each impact assessment category by setting a threshold value, against which the product or process is judged. This remains controversial, and will always be subject to debate.

The purpose of an LCA is to be able to compare processes or products and ascertain the most environmentally benign option.[23] Usually the comparison between different options is used to indicate the most sustainable option (relatively speaking). Alternatively, an indication of absolute sustainability is achieved by translating the results of the LCA(s) into a sustainability assessment, where the principle of comparison is then based on sustainability thresholds. Agreement on robust thresholds is not easy to come by, and they are not universal. The tolerable soil degradation caused by a given process operating in one area is different to that of another area. A certain quantity of emissions or land use required by a chemical plant may not damage biodiversity in Europe, but can be devastating in tropical regions. Therefore, it is not the volume of emissions that is important, but the impact they have. For this reason, sustainability certification schemes, for example, tend to lack definitive quantitative thresholds for indicators, and instead ask the operator of a process to justify why their actions do not adversely affect the environment. However, this means that the impact assessment of an LCA is not used to its full potential, merely clarifying resource use and emissions.

Just as the results of an LCA can be reported as a single end-point indicator, the next step is the grouping of different sustainability indicators for environmental, social and economic impacts to create a composite sustainability index.[24] Multidimensional sustainability assessments can take different forms, depending on whether the focus is retrospective or prospective, and whether the focus is on a product, an integrated process, or an entire region or nation.[25] A comprehensive list of sustainability criteria, especially social aspects, for evaluating industry have been compiled by Brent and co-workers.[26] Combining the interpretation of issues such as these with an LCA to account for the environmental impact gives a more complete picture of the situation.

There are a multitude of ways one can conduct an LCA. To enhance consistency and quality, international standards have been produced to define the relevant principles, ISO 14040,[12] and requirements, ISO 14044.[13]

However, these are not specific to bio-based products and the particularities of biomass. European standard EN 16760 defines best practice for life cycle assessments of bio-based products.[27] Additionally the French ‘Association Chimie du Végétal’ (ACDV) provides guidance on LCA for chemicals made from biomass.[28]

3.1.2 Alternative Tools for Environmental Sustainability Assessments

Various adaptations of the life cycle assessment (LCA) principle exist. A four dimensional evaluation, ‘Eco-LCA’,[29] produces a quantitative metric for each of the following: resource utilisation, resource availability, environmental impact, and economic effectiveness. The boundary of the assessment goes upstream as far as possible to include solar energy. In contrast, a typical LCA starts at the available raw materials. Another modification to LCA is offered by Eckelman.[30] What Eckelman realised is that an LCA relies on inputs to evaluate outputs. What goes unevaluated are the inherent issues of the process, such as the toxicity of the chemicals used and produced that are not emissions or waste. ‘Life cycle inherent toxicity’ is a new indicator that looks at the impact to human health of the product from a chemical process, not the inadvertent consequences. This is helpful as a way to represent the process because emissions can be variable, captured or released, whereas the intended product is a constant that identifies the process, and is the purpose of that process.

A combined economic and ecological assessment has been developed by Heinzle *et al.*,[31] in which early indicators of environmental impact (placed in the context of regulations) and economic impact (by way of feedstock cost, waste disposal cost, and operational/infrastructure cost) have been developed for the purpose of directing process design. Too often an LCA is applied retrospectively, whereas if used to inform design choices it can result in a more sustainable chemical industry. Expanding the boundary of the assessment to the surrounding region gives an ‘ecological footprint’, which is a sustainability indicator describing the impact of human activities within a given land area.[32] This reveals the intensity of resource depletion and waste creation, and whether this is within the capacity of the region. Obviously all regions combined constitute the whole planet, and if on average capacity is exceeded then current human activities are unsustainable (which they currently are).[33]

Another metric that uses land area-based units is the ‘sustainable process index’ (SPI).[34] The SPI has its basis in mass and energy flows between the environment and technosphere.[35] The sustainable process index is reported as the area required to supply a person with the product or service in question for a year. Finite land availability therefore imposes a limit to the scale of any process. Considered within the SPI are land requirements for biomass production, mining of non-renewable materials (for energy and feedstocks), the production facility and the staff. Also accounted for is the sustainable dissipation of releases and disposal. This is not to advocate the dilution of chemicals in the environment as was the Victorian approach, but managing the scale of emissions. In a case study, bio-ethanol (as a fuel) from sugar beet was evalauted.[34] The area required was calculated as 2.04 m^2 year kWh^{-1}, with 20% of the land needed for biomass production, but much more (63%) needed for the less obvious dissipation of emissions. If everyone used this bio-ethanol to fuel their cars, 37% of the Earth's surface would be dedicated only to sustaining this particular demand for energy, which is very revealing. Whereas a classic type of LCA reports land use as a mid-point indicator, the SPI elaborates this by extending its scope, while also providing more information in a way that is relevant to time and space (rather than providing a normalised, unitless number).

The 'Sustainability evaluator' is a LCA-type methodology that generates a numerical score for different metrics across social, economic and environmental sustainability categories to assist process design.[36] Whereas an LCA only reports emissions and depletions of energy and resources, in addition this tool shares some attributes with Eckelman's 'Life cycle inherent toxicity',[30] in so much as the use of chemicals is evaluated and their toxicity and other hazards are taken into account (Figure 3.3). Models of different process options can be compared. This was done for the manufacture of dimethyl

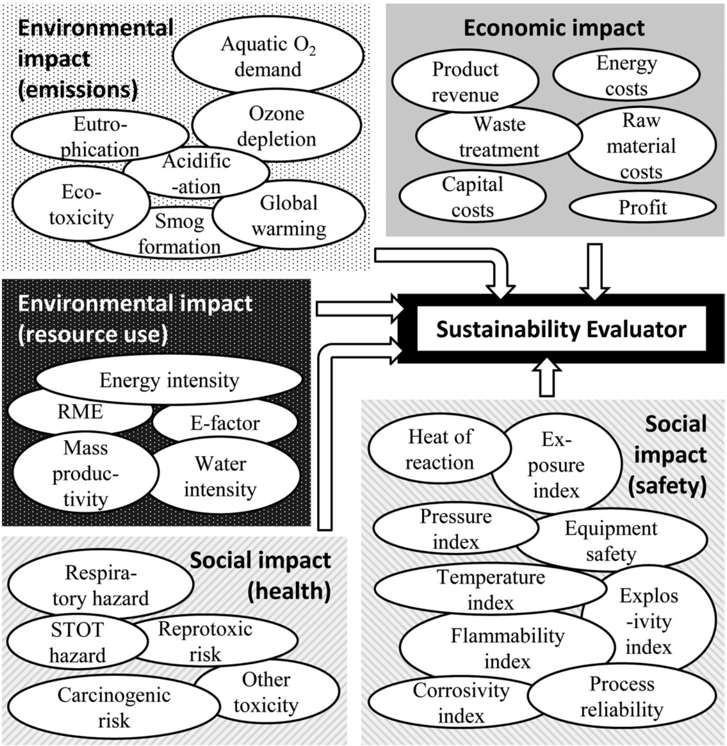


Figure 3.3 The metrics of the 'Sustainability evaluator' and how they relate to social, economic and environmental sustainability. RME is reaction mass efficiency,[173] and STOT is specific target organ toxicity.

ether,[36] a compressed gas fuel that also has potential as a solvent for natural product extraction.[37] To illustrate how some of the metrics work, the temperature index awards a score of zero (least impact) to processes that operate between 0 °C and 70 °C. Sub-zero processes and those between 70 °C and 150 °C are scored two, and so on. Higher scores indicate a higher impact. Some metrics are less precisely defined. Equipment safety is scored according to whether the following equipment is required: only equipment for non-flammable and non-toxic materials (0); heat exchangers, pumps, towers and drums (2); air coolers, reactors, and high hazard pumps (4); compressors and high-hazard reactors (6); and furnaces and fired heaters (8).

Another tool of this type is available, demonstrated for the design of a plant for the manufacture of cyclohexanone from benzene.[38] Cyclohexanone is a solvent for degreasing and polymer processing, and has been shown to be a viable solvent for graphene manufacturing.[39] The result shows that even though two routes (one *via* cyclohexene, the other *via* phenol) might have indistinguishable environmental impacts, the economic and social impacts can be much less severe in the case of the cyclohexene pathway. This reiterates the limitation of LCA as a tool purely for assessing environmental impact, which is not a problem in itself, but is an issue when it is assumed that environmental sustainability is the only relevant factor and a wider appreciation of other important issues is ignored.

A deconstruction of LCA has been used to evaluate the environmental impact of pharmaceutical production in terms of readily understandable actions. In the work of Soete *et al.*,[40] the most significant contributing practices extracted from LCA data were the amount of organic solvent needed, molar efficiency (or reactions), and the duration of a reaction. Generally, the chemicals required for the synthesis of an active pharmaceutical ingredient represent four fifths of cradle-to-gate life cycle resource consumption. Of this, reactants account for 13–33%, while solvents are responsible for 55–80% and the influence of the catalyst(s) is virtually insignificant.

Finally, the Organisation for Economic Co-operation and Development (OECD) has produced an online portal describing a 'Sustainable Manufacturing Toolkit'.[41] Inputs, processes and outputs are defined in terms of 18 indicators that could contribute to an environmental sustainability assessment (Table 3.2).[42] Each is a simple calculation reflecting recycled content,

Table 3.2 The OECD sustainable manufacturing indicators.

Input	Operation	Output (product)
Non-renewable materials	Water use	Recycled content
Restricted substances	Energy use	Recyclability
Recycled content	Renewable energy	Bio-based content
	Greenhouse gas intensity	Non-renewable materials
	Residuals intensity	Restricted substances
	Air releases	Energy consumption
	Water releases	Greenhouse gas emissions
	Land use	

renewable energy use, and GHG emission intensity amongst other attributes of environmental impact, which are all fully explained in the OECD portal.[42] A review of all the different 'footprinting' indicators has been compiled by Čuček.[43]

3.1.3 Solvent Assessment Models

It is difficult to compare the absolute impact of different solvents, and impossible to make blanket claims that one solvent is superior to another. This is because they have many different uses, and the choice of solvent and the practices of the user may have a significant influence in an application. Improved or reduced efficiency, longer or shorter application times, different quantities of solvent needed to achieve the same effect, and other variables mean that only on a case-by-case basis can a full LCA be implemented. Generic assessments are possible, but only for the production of solvents (cradle-to-gate), or their disposal (end-of-life), missing out the use phase. Two types of assessment are covered here, firstly the energy of solvent production (which can be offset by waste management options) (Section 3.1.3.1) and sustainability index ratings (Section 3.1.3.2).

3.1.3.1 Cumulative Energy Demand of Petrochemical Solvent Production

The energy required for the production of typical petrochemical solvents has been modelled extensively. Although the energy requirements are not the complete picture, the cumulative energy demand (CED) of a process correlates remarkably well with several other indicators of environmental burden (cradle-to-gate of course).[44] These indicators include mid-point indicators: land use (direct and indirect land use combined as the ecological footprint), global warming potential, and measures of exergy; and end-point indicators: 'Ecoscarcity',[45] 'Environmental Priority Strategy' (EPS),[46] and 'Eco-Indicator 99'.[14,15] It is therefore with some confidence that we can compare the CED of different solvents and have an idea (in a relative sense) which have the least environmentally damaging means of production.

Generally, the CED associated with petrochemical solvent production is below 120 MJ kg^{-1}, and it is often much lower depending on how many steps are required to transform the feedstock (natural gas, naphtha, aromatic crude oil fractions).[47] Methanol is a key chemical industry intermediate, most often made from natural gas. Not only is methanol a solvent in its own right, but it is also the precursor of many commonplace solvents, and not just those with C_1 groups (Figure 3.4). As in the original analysis by Capello *et al.*,[47] methanol will be treated as a feedstock when categorising solvents in terms of the number of synthetic steps required for production. As a justification for considering methanol as a feedstock and not an intermediate, the CED of methanol is still lower than the alternative naphtha and BTX feedstocks.

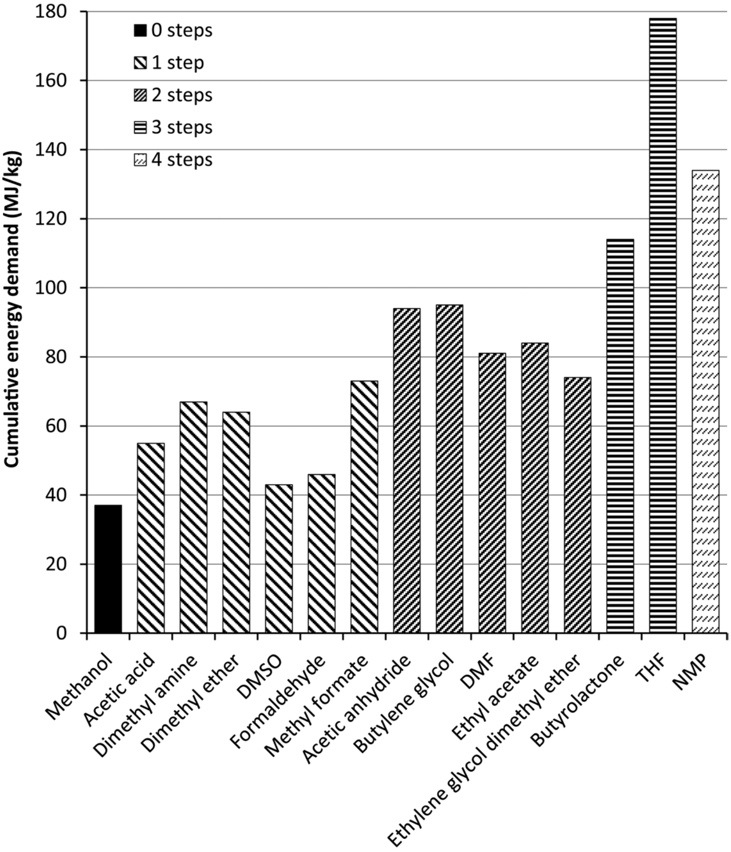


Figure 3.4 Energy of petrochemical solvent production from syngas-derived methanol.

Methanol is the industrial precursor of acetic acid, and therefore also downstream esters such as ethyl acetate that are considered solvents. Acetic acid itself is a solvent in select processes, for instance the manufacturing of PET.[48] With ethylene oxide, the methyl ethers of ethylene glycol ethers can be made, and by using acetylene butylene glycol, (1,4-butanediol) can be synthesised *via* formaldehyde. Oxidative cyclisation of 1,4-butanediol to butyrolactone is possible, which serves as an intermediate for THF and NMP production. Also considering that DMF is made by the carbonylation of dimethylamine, methanol has historically been a useful source of dipolar aprotic solvents. Capello *et al.* suggests that DMSO, another dipolar aprotic, is also made from methanol,[47] but in practice the dimethyl sulphide by-product from sulphate wood pulping is often oxidised to provide a source of DMSO (thereby it is made from renewable materials).[49]

The energy required to produce THF is substantial, and was once believed to be even higher in earlier estimates.[50] The suggested route is the dehydration of 1,4-butanediol, which is made especially energy intensive because the by-product water must be removed from the water miscible THF. The azeotrope between the two is 5 wt% water. Alternative ether solvents are being developed primarily because of safety concerns surrounding possible peroxide formation,[51] but the production of these solvents should be subject to the same scrutiny THF is afforded here. That would ensure excessive energy requirements are not inadvertently promoted through narrow solvent selection criteria.

Naphtha gives rise to a vast array of chemical intermediates *via* the alkene base chemicals (ethylene, propylene, 1-butene, 2-butene, butadiene). Linear hydrocarbons (pentane, hexane, heptane) are separated without any significant energy requirement, and find use as solvents for cleaning and the extraction of oils and waxes. Alcohols and ethers are obvious solvent products from the alkene base chemicals, typically achieved in 2 steps from naphtha (Figure 3.5). Ethanol was previously produced by the oxidation of ethylene to its oxide, followed by hydrolysis. Nowadays the influx of bio-ethanol has dwarfed petrochemical ethanol production, thinking in terms of all ethanol markets. The CEDs of ethanol and diethyl ether (the by-product of ethylene

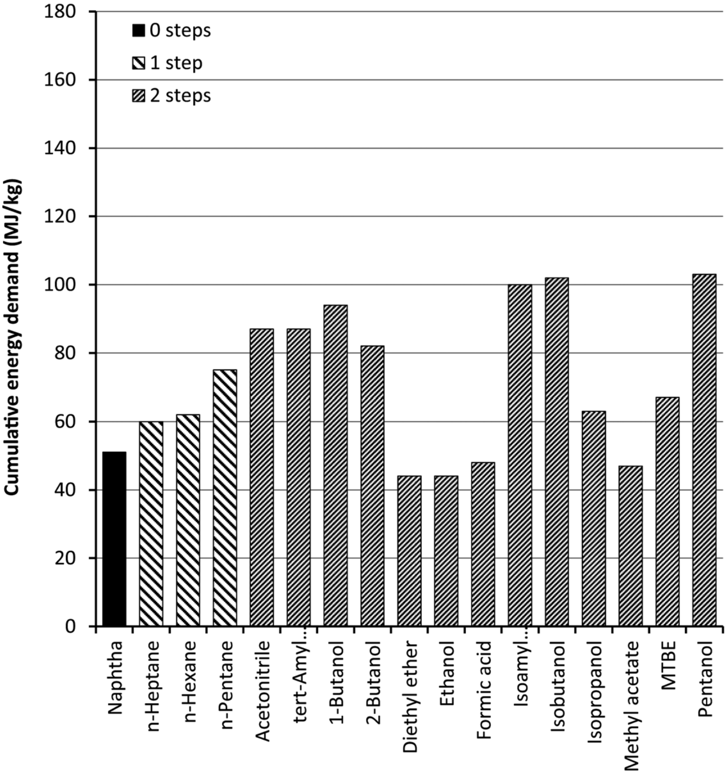


Figure 3.5 Energy of petrochemical solvent production from naphtha (1 or 2 steps).

oxide hydration) are much lower than the higher alcohols. This is because hydroformylation, requiring carbon monoxide with its own CED, is needed to produce propanol, butanol and pentanol. Figure 3.5 actually shows that ethanol has a lower CED than its precursor naphtha. This is because the measurement is in mass units, and the addition of significant mass (*e.g.* ethylene to ethanol, >60% mass increase per mole) using low energy processes can reduce the CED along the synthesis. In mole units, the CED must always increase with each separation or chemical transformation. Longer synthetic routes to solvents from naphtha provide access to the esters of the aforementioned alcohols (Figure 3.6).

The aromatics obtained from crude oil (benzene, toluene, and xylenes) are collectively referred to as BTX. Separation of each fraction provides the three most common aromatic solvents. Hydrogenation and subsequent oxidation provides access to cyclic aliphatic hydrocarbons and ketones, respectively (Figure 3.7). Cyclohexanone is produced by the oxidation of cyclohexane, while acetone is a co-product of cumene oxidation for the manufacture of phenol.

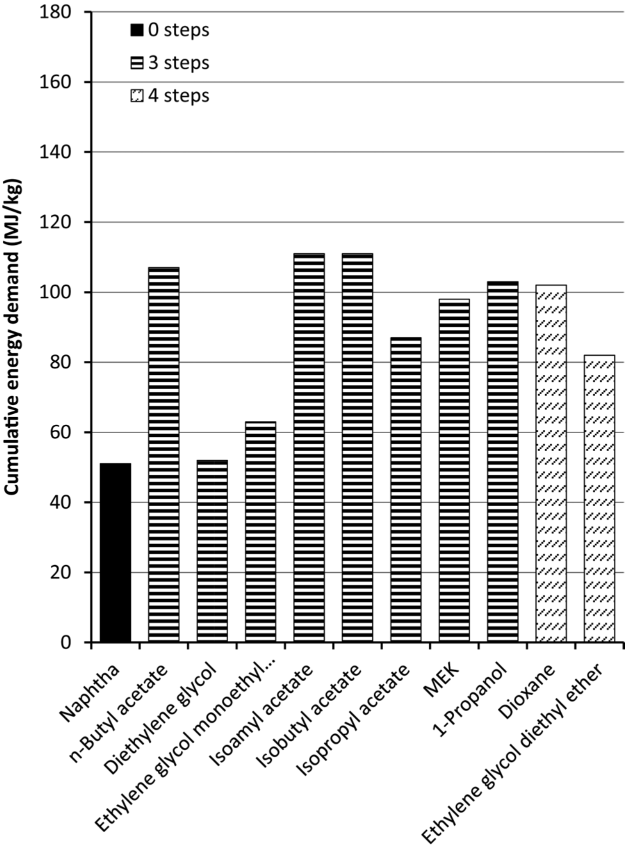


Figure 3.6 Energy of petrochemical solvent production from naphtha (3 or 4 steps).

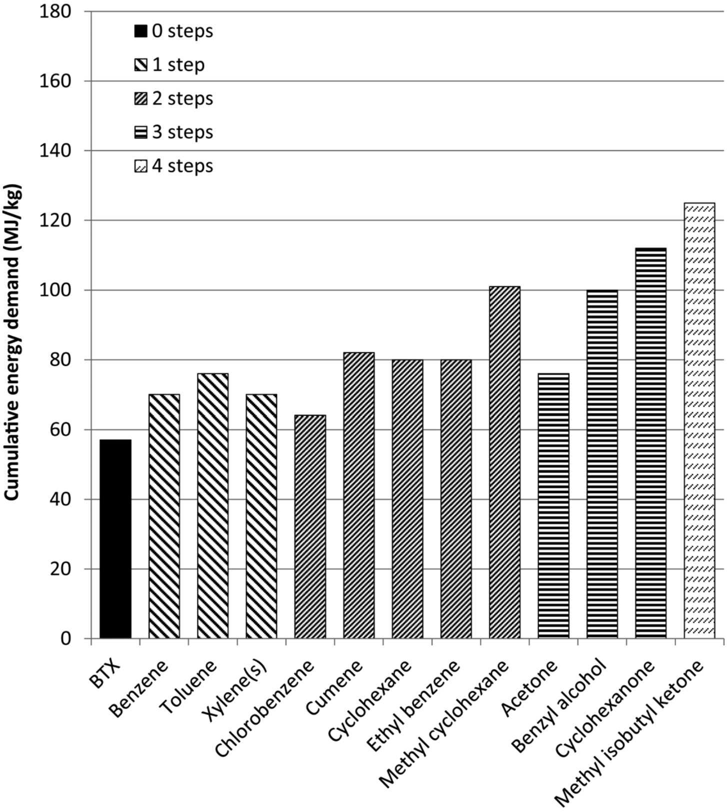


Figure 3.7 Energy of petrochemical solvent production from BTX splitting.

What this CED analysis suggests is that for solvents especially, given the proportions in which they are used in product formulations and processes, the length of the synthesis is important, as is the choice of reactions. When deciding on a solvent substitution or designing a new bespoke solvent synthesis, production should not be unavoidably energy intensive (of course additional savings can be made by optimising the development of pilot plants *etc*.). Otherwise, the work of Huijbregts demonstrates that the environmental impact will be higher,[44] and the expectation is that the price will be higher too. Chapter 5 will go on to show new production options for (bio-based) solvents that currently have a higher CED than conventional manufacturing processes. In the future, a reduction of the production CED is predicted as the technology (biotechnology for instance) matures. This might require integrated biorefineries, maximising feedstock usage to make better use of energy and meet price expectations.

The high CED of production associated with several prominent solvents can be offset by the end-of-life option applied.[50] Solvent waste management primarily takes two forms and both can favourably adjust the energy balance.

Recovery is the most satisfactory approach to maintain the material value of the solvent. Distillation is by far the most common technology for solvent recovery. The energy required to operate the distillation column(s) to recycle 1 kg of solvent is less than that required to produce 1 kg of virgin solvent. Therefore, solvent recovery is a way to offset the CED of production, and for some industries it provides a valuable product at a lower price point (70–80% of the virgin solvent).[52]

For some solvents, incineration after use is preferred to distillation. For the more calorific solvents, energy recovery during incineration offers a greater offset of the production CED than material recovery.[50] The choice can be seeded in efforts to reduce the environmental impact of solvent production as early as the process design stage, using an LCA approach.[4] There are tools and methods available specifically for the selection of the most favourable solvent end-of-life option,[53–55] as well as LCA studies demonstrating one way or another the ideal waste management strategy.[56–58] That said, in terms of overall environmental impact, elsewhere incineration has been claimed to always be inferior to distillation.[59] This is a helpful reminder that the scope of any evaluation is important and CED is only one indicator, albeit an important one. It also indicates that the historical process of distillation as the obvious means of recycling solvents needs re-evaluating, and low energy recovery options using membranes,[60] as well as new types of solvent that can be recovered and reused at low energy cost,[61] must be advanced towards commercial relevance. Meanwhile the solvent recovery industry is aligning itself with circular economy objectives,[62] offering a service that maintains the value of the solvent as much as possible.[63]

3.1.3.2 Sustainability Indices

There is an innate human desire to put numbers to the things we observe, and so indices that rank solvents are popular, whether this is in the form of a solvent selection guide,[64] or a sustainability index. GlaxoSmithKline (GSK) go some way towards the latter with a solvent 'renewability index'.[65] This combines the proportion of renewable (bio-based) carbon in feedstocks and energy, cradle-to-gate. The result is scaled from 1–10 for comparisons between solvents. Data for eight solvents was reported,[65] including ethanol, with none scoring more than 5 out of 10. There was no difference between tetrahydrofuran (THF) made from corn starch compared to 2-methyltetrahydrofuran (2-MeTHF), the obvious bio-based substitute for THF.

Nexant is a chemicals and energy sector consultancy firm who have produced a 'solvent sustainability index', although it is described as a tool to quantify "greenness" rather than true sustainability.[66] The following categories are evaluated: feedstock, health hazard, fire hazard, reactivity, volatility, VOC regulatory status, odour, and biodegradability. Water is reported with the maximum score of 100%, and other solvents scaled accordingly. For instance, glycerol (from vegetable oil triglycerides) scores 81%. Bio-ethanol (54%) is superior to petrochemical ethanol (44%). Bio-based ethyl acetate (59%)

is also considered to be greener than conventional non-renewable ethyl acetate (49%). Similarly, bio-based acetone (65%) scored 10% higher than conventional acetone. Limonene is penalised for its ecotoxicity (58%).

3.2 Sustainability Standards and Certification

Certification of sustainability is available now for a range of products, materials, and operations. One of the most prominent sustainability issues is biomass intended for biofuels. Different types of biomass can be certified under the terms of their own specific sustainability schemes. Biomass certification is relevant to bio-based solvents of course as it addresses the feedstock and sometimes chain-of-custody practices along the supply chain too. In addition, chemical products can be certified under certain schemes, and therefore sustainability certification becomes applicable to bio-based solvents. The most relevant standards and certification schemes for sustainable solvents are briefly reviewed here, after an overview of perhaps the most ambitious application of biomass (feedstock) sustainability criteria in the form of the European Union's renewable energy strategy. For reviews with an international perspective on biomass certification, use the references provided.[67–69]

Sustainability criteria must be met for biofuels (for transportation) and bio-liquids (for electricity and heating) used in the European Union.[70] This is defined in the 'Renewable Energy Directive' (RED, (2009/28/EC)).[71] Essential aspects of this ruling are that from 2017 biofuels must offer a 50% greenhouse gas emission saving compared to fossil fuels. This is a bottom-up criterion (see Chapter 1, Section 1.3.1). The biomass cannot be grown in land with high biodiversity or high carbon stock. The European specific version of the RSB sustainable biofuel production standard and certification is an example of an endorsed method to prove compliance with the RED (Section 3.2.1).

3.2.1 Product Certification: RSB

The 'Roundtable on Sustainable Biomass' (RSB) issues certification for bio-based products using their own standardised protocol, RSB-STD-02-001 (version 1.4, 2015).[72] The standard is implemented as a third party verification on behalf of bio-based product manufacturers and the producers of intermediate chemicals.[73] Requirements for the original biomass must meet the standards specified in RSB-STD-01-001 (version 2.1, 2011), which describes the requirements of sustainable biofuel production.[74] Manufacturers must also provide evidence of the bio-based (carbon) content of their product, which shall be no less than 25% (annual average). The analysis and calculation of bio-based content is explained in Chapter 4 (Section 4.2). There are additional rules on chain-of-custody allocation and product claims. Any claims regarding greenhouse gas (GHG) emissions must be justified using life cycle analysis or the RSB's own methodology (RSB-STD-01-003-01, version 2.1, 2012).[75] This part overrules the GHG requirements of RSB-STD-01-001, which is tied to biofuel regulations.

Clearly the actual sustainability of a bio-based product (under RSB certification) is limited to the biomass contained within it. If the product has a relatively low amount of bio-based content (*e.g.* 25% is enough to claim a solvent is bio-based according to European standard EN 16766,[76] see Chapter 4, Section 4.2.1), it is not necessarily a good reflection of the sustainability of the entire product, or the process that created it. Fortunately, bio-based solvents typically have a high bio-based content, often being fermentation products or essential oils for example. Feasibly they may be formulated as blends with petrochemical solvents, but this is unlikely to ever become a widespread practice. More obviously, occasionally bio-based solvents may be produced by chemical synthesis with a low bio-based content because of the choice of reactants. For example, an ester of bio-based lactic acid and petrochemical 2-ethylhexanol has (a calculated) 27% bio-based carbon content. Fossil feedstocks are fundamentally unsustainable because the longevity of the supply is unknown, and certainly finite. However, it is not practical to rule out any solvent with less than 100% bio-based content as unsustainable. In fact, because LCA is not time bound, fossil-derived products can easily appear superior with respect to environmental sustainability than bio-based products. Remember, the fossil feedstocks do not bear the consequences of land use or biodiversity issues to the same extent as has marred biomass use for non-food or feed applications in the past. This paradox suggests that current biomass processing practices are inefficient, requiring too much land and using too little of the inedible portion of biomass crops. Looking to the future, minimum bio-based content expectations must be progressively increased as the strength and size of the bio-based economy grows, while guaranteeing the impact on people, profit, and the planet is only beneficial.

The rules for sustainable biomass established by RSB standard RSB-STD-01-001 are presented in Table 3.3 and have been labelled as economic, social or environmental criteria. The requirements for GHG emissions are not listed because these are superseded by the requirements of RSB-STD-02-001 (which are only for making additional claims, and not essential to the certification scheme). Please note RSB-STD-01-001 is the global standard. There is also a European version for biofuels that allows the targets of the European Renewable Energy Directive (2009/28/EC) to be demonstrated.[77] The quantitative indicators for each criteria allow for a definitive assessment. The original context for RSB standard RSB-STD-01-001 was biofuels, and so the entries in Table 3.3 have been adjusted to remove reference to biofuels and in some cases paraphrased for brevity. Please refer to the latest version of the standard for full indictors and the minimum requirements needed to fulfil them. Note that RSB-STD-02-001 is not designed for self-certification. Each indicator may apply to any combination of the biomass producer, biomass processor, or final product manufacturer throughout the supply chain. Guidance in RSB-STD-01-001 determines the acceptable methods by which to prove adherence to the requirements of each indicator.

3.2.2 Product Certification: ISCC PLUS

'International Sustainability and Carbon Certification' (ISCC) are another third party certification agency that operate a sustainability scheme for end products. This is known as ISCC PLUS, which is based on several different standards covering different considerations throughout the supply chain.[78] As in the approach of RSB, the sustainability criteria only apply to the feedstock, as documented in ISCC PLUS 202 (version 3.0, 2016).[79] For bio-based plastics, an additional standard is used, ISCC PLUS 260-02 (version 1.0, 2012),[80] but the information is limited, merely indicating how the collection of ISCC standards should be used together. The sustainability requirements presented in ISCC PLUS 202 are broadly the same as those in RSB-STD-01-001. The criteria are grouped under six principles, which neatly divide into two principles for each of the three pillars of social, environmental, and economic sustainability (Table 3.4).

As in Table 3.3, compliance with regulations is assigned as an economic criterion. This is somewhat for convenience for the purpose of explaining the topic within this book, but because profitability is in itself usually a sufficient motivator in the dominant business model, the concept of economic sustainability has taken a broader perspective in order to direct operations towards achieving a more stable and beneficial approach for the global economy. An economy is "*a system of relationships focused on the production, distribution, exchange and consumption of goods and services*",[81] and so sustainability must "*cultivate economic opportunities ... meet social needs and cultivate equitable relationships*" if we are to continue to strive for greater equality yet greater industrialisation.[82] Regulation is a necessary tool to manage and protect the economy, and determines what business relationships are suitable for sustainable development.

The details on biodiversity and high carbon stock provided in ISCC PLUS 202 are helpful given the emphasis of these criteria in the EU Renewable Energy Directive (2009/28/EC). The key date in this respect was January 2008, with land categorised as having high biodiversity value or high carbon stock not being suitable as a source of raw material from this time onwards. The status of these lands cannot be changed in order to justify the production of biomass (for biofuels). Highly biodiverse lands include natural forest (as in native tree species not yet disturbed by commercial human activity), some grasslands, protected nature reserves and the habitats of endangered species. Land with high carbon stock unsuitable for conversion for biomass production are wetlands, forests with significant canopy cover (greater than 30% coverage), and peatland. However, if the harvesting of biomass is part of a conservation effort, this is permitted. This is consistent with the EU Renewable Energy Directive (2009/28/EC) and the tools available in support of it.[83]

An interesting topic is addressed by ISCC PLUS 260-05 (version 1.1, 2015),[84] which is dedicated to feedstocks that are either a waste, or renewable but of non-biological origin. In the introduction to this standard, the need to replace fossil substances with low-carbon feedstocks is recognised. Waste is stated as having essentially no risk of land use change

Table 3.3 RSB sustainable biomass requirements.[74]

Criteria	Indicator
Economic: Operations shall follow all applicable laws and regulations	*Operations shall comply with all applicable laws and regulations of the country in which the operation occurs and with relevant international laws and agreements*
Economic: Sustainable operations shall be planned, implemented, and continuously improved through an open, transparent, and consultative impact assessment and management process and an economic viability analysis	*Operations shall undertake an impact assessment process to assess impacts and risks and ensure sustainability through the development of effective and efficient implementation, mitigation, monitoring and evaluation plans*
	Free, Prior & Informed Consent (FPIC) shall form the basis for the process to be followed during all stakeholder consultation, which shall be gender sensitive and result in consensus-driven negotiated agreements
	Operators shall implement a business plan that reflects a commitment to long-term economic viability
Environmental: Products shall contribute to climate change mitigation	Not applied to bio-based products
Social: Operations shall not violate human rights or labour rights, and shall promote decent work and the well-being of workers	*Workers shall enjoy freedom of association, the right to organise, and the right to collectively bargain*
	No child labour, slave labour, or forced labour shall occur
	Workers shall be free of discrimination of any kind
	Workers' wages and working conditions shall respect all applicable laws and international conventions. Men and women shall receive equal pay for work of equal value
	Conditions of occupational safety and health for workers shall follow internationally-recognised standards
	The rights outlined in this principle shall apply equally when labour is contracted through third parties
Social: In regions of poverty, the operations shall contribute to the social and economic development of local, rural and indigenous people and communities	*In regions of poverty, the socio-economic status of local stakeholders impacted by the operation shall be improved*
	In regions of poverty, special measures that benefit and encourage the participation of women, youth, indigenous communities and the vulnerable in the operation shall be designed and implemented
Social: Operations shall ensure the human right to adequate food and improve food security in food insecure regions	*Operations shall assess risks to food security in the region and locality and shall mitigate any negative impacts that result from operations*
	In food insecure regions, operations shall enhance the local food security of the directly affected stakeholders
Environmental: Operations shall avoid negative impacts on biodiversity, ecosystems, and conservation values	*Conservation values of local, regional or global importance within the potential or existing area of operation shall be maintained or enhanced*
	Ecosystem functions and services that are directly affected by the operation shall be maintained or enhanced
	Operations shall protect, restore or create buffer zones
	Ecological corridors shall be protected, restored or created to minimize fragmentation of habitats
	Operations shall prevent invasive species from invading areas outside the operation site

Environmental: Operations shall implement practices that seek to reverse soil degradation and/or maintain soil health	*Operators shall implement practices to maintain or enhance soil physical, chemical, and biological conditions*
Environmental: Operations shall maintain or enhance the quality and quantity of surface and ground water resources, and respect prior formal or customary water rights	*Operations shall respect the existing water rights of local and indigenous communities* *Operations shall include a water management plan which aims to use water efficiently and to maintain or enhance the quality of the water resources that are used for operations* *Operations shall not contribute to the depletion of surface or groundwater resources beyond replenishment capacities* *Operations shall contribute to the enhancement or maintaining of the quality of the surface and groundwater resources*
Environmental: Air pollution from operations shall be minimised along the supply chain	*Air pollution emission sources from operations shall be identified, and air pollutant emissions minimised through an air management plan* *Operations shall avoid and, where possible, eliminate open-air burning of residues, wastes or by-products, or open air burning to clear the land*
Environmental: The use of technologies in operations shall seek to maximise production efficiency and social and environmental performance, and minimise the risk of damages to the environment and people	*Information on the use of technologies in operations shall be fully available, unless limited by national law or international agreements on intellectual property* *The technologies used in operations including genetically modified organisms shall minimise the risk of damages to environment and people, and improve environmental and/or social performance over the long term* *Micro-organisms which may represent a risk to the environment or people shall be adequately contained to prevent release into the environment* *Good practices shall be implemented for the storage, handling, use, and disposal of chemicals* *Residues, wastes and by-products from feedstock processing and production units shall be managed such that soil, water and air physical, chemical, and biological conditions are not damaged*
Social: Operations shall respect land rights and land use rights	*Existing land rights and land use rights, both formal and informal, shall be assessed, documented, and established. The right to use land for operations shall be established only when these rights are determined* *All negotiated agreements for any compensation, acquisition, or voluntary relinquishment of rights by land users or owners for new production operations shall be consensual*

impacts (neither direct or indirect) within ISCC PLUS 260-05.[84] The types of waste from biological origin included in the scope are agricultural wastes and residues, process-specific and industry-specific wastes and residues, and end-of-life wastes and residues. The non-biological (but renewable) wastes included in ISCC PLUS 260-05 are organic municipal solid wastes

Table 3.4 ISCC principles for establishing sustainability indicators.

Social	Economic	Environmental
Safe working conditions through training and education, use of protective clothing and proper and timely assistance in the event of accidents	Biomass production shall take place in compliance with all applicable regional and national laws and shall follow relevant international treaties	Biomass shall not be produced on land with high biodiversity value or high carbon stock
Biomass production shall not violate human rights labour rights or land rights	Good management practices shall be implemented	Biomass shall be produced in an environmentally responsible way

(*e.g.* plastic), carbon dioxide from natural sources, carbon dioxide from waste-streams, and either syngas component (carbon monoxide and/or hydrogen), again from waste streams. There is potential for this list to be expanded, pending a decision from ISCC. Importantly the waste must not be created deliberately as a feedstock, and the supply chain from the point of origin must be certified, and traceability assured. The value of "waste" is variable, as sometimes the waste is a surplus of otherwise useful material (*e.g.* wheat straw), and other times the abundance of a waste product stimulates a market (as was the case for glycerol made during biodiesel production). The biological wastes must comply with sustainability criteria, specifically meaning ISCC PLUS 202. For example, if waste biomass from the forestry industry was used as a feedstock, the primary biomass product (*i.e.* timber) would need to be certified as sustainable. If the operation producing and then supplying the waste is not itself sustainable, then the long term availability of the waste feedstock is not assured. This is an important point to remember because it is easy to assume that we can use wastes freely as feedstocks as part of industrial symbiosis relationships, but the users of these so-called wastes are in the middle of a supply chain, and therefore vulnerable to product demand and feedstock availability fluctuations on both sides. Contrariwise, mismanagement of the waste conversion process may destabilise a key aspect of the value chain that other operations have become financially dependent on.

3.2.3 Product Standardisation: Sustainability Criteria for Bio-Based Products

As of 2016, the 'European Committee for Standardisation' (CEN) will complete its ambitious development of standards to enhance the bio-based product market in Europe. Standards are technical documents, formed in agreement with relevant stakeholders, that define the requirements of certification and test methods, provide harmonised definitions, and introduce other types of guidelines for business, products and services. The purpose of a standard is a reference point for agreed practices, resulting in higher efficiency, reliability, and quality.

The technical committee responsible for bio-based products at CEN has now created a number of technical reports and European standards.[85] Of particular relevance here is EN 16751, dedicated to sustainability criteria for bio-based products.[86] It is based on the ISO (international) standard ISO 13065 'Sustainability Criteria for Bioenergy' and features many of the same criteria and indicators, arranged under the same principles of social, economic, and environmental sustainability.[87] The scope of the standard is restricted to the impact of the bio-based content within a product, as is true of the RSB certification. Equally the criteria established in EN 16751 can be applied to the production of sustainable biomass, but additionally it can be extended to cover the production of the bio-based product too. The extension of the scope to include production of bio-based products is a welcome advance, even if there is little difference between the indicators of EN 16751 and a certification scheme only looking at biomass production. How the partitioning of biomass and non-renewable materials is implemented is not clear from the text in the standard, but allocation of environmental burdens would be necessary. For blends of bio-based solvents and petrochemical solvents this is done directly, but for partially bio-based solvents the bio-based content will determine the degree of allocation in the production phase.

The purpose of EN 16751 is only for the communication of sustainability information. No thresholds are established for the indicators in the standard because it is applicable to all bio-based products. Thresholds depend on different types of product. All criteria must be addressed by the operator and may be derived from certificates (awarded for sustainable biomass, for example). It is stated in the general requirements of EN 16751 that indicators shall be met using scientific approaches. Only where the indicator is incompatible with quantitative data can policy and ethical conventions be referred to. The environmental criteria are more numerous than the social and economic requirements. These are summarised in Figure 3.8 (climate), Figure 3.9 (water), Figure 3.10 (soil), Figure 3.11 (biodiversity), Figure 3.12 (energy and material resources), Figure 3.13 (waste), Figure 3.14 (labour rights), Figure 3.15 (land use rights), Figure 3.16 (water use rights), Figure 3.17 (local development), and Figure 3.18 (economic sustainability), and paraphrased where appropriate. The format is similar to sustainable biomass certification scheme requirements.

3.2.4 Biomass Certification: Palm Oil

Responsible for one of the more prominent certification schemes dedicated to a specific biomass, the Roundtable on Sustainable Palm Oil (RSPO) have a huge responsibility in maintaining standards for a product as controversial as palm oil. Palm oil is not a major feedstock for solvents, but in one instance,

Climate protection and air quality: Promote good air quality and reduce GHG emissions.

Criterion: The operator provides information on how greenhouse gas (GHG) emissions and removals related to their operations are managed.

Indicators: Describe procedures taken to identify GHG emissions and removals related to their operations. List the identified emission sources and removals and quantify them if possible

Describe the measures taken to reduce GHG emissions.

Criterion: The economic operator provides information on how emissions to air are managed with the objective to promote good air quality.

Indicators: Describe the procedures taken to identify air pollutant sources and emissions. List the relevant air pollutant sources and emissions identified.

Describe the measures taken to reduce the air pollutant emissions.

Figure 3.8 Climate criteria of EN 16751.[86]

Water: Conserve and protect water resources.

Criterion: The operator provides information on how quality and quantity of water withdrawn and released are addressed.

Indicators: Describe procedures taken to identify potential impacts on water quality and quantity. Impacts to water quantity and quality should consider impacts to water sources and receiving bodies.

Describe measures taken to address the impacts on water quality and quantity.

Figure 3.9 Water quantity and quality criteria of EN 16751.[86]

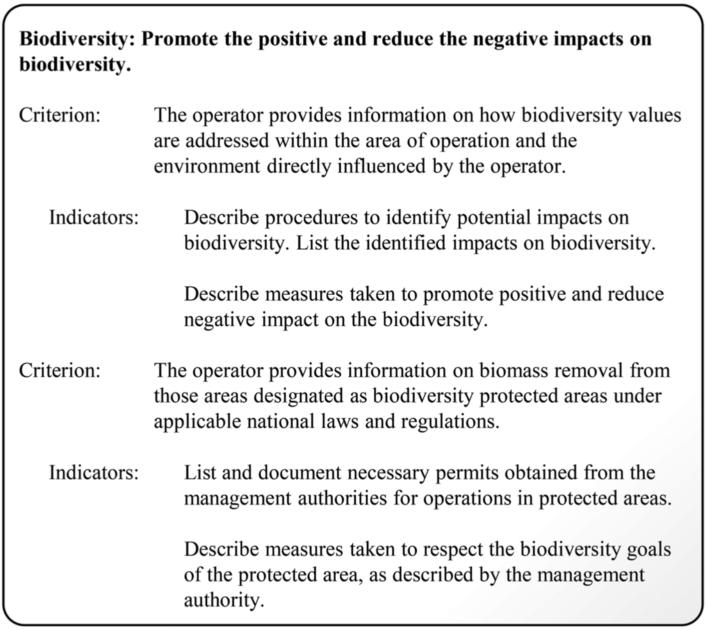
Soil: Protect soil quality and productivity.

Criterion: The operator provides information on how soil quality (*e.g.* organic matter and nutrients content in soil), productivity and erosion are addressed.

Indicators: Describe procedures taken to identify potential impacts on soil quality, productivity and soil erosion forces. List the relevant identified soil impacts.

Describe measures taken to address those impacts on soil quality, productivity and soil erosion forces.

Figure 3.10 Soil criteria of EN 16751.[86]



Biodiversity: Promote the positive and reduce the negative impacts on biodiversity.

Criterion: The operator provides information on how biodiversity values are addressed within the area of operation and the environment directly influenced by the operator.

Indicators: Describe procedures to identify potential impacts on biodiversity. List the identified impacts on biodiversity.

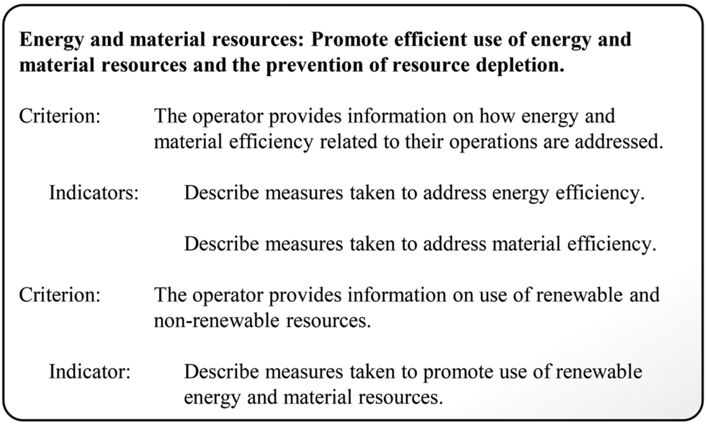
Describe measures taken to promote positive and reduce negative impact on the biodiversity.

Criterion: The operator provides information on biomass removal from those areas designated as biodiversity protected areas under applicable national laws and regulations.

Indicators: List and document necessary permits obtained from the management authorities for operations in protected areas.

Describe measures taken to respect the biodiversity goals of the protected area, as described by the management authority.

Figure 3.11 Biodiversity criteria of EN 16751.[86]



Energy and material resources: Promote efficient use of energy and material resources and the prevention of resource depletion.

Criterion: The operator provides information on how energy and material efficiency related to their operations are addressed.

Indicators: Describe measures taken to address energy efficiency.

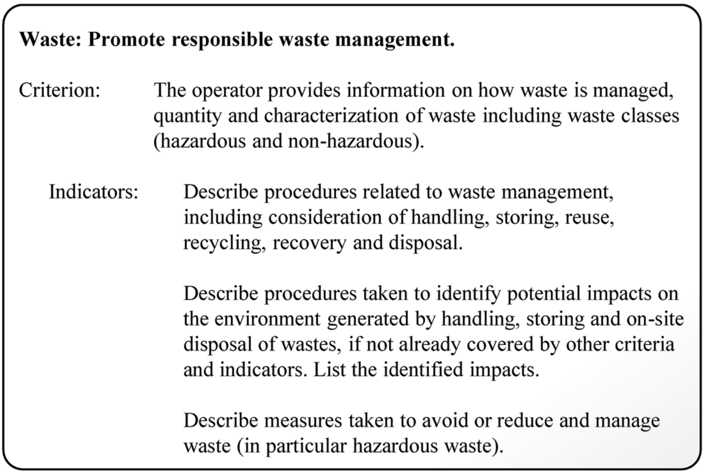
Describe measures taken to address material efficiency.

Criterion: The operator provides information on use of renewable and non-renewable resources.

Indicator: Describe measures taken to promote use of renewable energy and material resources.

Figure 3.12 Resource criteria of EN 16751.[86]

RSPO certified palm oil is used by glycerol and propylene glycol producer Oleon.[88] Speaking in broader terms, many of the sustainability principles and criteria that are used to characterise sustainable palm oil production are important more generally.[89] If these are upheld (by adhering to the specified indicators), then how the sustainable palm oil is traded through the supply chain must also satisfy the RSPO standard.[90] Environmental, social, and economic criteria apply as would be expected. Other mandatory principles cover



Waste: Promote responsible waste management.

Criterion: The operator provides information on how waste is managed, quantity and characterization of waste including waste classes (hazardous and non-hazardous).

Indicators: Describe procedures related to waste management, including consideration of handling, storing, reuse, recycling, recovery and disposal.

Describe procedures taken to identify potential impacts on the environment generated by handling, storing and on-site disposal of wastes, if not already covered by other criteria and indicators. List the identified impacts.

Describe measures taken to avoid or reduce and manage waste (in particular hazardous waste).

Figure 3.13 Waste management criteria of EN 16751.[86]

Labour rights: Respect labour rights.

Criterion: The operator provides information on how labour rights are addressed.

Indicator: Describe measures taken to safeguard rights related to trade unions and collective bargaining, forced and compulsory labour, child labour and discrimination.

Criterion: The operator provides information on how working conditions are addressed.

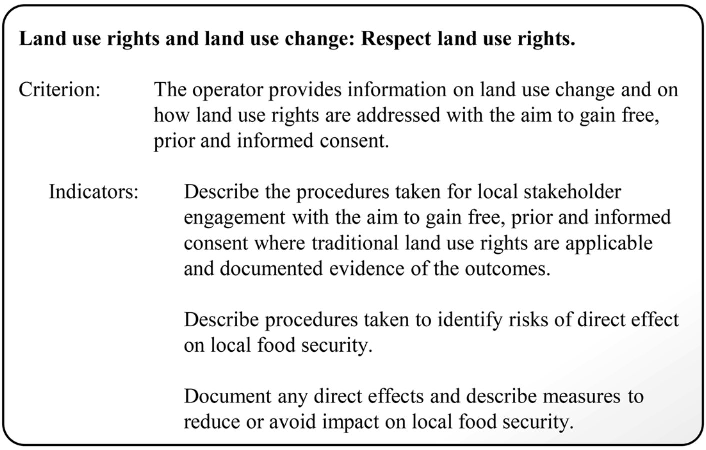
Indicator: Describe policies, practices and measures taken related to working conditions, including consideration of knowledge required, training, health, safety and hygiene.

Criterion: The operator provides information about the living conditions of employees at least if these are living on site.

Indicator: Describe measures taken to address living conditions and satisfaction of basic needs of the employees (*e.g.* access to drinking water, condition of housing, possibility for children to attend schools).

Figure 3.14 Labour rights (social) criteria of EN 16751.[86]

a commitment to transparency, regulatory compliance, appropriate practice (growers and millers), consideration of employees, affected individuals and communities, responsible development and finally a commitment to continuous improvement in key areas of activity (*e.g.* reducing chemical use, environmental impact, waste and pollution).



Land use rights and land use change: Respect land use rights.

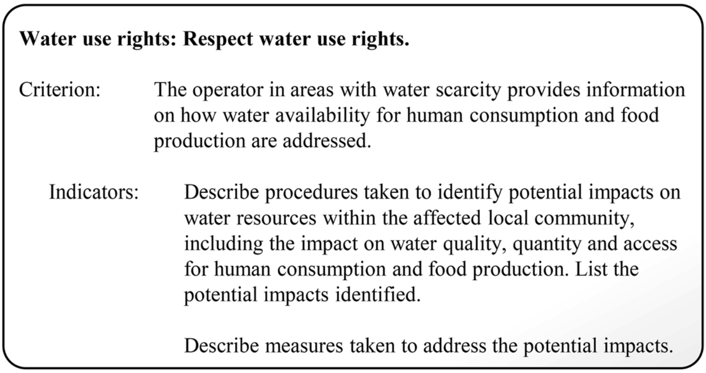
Criterion: The operator provides information on land use change and on how land use rights are addressed with the aim to gain free, prior and informed consent.

Indicators: Describe the procedures taken for local stakeholder engagement with the aim to gain free, prior and informed consent where traditional land use rights are applicable and documented evidence of the outcomes.

Describe procedures taken to identify risks of direct effect on local food security.

Document any direct effects and describe measures to reduce or avoid impact on local food security.

Figure 3.15 Land use (social) criteria of EN 16751.[86]



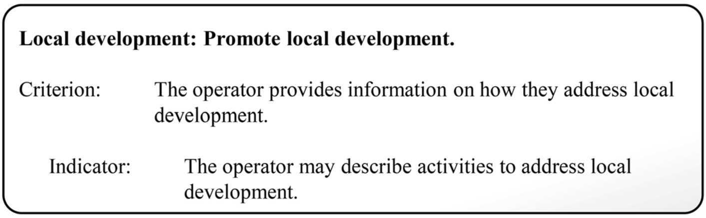
Water use rights: Respect water use rights.

Criterion: The operator in areas with water scarcity provides information on how water availability for human consumption and food production are addressed.

Indicators: Describe procedures taken to identify potential impacts on water resources within the affected local community, including the impact on water quality, quantity and access for human consumption and food production. List the potential impacts identified.

Describe measures taken to address the potential impacts.

Figure 3.16 Water use rights (social) criteria of EN 16751.[86]

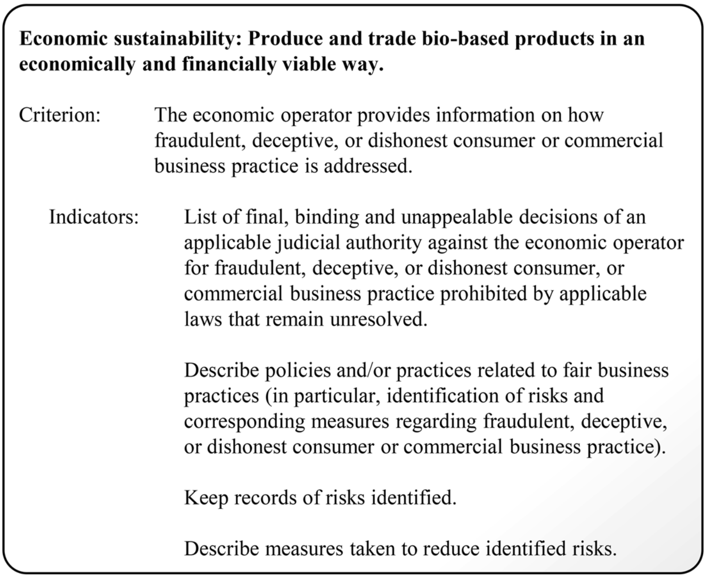


Local development: Promote local development.

Criterion: The operator provides information on how they address local development.

Indicator: The operator may describe activities to address local development.

Figure 3.17 Local development (social) criteria of EN 16751.[86]



Economic sustainability: Produce and trade bio-based products in an economically and financially viable way.

Criterion: The economic operator provides information on how fraudulent, deceptive, or dishonest consumer or commercial business practice is addressed.

Indicators: List of final, binding and unappealable decisions of an applicable judicial authority against the economic operator for fraudulent, deceptive, or dishonest consumer, or commercial business practice prohibited by applicable laws that remain unresolved.

Describe policies and/or practices related to fair business practices (in particular, identification of risks and corresponding measures regarding fraudulent, deceptive, or dishonest consumer or commercial business practice).

Keep records of risks identified.

Describe measures taken to reduce identified risks.

Figure 3.18 Economic sustainability criteria of EN 16751.[86]

Three mechanisms for distributing sustainable palm oil exist: segregation, mass balance, and book-and-claim (Figure 3.19).[91] Segregation of the product means a batch is accompanied by its paperwork from the grower, to the miller, transporter(s), refiner, and the end product manufacturer without touching unsustainable palm oil. This is ideal but not always feasible depending on scale and destination. A mass balance allocation requires that when certified and non-certified palm oil is mixed for processing or transportation purposes, the end-product is separated into batches. A volume of final product proportional to the amount of sustainable palm oil feedstock used receives the accreditation. It is not possible under the mass balance rules to artificially elevate the amount of sustainable palm oil or claim a larger batch of product is partially sustainable (or more precisely partially made from sustainably produced palm oil). The palm oil used as a feedstock by Oleon is certified under a mass balance approach.[88] Book-and-claim sees certification for a given volume of sustainably produced palm oil transferred to an equal volume of unsustainable palm oil for reasons of convenience with respect to transportation and consumer expectation. The palm oil that was physically obtained from the certified plantation loses its certificate and is treated as an unsustainable product.

The supply chain mechanisms in Figure 3.19 make interesting reading when comparing the three methods regarding what is allowed in claims of bio-based content (see Chapter 4, Section 4.2). The crucial difference between establishing the sustainability of palm oil and the bio-based content of bio-based products is that there is no analytical test for sustainable materials, meaning paperwork is the only mechanism by which to attribute

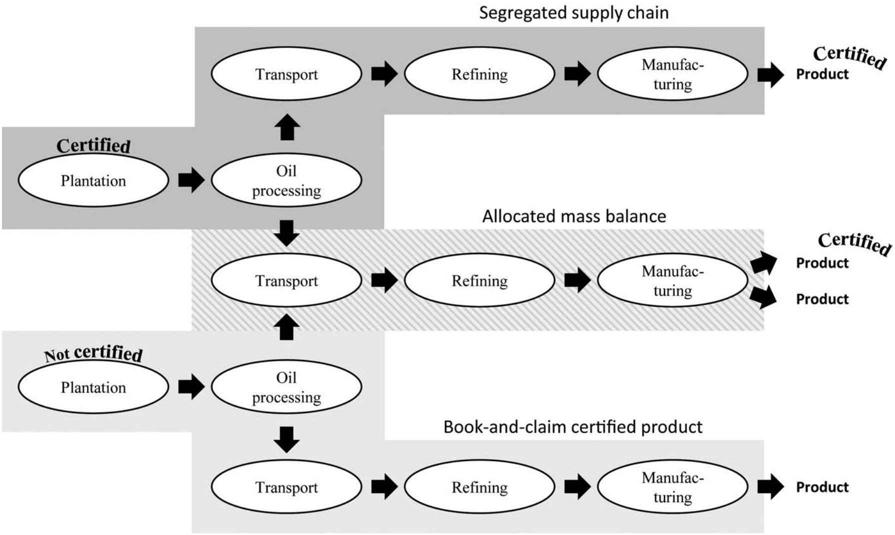


Figure 3.19 The supply chain models for sustainably produced palm oil. Certificates from the segregated supply chain (dark grey region) product can be transferred to the uncertified product (light grey region) by book-and-claim.

sustainability accreditation. Bio-based content is conferred across chemical reactions and (on a carbon atom basis at least) remains detectable by radiocarbon analysis. Therefore, neither mass balance allocations or book-and-claim are viable mechanisms of assigning bio-based content.

3.2.5 Biomass Certification: Sustainable Forestry Products

Two international forestry agencies, the Programme for the Endorsement of Forest Certification (PEFC) and the Forest Stewardship Council (FSC), provide certification. 'Sustainable Forest Management' (PEFC ST 1003) requires the maintenance and conservation of biomass yielding forests.[92] Ten principles with numerous criteria define the equivalent FSC forest stewardship standard.[93] The themes are not dissimilar to other certification schemes, including legal compliance, workers' rights, the rights of indigenous peoples, and conservation. In addition, the organisation responsible shall maintain and sustain the environmental and social benefits of the forest, while avoiding negative environmental impact in search of long term economic viability.

In the context of bio-based solvent production, a lignocellulosic feedstock coming from forestry processes should be sourced from certified plantations. Synergy with existing paper and pulp plantations and mills is ideal as low value by-products such as sawdust can be used as the feedstock for bio-based solvents.[94]

3.2.6 Biomass Certification: Sugar

Sugar, alongside starch, remains a primary feedstock for bio-based chemical products. Therefore, it is important to recognise how the sustainability of foodstuffs when used as chemical feedstocks can be formally recognised. Bonsucro is a certifier of sugarcane production for bio-ethanol.[95] The standard that underlines the certification is unusual as it contains thresholds for its indicators. This is a positive step towards a comprehensive and quantitative sustainability assessment, albeit mostly for biomass production. Other factors become important when we start to think of the production and use of bio-based products made from sugars, which is inevitably followed by end-of-life issues and the impact that too causes. Despite this, (cradle-to-gate) LCA studies have shown that the production of biomass remains a very significant contributor to the environmental impact of bio-based solvents (Section 3.3.2). This means the choice of biomass is important, and to make that decision the sort of scheme offered by Bonsucro is helpful.

The Bonsucro standard comprises six principles: legal compliance, human rights, efficiency, biodiversity/ecosystems, continuous improvement, and the regulatory requirements established by the European Renewable Energy Directive (2009/28/EC) for biofuels.[71] The two principles dedicated to process efficiency (Table 3.5) and biodiversity (Table 3.6) are of interest when seeking environmental sustainability.

Table 3.5 Bonsucro sustainable sugarcane production principle: manage input, production and processing efficiencies to enhance sustainability.

Criteria	Indicator	Threshold
To monitor production and process efficiency and to measure the impacts of production and processing so that improvements are made over time	Total raw materials used per kg product	<11 kg kg^{-1} (no ethanol production) or <20 kg kg^{-1} (sugars fermented to bio-ethanol)
	Yield of production	>8–49 tonnes per hectare (rain-fed) and >73–117 tonnes per hectare (irrigated), depending on the geographical region (as specified in the standard)
	Mill overall time efficiency	>75% of maximum operation time achieved
	'Factory Performance Index'	>90% sugars recovered from sugarcane
	Industrial efficiency	>75% (Total Sugars As Invert, TSAI)
To monitor global warming emissions with a view to minimising climate change impacts	Net greenhouse gas (GHG) emissions per tonne of sugarcane	<40 kg CO_2-eq.
	Net GHG emissions per tonne of sugar	<400 kg CO_2-eq.
	Net GHG emissions per MJ of bio-ethanol	<0.024 kg CO_2-eq.

Table 3.6 Bonsucro sustainable sugarcane production principle: actively manage biodiversity and ecosystem services.

Criteria	Indicator	Threshold
To assess impacts of sugarcane enterprises on biodiversity and ecosystems services	Dissolved oxygen in effluent flow receiving stream	>2.5 ppm
	Percentage of areas defined internationally or nationally as legally protected or classified as of 'High Conservation Value' planted as sugarcane after the cut-off date of 1st January 2008	0%
	The key environmental issues are covered by an appropriate and implemented environmental impact and management plan	>90%[a]
	Ratio of N and P fertiliser applied to fertiliser recommended (expressed in eq. phosphate), by soil or leaf analysis	<1.05
	Agrochemicals applied per hectare per year	<5 kg per hectare
	Banned agrochemicals applied per hectare per year	0 kg per hectare

[a] Nine of the ten key issues to be actively and successfully addressed: biodiversity, ecosystem services, soil quality, water quality, air quality, climate change, agrochemical use, artificial fertiliser, cane burning, and waste/noise.

Table 3.5 has definite requirements on the efficiency of biomass production and the technology used to convert it into sugar and/or bio-ethanol. Limits on greenhouse gas (GHG) emissions are also imposed, which can be calculated by LCA. Table 3.6 limits the use of fertiliser and pesticides. The indicators of environmental sustainability usually found in sustainability standards and certification schemes are bundled together by Bonsucro in the form of a requirement to develop and implement an 'environmental impact and management plan'. In it, key issues must be addressed (see Table 3.6 footnote). For each issue, potential environmental impacts must be identified. Then the sugarcane mill operator shall define measurable objectives, against which progress is continually monitored to make improvements. A public consultation is required to reach agreement on the 'environmental impact and management plan'.

3.3 Published Examples of Sustainable Solvents

"Sustainable" is far too frequently applied as an adjective to describe bio-based solvents and equally solvents made from other resources. Justified usage of this term must be proceeded by a sustainability assessment. It is far from acceptable to assume any product is sustainable without considering the far reaching issues that it entails. There are a number of LCAs and similar assessments based on solvent manufacturing and disposal (Section 3.1.3), but there is a lack of studies specifically set up to definitively characterise a process of solvent manufacturing (or the solvent itself) as sustainable. Even for product certification, it tends to be the feedstock that is certified and not the actual end product, and the same applies to the larger food and fuel sectors. Assessments relevant to understanding the sustainability of solvents are preceded in this sub-chapter by examples of claims made without formal assessment. Additionally, a review of biorefinery sustainability assessment frameworks has been provided as Section 3.3.3 to elaborate on how the impact of solvent production can be considered in a systematic manner.

3.3.1 Colloquial Statements of Solvent Sustainability

During the course of green chemistry establishing itself as a new chemical discipline, innovations have been considered as "green" far too eagerly, only for subsequent data to eventually inform more considered opinions and the position gradually revoked. Ionic liquids were more or less universally praised as green solvents at the turn of the century because of their negligible volatility,[96] but safety concerns over certain ions,[97,98] limited mammalian toxicity data,[99] and environmental fate,[100,101] including biodegradability,[102] have meant the greenness of ionic liquids is now strongly disputed. Ionic liquids or the processes they are added to are still claimed to be green,[103,104] but it has become a less prevalent practice.

It is important not to limit a conclusion on the sustainability or greenness of a solvent to just one contributing factor. With ionic liquids it was volatility. However, the synthesis of ionic liquids sometimes requires more volatile solvents than can be replaced by the resultant ionic liquid. In Figure 3.20 the synthesis of a classic ionic liquid, 1-butyl-3-methyl imidazolium tetrafluoroborate ([bmim][BF_4]), is represented as a Sankey diagram. The mass of each chemical required is represented by the width of each pentagon, with the pentagons acting as arrows. Data was taken from the procedure of Crowhurst *et al.*[105] Reactants and solvents (toluene in this case) are shown as inputs. 1-Butyl-3-methyl imidazolium chloride is an isolated intermediate, bridging the two reactions (alkylation and anion exchange) indicated by the light grey regions of the Sankey diagram. The product is labelled as output 1, with waste toluene (2), unreacted 1-methyl imidazolium and 1-chlorobutane (3), sodium chloride (4) and decomposition products (5) also labelled. The pie chart in Figure 3.20 collects these outputs of the reaction to show that the product accounts for 39% of the total mass of the indicated materials, while toluene accounts for 23%. Other wastes make up the remaining 38%, although in this analysis, wash solvents (ethyl acetate, dichloromethane, water) could not be included because of a lack of data. These auxiliary solvents will almost certainly triple the amount of solvent use accounted for here. In addition, the full impact of the synthesis is not appreciated just from what happens in research laboratories, as the reactants also had to be made beforehand at a different facility (a complete 'synthesis tree' for [bmim][BF_4] is provided in Chapter 4).[61,106]

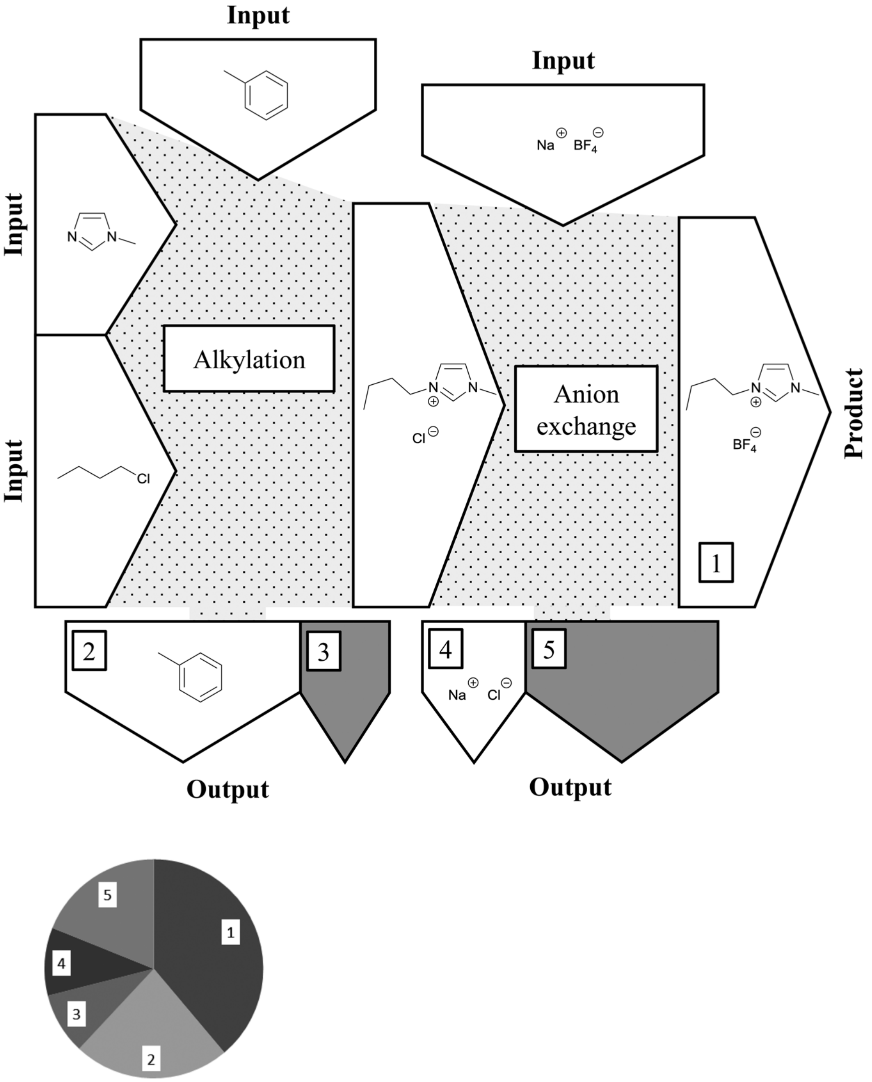


Figure 3.20 A Sankey diagram demonstrating the scale of solvent use in a recent ionic liquid synthesis. The relative mass of the product and wastes is shown in the pie chart.

For solvents, the advantages transferred to the application, be it faster reaction rates or superior formulations, are also important. A solvent substitute may require more energy to manufacture than its predecessor, but allow the energy required in its application to be reduced to more than compensate. Particularly for ionic liquids, the potential to recover and reuse them will, over time, minimise the impact of their synthesis.

Nowadays, "sustainable" is being used in place of "green" as a superior description of different types of solvents, not just ionic liquids of course.[107] Here we will provide a survey of instances in the peer-reviewed scientific literature where a solvent is claimed to be sustainable, yet no evidence is provided. The purpose of this section, through highlighting bad practice, is not to chastise the authors responsible, but to establish the present day habits dictating how the claim of sustainability is used to describe solvents. For fairness, past publications by the authors of this book are also included in this exercise! The state-of-the-art can only progress if chemists accept the meaning of sustainability as a culture for positive change and not a physical attribute of a substance. The burden of proof is high, but so is the responsibility of scientists to demonstrate their work is a sustainable development to the benefit of the planet and its people, and profitable enough to ensure that it is put into practice so that those benefits can actually be realised.

Water, regarded as "nature's solvent", is the most abundant, benign, and safe solvent available. However, for this very reason, the use of water in chemical processes and products as a solvent can lead to major and inexcusable issues relating to the contamination of water (see Chapter 4, Section 4.4). Dinjus and Kruse posed the question 'hot compressed water, a suitable and sustainable solvent and reaction medium?' in their 2004 article of the same name.[108] However, they did not go on to answer the question fully. A bolder statement found in a recent publication made no such hesitation, saying "*we developed a sustainable system consisting of ethyl lactate–water media in the presence of 1 mol% $Pd(OAc)_2$*" for Suzuki cross-coupling reactions.[109] The scarcity of palladium,[110] which was not recovered, and the purposeful organic contamination of water (inherent to their procedure) does not provide a strong basis for a sustainable reaction system. Furthermore, ethyl acetate is used as an extraction solvent in a 15 times excess over the amount of reaction solvent, which was 1 : 1 v/v water-ethyl lactate. Therefore, the discussion of solvent sustainability would have been better addressed towards the work-up solvent, which accounts for 92% of the total waste (excluding chromatography, which was also required). In total, 375 g of ethyl acetate were required for every gram of product (example of biphenyl, 93% yield).[109] It is common to overlook the impact of purification and analytical solvents despite their greater contribution to waste streams when compared to reaction solvents.

Conventional fossil-derived solvents are sometimes claimed to be sustainable, such as acetone,[111] and polyethylene glycols,[112] but without evidence. The same is true of bio-based solvents where renewable and sustainable can be confused. Limonene,[113] and 2-methyltetrahydrofuran,[114] have been subject to these claims. Neither of these solvents is without health and safety hazards (or eco-toxicity in the case of limonene). Similarly, furfuryl alcohol,[115] and tetrahydrofurfuryl alcohol,[116] have been used in so-called sustainable processes, but both are suspected of severe chronic toxicity, which suggests that they are not optimal solvents and their use may be curtailed by regulations.

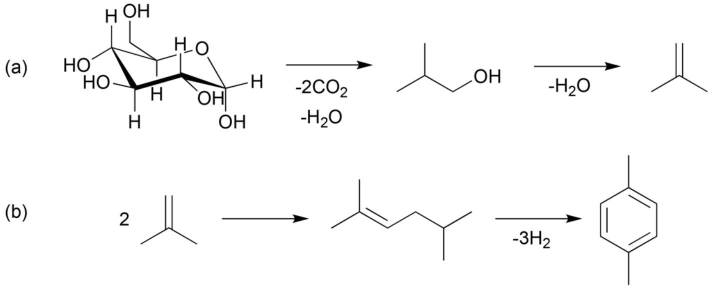
Organic carbonate solvents are known for their benign environmental, health and safety profile.[117] However, this does not translate to a sustainable solvent. Despite this, many authors have concluded that diethyl carbonate and cyclic carbonate solvents are sustainable.[118–120] The sustainability of a green solvent cannot be demonstrated only by proving it to work successfully in a reaction.

Glycerol is another low-toxicity, but also bio-based, solvent. It is assumed to be sustainable in an otherwise impressive review article about the solvent applications of glycerol.[121] The sustainability impact of glycerol is very much dependent on how the vegetable oil feedstock is produced and how it is disposed of, but the potential is there for a very acceptable environmental, social and economic impact. Glycerol can be modified for solvent uses by direct chemical transformation or as a mixture forming a deep eutectic solvent system. Glycerol derivatives can take a huge number of forms, with varying toxicity profiles and sustainability concerns.[122] Glycerol-based deep eutectic solvents have been described as representing "*a sustainable way of preparing non-toxic, tuneable solvent systems*",[123] but such a claim must be backed by evidence. Deep eutectic solvents (see Chapter 4, Section 4.6) are widely described as being a sustainable medium for reactions and extractions.[124–127] Many are formed from edible biomass, including sugars directly. The high viscosity of deep eutectic solvents presents technological challenges, and maintaining the dryness of these (usually) hygroscopic mixtures is energy demanding. Therefore, the sustainability of deep eutectic solvents is not above questioning just because they are made of renewable and non-toxic components.

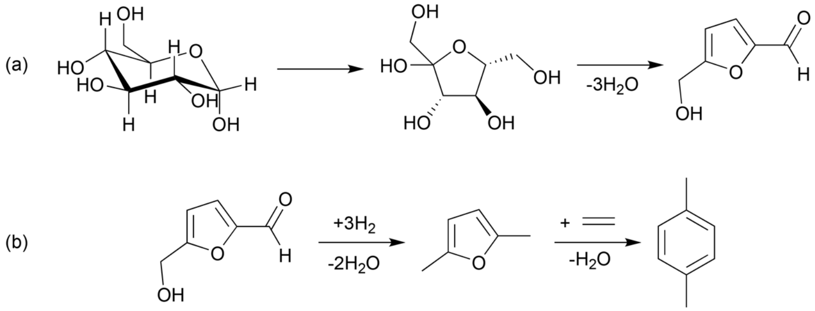
3.3.2 Solvent Assessment Case Studies

There are of course evaluations of solvent sustainability, or at least aspects of it, conducted in an appropriate manner. Several LCA studies of solvents exist, although these are very much restricted in scope to cradle-to-gate, biomass production and manufacturing issues. In cases where the product is the same (bio-ethanol and petrochemical ethanol for instance, or a comparison between different sources of biomass feedstocks) a valid judgement can be made just on the strength of a cradle-to-gate LCA. In this part of the book, LCA and technoeconomic assessments looking at just the production of solvents are considered. Summaries of other LCA evaluations addressing the application of solvents and solvent selection can be found elsewhere in the book, especially in Chapter 2 (*e.g.* replacing NMP,[128] in monomer synthesis), as can assessments of neoteric solvents in Chapter 4 (*e.g.* LCA of an ionic liquid,[106] cradle-to-grave). Broader economic-environmental assessments of bio-based platform molecules also provide relevant data, even if the complete synthesis of the solvent is not covered, just the production of intermediates.[129]

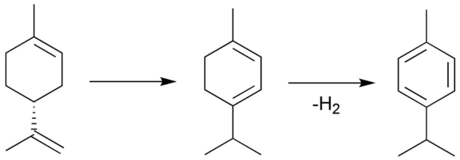
An interesting target for a bio-based chemical is *p*-xylene. Presently it is obtained from crude oil, but several routes from biomass are appealing, driven by a desire to make renewable polyethylene terephthalate plastic. A bio-based *p*-xylene chemical intermediate would also be a viable product for its traditional solvent applications. Two renewable manufacturing options are (1) the reaction of isobutene made from isobutanol (Scheme 3.1), and (2) a Diels–Alder cyclisation of fructose-derived 2,5-dimethylfuran with ethylene gas (Scheme 3.2).[130] Of these, a techno-economic analysis has shown that the latter is capable of producing the lower cost product, despite being less technologically developed at present.[131] The cost of biomass is a major factor, and in the case of the isobutene route, the fermentation procedure to make isobutanol is also responsible for the higher price of *p*-xylene calculated. The economics of the 2,5-dimethylfuran route could be improved by addressing the use of tetrahydrofuran as a solvent for the conversion of 5-(hydroxymethyl)furfural (HMF) into 2,5-dimethylfuran. An LCA of the process shown in Scheme 3.2 indicates that a wood-derived lignocellulose feedstock is environmentally superior to a starch feedstock.[132] Except for land use, lignocellulose was superior to starch in other indicators (including global warming potential, eutrophication, and the human toxicity of emissions). Tetrahydrofuran was responsible for 24% of the entire life cycle contribution, equal to that of the wood chip feedstock.



Scheme 3.1 The production of *p*-xylene by (a) the fermentation of glucose to isobutanol followed by dehydration, and (b) dimerisation and dehydrogenation.



Scheme 3.2 The production of *p*-xylene by (a) the conversion of glucose to fructose, followed by dehydration to HMF; (b) HMF is then reduced to 2,5-dimethylfuran and finally used in a Diels–Alder cycloaddition with ethylene.



Scheme 3.3 The catalytic isomerisation and dehydrogenation of *d*-limonene to yield *p*-cymene.

A lesser known member of the aromatic hydrocarbon solvent catalogue is *p*-cymene. It is possible to produce *p*-cymene from the limonene in citrus oils (Scheme 3.3).[133] A combined techno-economic and environmental assessment of the process of making *p*-cymene and pectin from waste orange peel showed how best to design the process.[134] Counterintuitively, it is not advantageous to co-produce electricity by gasification of the biomass residue, because of high capital costs. It was also shown that electricity generation significantly increases acidification potential due to liberated carbon monoxide and carbon dioxide. Small reductions in environmental impacts caused by the biomass residue if not used for electricity generation (human toxicity indicators, photochemical oxidation potential) does not compensate for this.

When using biomass for solvent production, the regionality of the feedstock should be considered for greater sustainability and less reliance on fossil fuels for transportation. Citrus plantations are concentrated in tropical regions, Brazil being the largest producer.[135] Therefore, there is an argument that the use of limonene and *p*-cymene as solvents, especially when substituting petrochemical solvents in low value applications such as degreasing, is best localised to the country of origin.[136] The environmental impact of the citrus oil production itself is quite favourable in many respects compared to hydrophobic fossil-derived solvents.[137] One area in which bio-based solvents will always appear unfavourable compared to petrochemical solvents is land use and biodiversity, which is true of limonene and downstream solvent products such as *p*-cymene.

The synthesis of 2-methyltetrahydrofuran (2-MeTHF) from different lignocellulosic feedstocks has been evaluated by LCA.[138] Khoo *et al.* analysed global warming potential, acidification, eutrophication, energy use, and land use mid-point indicators. For the three low-value feedstock options – Brazilian sugarcane bagasse (the pulp remaining after sugar extraction), USA corn stover (leaves and stalks), and Chinese rice straw – a mixed picture emerges (Figure 3.21). Sugarcane bagasse has the highest energy consumption demand. This includes transportation of the biomass as well as processing. Otherwise, sugarcane bagasse is very appealing as a feedstock. Corn stover, the popular feedstock option in practice, requires the most biomass for every kilogram of 2-MeTHF produced, and therefore has the highest land requirement, and has high acidification and eutrophication potentials. 2-Methyltetrahydrofuran made from rice straw is also highly damaging in terms of its acidification

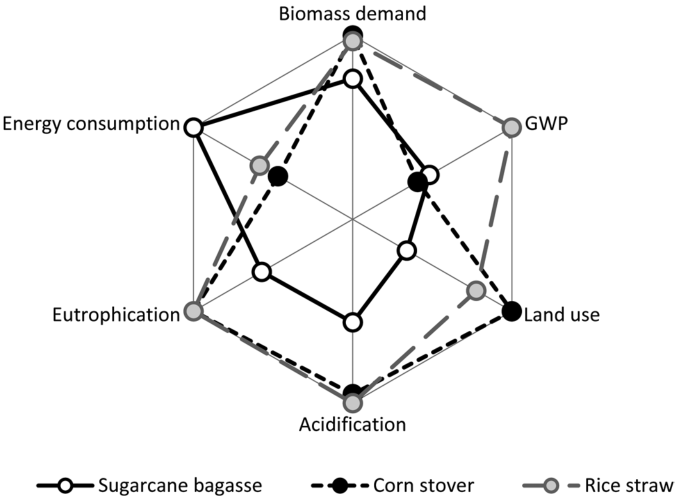
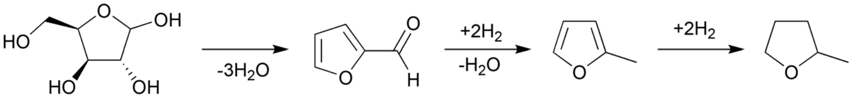


Figure 3.21 The relative environmental impact of 2-MeTHF produced from three different feedstocks, normalised to the highest value.

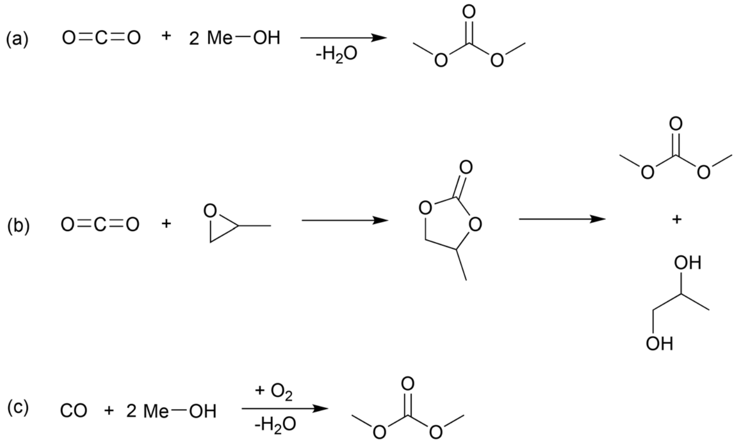


Scheme 3.4 The synthesis of 2-MeTHF from xylose (obtained by hydrolysing hemicellulose) *via* furfural.

and eutrophication potential, and has a particularly high global warming potential associated to it because rice farming releases significant amounts of N_2O and methane. The production of the biomass was the major factor behind the overall environmental impacts, much more so than the chemical transformation of hemicellulose into the end product (Scheme 3.4).

Alternatively, Slater *et al.* in their examination of 2-MeTHF production from corn stover (a commercialised process) use the benchmark of petrochemical tetrahydrofuran (THF).[139] The life cycle emissions of 2-MeTHF production are lower than those of THF production. Many indicators are more favourable in Slater's analysis because of the total allocation of environmental burdens onto corn for food production. Using this assumption, the impact of fertilisers and land use created by the production of 2-MeTHF from agricultural wastes was zero. This is fair considering the yield of corn is unchanged, and the use of corn stover (plant stalks and leaves) requires no additional farming practices.

The synthesis of *N*-methyl pyrrolidinone (NMP) from glutamic acid has been reported (see Chapter 4, Section 4.1.6).[140] Accompanying this work are environmental,[141] and technoeconomic assessments.[142] Compared to conventional NMP, the negative environmental impacts of bio-based NMP



Scheme 3.5 Three routes to dimethyl carbonate: (a) direct condensation of carbon dioxide and methanol; (b) methanolysis of propylene carbonate; (c) oxidative carbonylation of methanol.

production are lower for many indicators (acidification potential, eutrophication potential, global warming potential) but considerably higher for others (especially ozone layer depletion, but also photochemical oxidation potential and land use). The high ozone layer depletion potential is due to the formation of intermediate methyl bromide, which was assumed to be released as part of the assessment.[141] Thus the potential for environmental damage is high, but with proper safety procedures in place, and ideally a different alkylating agent, the actual environmental damage can be controlled to much lower levels.

An abbreviated economic, social and environmental assessment of dimethyl carbonate (DMC) production has been used to evaluate three synthetic routes (Scheme 3.5).[143] A normalised impact registered across ten indicators, as given in Figure 3.22, shows that route (a) and route (b) have many advantages over the commercialised route (c). Route (b) is a modification of another commercial process,[144] using an ionic liquid solvent.[145] However the indicators used are inadequate to call this a sustainability assessment. Instead, the methodology is helpful to narrow down manufacturing process options, after which full LCA and technoeconomic assessments will be needed.

Whereas some techno-economic assessments indicate that bio-based products are competitive, as has been said of ethyl acetate,[146] biotechnology, despite being at an advanced stage of commercialisation, hampers bio-based product manufacturing with low and variable yields.[147] Separation of products from the aqueous fermentation broth is another issue. 1-Butanol and isobutanol are desirable targets to serve the fuel and commodity chemical markets, but also find use as solvents. Butanol manufacturing from sugarcane can be conducted in a variety of ways, diverting the feedstock into acetone,

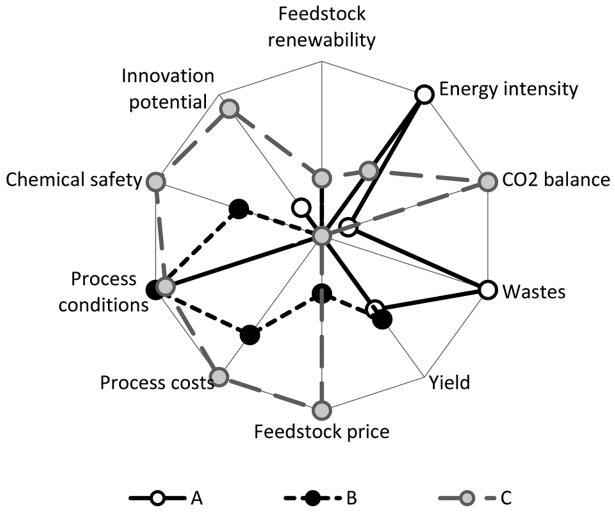


Figure 3.22 Normalised impacts of dimethyl carbonate synthesis across social, economic and environmental indicators.

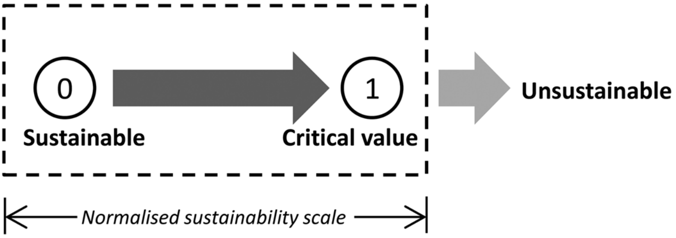
butanol, ethanol (ABE fermentation), and sugar production in different proportions. There is also the option to use wild or genetically modified microorganisms. Regardless, the environmental impact of 1-butanol production is not greatly affected by these choices within a cradle-to-gate scope.[148] The amount of fugitive ethanol emission does however influence the photochemical oxidation potential quite significantly. Isobutanol is produced from saccharified corn stover instead of 1-butanol by using *E. coli* instead of *Clostridia* bacteria as the fermenting microorganism.[149,150] Given that certain fermentation yields are achieved, the process becomes economically feasible.[151] The production of butanols is more energy intensive than it is for bio-ethanol given the higher boiling points of 1-butanol and isobutanol, but the life cycle emissions are reasonably similar.

3.3.3 Biorefinery Case Studies

A biorefinery is the operational infrastructure that converts biomass into products.[152] Just as biomass production is subject to sustainability criteria (in the form of certification, Section 3.2), biorefineries must be operated to a certain standard of sustainability, so ideally the feedstock and the process should both be evaluated, as is true of cradle-to-gate life cycle assessments. Biorefineries are replacing oil refineries, but the technology involved is different, requiring fermentation and chemical reduction, whereas oil refineries operate gas phase separations and oxidation chemistry among other chemical processes that add functionality to hydrocarbons.[153] This is due to the nature of the feedstocks they convert. Generally speaking, the transition to biomass as a feedstock does have long-term advantages,[154] but it is important to remember that the feedstock has a major impact on sustainability, often more so than the processes that convert it into functional chemicals.[155] Intensification of biomass production is needed, but this cannot be achieved by neglecting the protection of diverse ecosystems and replacing them with monoculture farming practices. This is why comprehensive certification schemes are used to dictate the terms on which biomass (chiefly for biofuels) is produced.

A biorefinery must embrace the large variety of different feedstocks available. The biomass needed for bio-based solvent synthesis can either be produced directly for use as a chemical feedstock or obtained as a waste or by-product of other industries, as already alluded to in mentions of glycerol production earlier in this chapter, for example. One might automatically say that valorisation of a waste product is superior given the issues with biomass production (land use where monoculture farming destroys (directly or indirectly) biodiverse ecosystems, the impact of agrochemicals on soil and water, *etc*.).[156] This is not necessarily true and must be proven with tools such as LCA. Taking bio-ethanol as an example, what has been found is that production of bioethanol from food waste has an advantageously negative net balance in carbon dioxide emissions when the alternative of landfill is factored in.[157] Conversely, bioethanol production from low fibre quality waste paper can have significant environmental impacts that must prompt a re-evaluation of the process.[158] Lignocellulosic bioethanol is (in theory) less damaging than first generation bioethanol, but the additional pre-treatments of the biomass have a large impact on the environmental consequences.[159] These findings should be contrasted against arguments in favour of first generation bioethanol, meaning that made from food-grade carbohydrate. A 25% decrease in environmental impact indicators is achievable just by implementing process optimisation technologies that are now routine in new (first generation) bioethanol plants.[160] This shows that the processes chosen in order to conduct the synthesis of bio-based solvents (for example) remain important. It is also true that first generation bio-ethanol production provides more jobs to communities, according to a recent social-LCA on a Brazilian case study.[161] This should be balanced against the advantages of a second generation (cellulosic) bio-ethanol supply chain, where on average the jobs created are better paid and lower risk, and more accessible to women.

To specifically address the sustainability of biorefineries, El-Halwagi *et al.* have produced a techno-economic assessment that introduces safety considerations in the form of risk metrics.[162] This is part of the design decision making process, where the balance between costs and safety for the correct choice of equipment is modelled to assess the risks involved. The location of a biorefinery is also important, because its geographical position relative to farms, storage facilities, worker communities, and product markets dictates the success of the bio-based product supply chain and to some degree its environmental impact.[163,164]



Environmental load

Indicator: Reduction of baseline emissions.

Scale: (0) The reduction of baseline emissions in the biorefinery (relative to a reference system) is infinitely greater than the defined reductions target; (1) The reduction of baseline emissions by the biorefinery is equal to the reductions target.

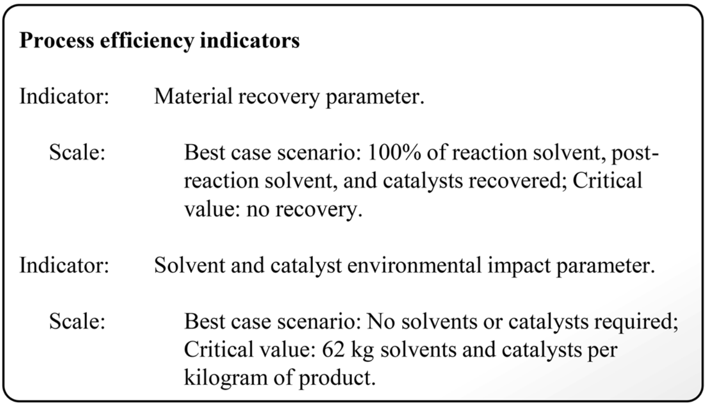
Indicator: Sustainable land use.

Scale: (0) No net land-use change is needed to operate the biorefinery; (1) The land-use change caused by the biorefinery's operation is at the limit of causing a net biodiversity loss.

Figure 3.23 An example of a normalised sustainability indicator scale with two representative environmental sustainability indicators provided.

A framework for evaluating integrated (multi-product) biorefineries with indicators has been proposed by Sacramento-Rivero.[165] The results are normalised so that each indicator provides a comparative scale. This means that the outcome of mid-point indicators can be evaluated on a fair basis without losing information as a combined end-point indicator. On the proposed scale, zero impact is sustainable, and 1 is the point of "*systemic collapse*".[165] Therefore there is no obligation to weight the different indicators against one another. If one indicator exceeds the critical impact value, the biorefinery operation is unsustainable. Five principle areas are categorised into feedstock, process, products, environment, and corporate responsibility. These themes are represented by 14 indicators in total (Figure 3.23). With the necessary data, the results of the sustainability assessment can be represented as a radar/spider diagram in the same way as Figure 3.21,[138] and Figure 3.22.[143] In an update to his previous work, Sacramento-Rivero *et al.* provide an evaluation of a conceptual lignocellulosic (switchgrass feedstock) biorefinery using this methodology.[166] A similar system by which to evaluate biorefinery processes (economic, environmental, risk) has been developed by Patel *et al.*[167]

More generally, a tool for designing sustainable chemical processes has been developed by Ruiz-Mercado, Gonzalez, and Smith ('GREENSCOPE').[168–170]



Process efficiency indicators

Indicator: Material recovery parameter.

Scale: Best case scenario: 100% of reaction solvent, post-reaction solvent, and catalysts recovered; Critical value: no recovery.

Indicator: Solvent and catalyst environmental impact parameter.

Scale: Best case scenario: No solvents or catalysts required; Critical value: 62 kg solvents and catalysts per kilogram of product.

Figure 3.24 An example of a normalised sustainability indicator scale (efficiency indicators relevant to solvent use).

In it, indicators of sustainability are quantified by their position on a numerical range defining the ideal and worst tolerable scenarios in the same way as Sacramento-Rivero.[165] Sixty-six environmental indicators, 26 efficiency indicators, 33 economic indicators, and 15 energy indicators were developed in total. Examples are found in Figure 3.24.[168] This goes to demonstrate how advanced and elaborate these schemes have become.

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CHAPTER 4

Alternative Solvents

4.1 Types of Bio-Based Solvent

Bio-based solvents in the first instance are only defined by the origin of the material they are made of. Therefore, a neoteric solvent might be bio-based, but here only conventional liquid solvents are considered in the following discussion on aqueous solvents (Section 4.4), supercritical fluids (Section 4.5), and ionic liquids and deep eutectic solvents (Section 4.6). Feedstock options for the production of bio-based solvents are diverse, with the various forms and components of lignocellulose being a rich source of bio-based solvents, as are sugars and starches, vegetable oils and essential oils. It is also possible to categorise bio-based solvents according to how they are made (fermentation, extraction, thermochemical processes, anaerobic digestion, *etc.*), or by what is made (alcohols, esters, ethers, *etc.*). Different bio-based solvents will be presented in order of feedstock, and the most notable commercial examples supplemented with data sheets in Chapter 6 with an emphasis on environmental, health, and safety (greenness) data. Information relating to the sustainability of the feedstock and the manufacturing process is also provided where available (see Chapter 6). For comprehensive physicochemical data please refer to other texts, for example Smallwood's 'Handbook of Organic Solvent Properties',[1] and 'Solvent Effects in Chemistry'.[2] For further information on the biomass feedstocks and their conversion into functional chemicals, specialist books are available.[3,4] The discussion in this part of the book will introduce academic examples of bio-based solvents that may find industrial applications in the future. The transition from discovery to commercialisation is exemplified with a case study on dihydrolevoglucosenone (Section 4.1.2.1).

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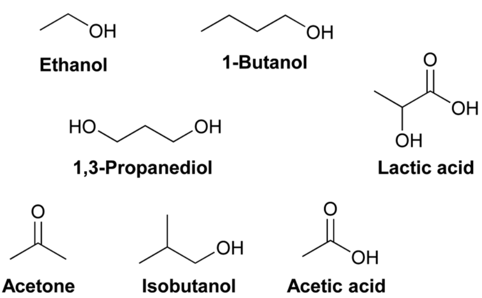
4.1.1 Carbohydrate-Derived Solvents Produced Using Biotechnology

In a maturing industrial sector, bio-based chemicals are being produced by revisiting old technology. Fermentation of a sugar or starch feedstock will typically produce ethanol, although this depends on the microorganism used. The annual bio-ethanol market is truly huge, growing from 10 billion litres in the 1970's to something closer to 80 billion litres nowadays.[5] This growth is almost entirely fuel driven, to the extent that it distorts estimates of the bio-based solvent market.[6] Important producers are Brazil (sugarcane), USA (corn starch), China (corn and wheat),[7] and Europe (sugar beet). Use of bio-ethanol as a solvent is complemented by the many solvent products made from ethanol, including esters and ethers.[8] Attention is now turning to non-food competitive lignocellulose feedstocks for bio-ethanol production.[9] A few examples of cellulosic bio-ethanol plants utilising corn stover now exist,[10,11] despite other projects being halted.[12,13]

Other fermentation processes yield different small molecule products. These include acetic acid, 1-butanol and 1,3-propanediol (Scheme 4.1),[14] all of which have been commercialised (see Chapter 6 for details). Lactic acid is also an example of a fermentation product, primarily made for polylactic acid manufacture.[15] As an additional use, a wide range of chemistries can be conducted in lactic acid as the solvent,[16] or it can be esterified to make a lactate ester.[17] Fermentation to give alkenes, either directly using genetically modified bacteria or by dehydrating conventional alcohol products, means a wide range of potential bio-based solvent products can in theory be obtained from the familiar base chemicals currently produced by the petrochemical industry.[18] Alternatively, new synthetic procedures can be used to access familiar end-products. There is some interest in alternative routes to acetonitrile (and replacements for acetonitrile). Acetonitrile is presently obtained as a by-product of acrylonitrile manufacturing.[19] This usually provides satisfactory volumes of acetonitrile, except when the polymer industry is scaled back, as was the case in this millennium's global financial crisis.[20] Bio-ethanol can be used to make acetonitrile *via* ethylamine,[21] with bio-based ethylamine now commercially available.[22]



Scheme 4.1 A selection of fermentation products that can be applied as solvents.

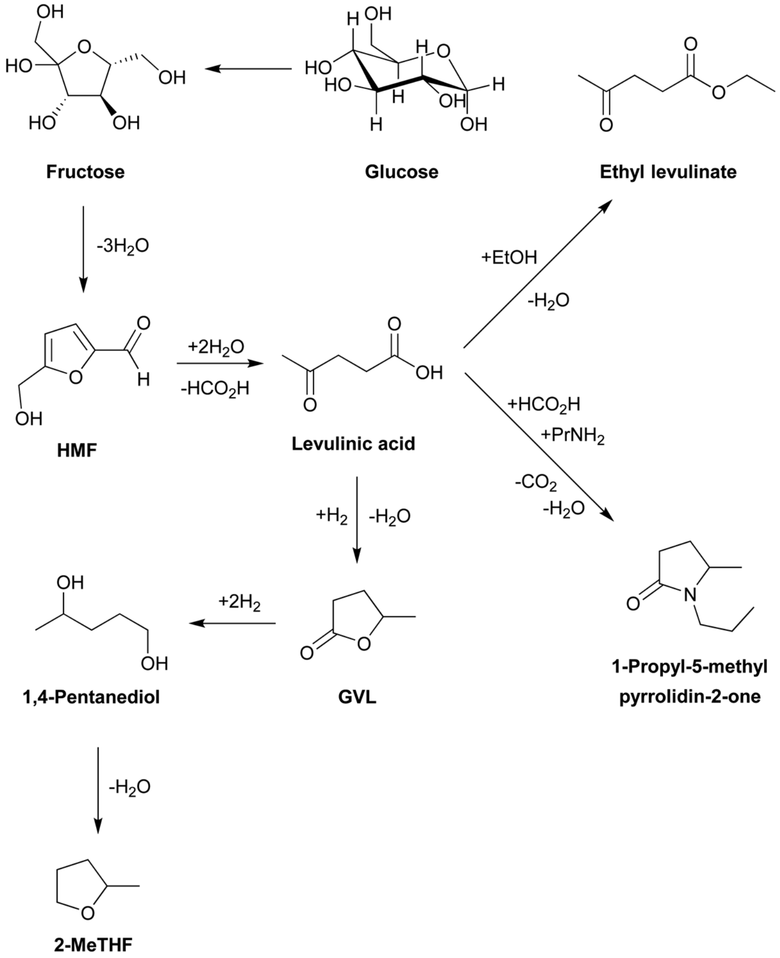
As the status of fermentation technology improves, it has become possible to directly produce isobutene from sugars by adapting the isobutanol metabolic pathway of bacteria, for example.[23–25] Bio-based isobutene could be used to make *t*-butyl ethers alongside plastics and fuels. 'Myralene™-10' is the key ingredient of a bio-based solvent cleaning formulation,[26] made by hydrogenating *β*-farnesene.[27] *β*-farnesene is an olefinic fermentation product made from sugar by genetically modified yeast,[28] or from carbon dioxide by genetically modified bacteria.[29]

Instead of fermentation, the anaerobic digestion of otherwise low value materials facilitates a way of processing renewably sourced feedstocks, ideally wastes, in such a way as to contribute to the existing commodity chemical production industry through the synthesis of methane. Methane as natural gas is the precursor to syngas (carbon monoxide and hydrogen) and in turn this is used to make methanol commercially.[30] Bio-methanol production equates to 0.34 million tonnes per year, less than 1% of the total methanol production.[31] This is not only sourced from anaerobic digestion, but from the traditional gasification of wood (methanol being 'wood alcohol'), paper and pulp liquors, and glycerol and carbon dioxide precursors.[32] Syngas and methanol obtained from renewable resources allow the production of several bio-based solvents, including acetic acid and therefore esters made from acetic acid or indeed methanol.[8]

4.1.2 Carbohydrate-Derived Solvents Produced Using Thermochemical Processes

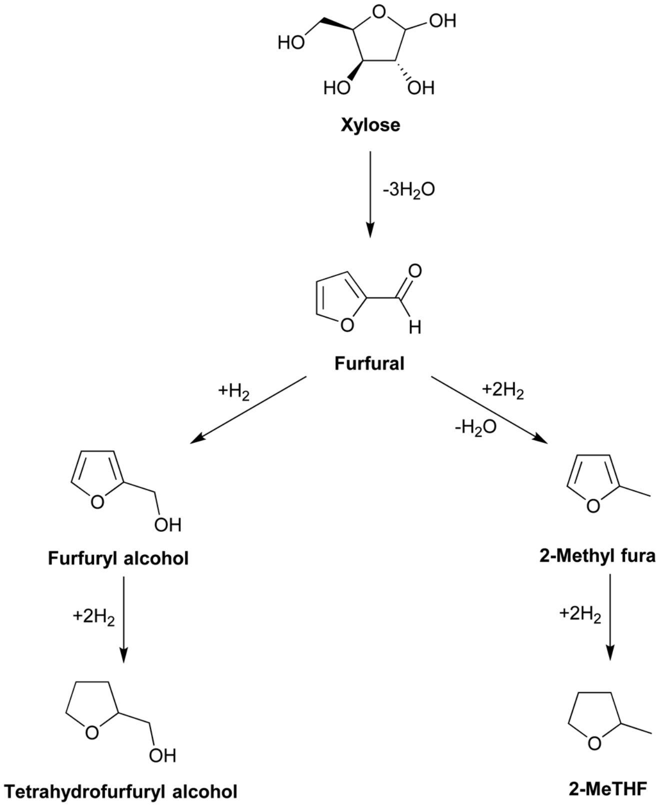
Generally, the chemical functionalities contained in bio-based solvents are the same as conventional solvents. However, the chemical basis of biomass feedstocks is different to that of crude oil fractions, and so many of the easily obtainable small molecules that could be considered solvents or precursors to solvents that can be derived from biomass will not be equivalent to conventional solvents. This is evident when thermochemical processes are used to convert biomass instead of biological approaches. For example, while bio-ethanol is indistinct from petrochemical ethanol, 2-methyltetrahydrofuran (2-MeTHF) is not structurally identical to the solvent tetrahydrofuran (THF) it usually replaces,[33,34] and the analogy is not necessarily this clear. *γ*-Valerolactone (GVL) can substitute reprotoxic amide solvents for example.[35,36] Structurally equivalent solvents can be referred to as orthodox or conventional bio-based solvents. The phrase 'neoteric solvent' describes structurally novel solvents, although it is most frequently used to describe ionic liquids and other types of unusual solvents.

Several unconventional bio-based solvents are formed from the thermochemical dehydration and hydrogenation of biomass. The most relevant intermediate is 5-(hydroxymethyl)furfural (HMF), made by the dehydration of fructose. From HMF, levulinic acid (and hence its esters), 2-MeTHF and GVL can be made (Scheme 4.2). Amide solvents are also possible with the introduction of an amine reactant.[37] Levulinic acid ketals are made by Segetis (acquired by GFBiochemicals),[38,39] for the plasticiser market, demonstrating another avenue of chemistry also applicable to the production of solvents.[40]



Scheme 4.2 Solvents made from levulinic acid.

The more common way to make 2-MeTHF (from furfural) was shown in Chapter 3, Section 3.3.2. Furfural, obtained from pentose sugars (and therefore also hemicellulose) is analogous to HMF obtained from hexose sugars (and therefore also cellulose). A range of furan solvents in addition to 2-MeTHF can be made from furfural (Scheme 4.3), and this is the preferred manufacturing route. 2-Methyl tetrahydrofuran is now regularly used in a variety of synthetic transformations,[34] including polymer synthesis.[41] Aqueous tetrahydrofurfuryl alcohol has been shown to work as an effective solvent for transformations of HMF.[42] Despite their aromaticity, furan-derived solvents are not usually applied as substitutes for aromatic hydrocarbon solvents. To obtain the conventional benzene, toluene, and xylene solvents from biomass, it is possible to perform catalytic fast pyrolysis of cellulose,[43,44] or aqueous phase reforming of sugars.[45,46]

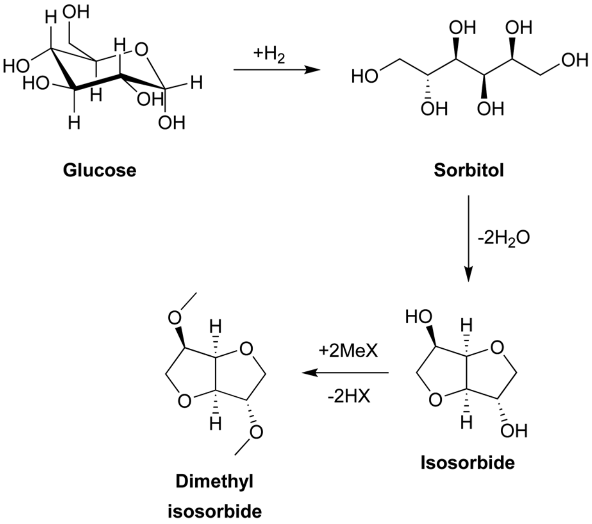


Scheme 4.3 Solvents made from furfural.

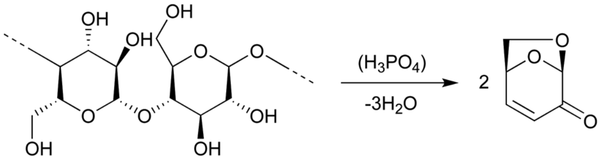
Other platform molecules to consider are levoglucosenone and isosorbide. The former is discussed at length in the following case study (Section 4.1.2.1). Dimethyl isosorbide is an obvious solvent product to make from the isosorbide intermediate (Scheme 4.4). It's uses are quite limited at present, but the isosorbide platform molecule has lots of promise in a number of applications beyond solvents.[47] Sorbitol is made from glucose by hydrogenation.[48,49] It is an established product, used widely in food and cosmetic formulations. An acid catalysed cyclisation of sorbitol affords the bicyclic diol isosorbide.[50] It is also possible to use cellulose as the feedstock and perform the reaction to isosorbide directly in one pot.[51] Ideally the finally transformation to dimethyl isosorbide is performed with a green methylating agent.[52] Dimethyl isosorbide is a strongly dipolar solvent, akin to acetonitrile in terms of polarity.[53]

4.1.2.1 Cyrene (Circa Group)

The paper and pulp industry is looking to develop alternative wood-based products as paper use in traditional markets continues to decrease.[54] Although overall demand for paper and cardboard for packaging is growing,



Scheme 4.4 The synthesis of dimethyl isosorbide.



Scheme 4.5 The synthesis of levoglucosenone from cellulose.

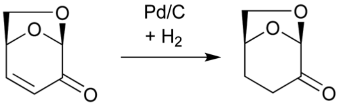
the output of western producers is declining.[55] Converting pulp and paper mills into integrated biorefineries for paper and chemical production makes use of the existing biomass sources, infrastructure, and supply chain.[56] Niche but high value products are an obvious target,[57] valorising the waste streams of the paper industry. Circa is an Australian company that seeks to use abundant cellulosic wastes to produce fine chemicals.[58] The initial intention of the company was to convert the carbohydrate in woody biomass into levulinic acid. However, in what became their now patented Furacell™ process, instead Circa came across a method of producing levoglucosenone (Scheme 4.5).[59] The Furacell™ process is somewhat 'feedstock-agnostic', meaning the feedstock requirement is not specific to a single resource. Different cellulose rich (>30%) sources of biomass can be used, with sawdust and waste paper obvious candidates given the context of this operation.[60]

The Furacell™ process has now been scaled-up to a 50 tonne per year demonstration plant, associated with a paper mill in Tasmania, Australia.[61,62] The conversion of cellulose to levoglucosenone requires phosphoric acid at a temperature of 430 °C, resulting in the desired dehydration reaction. Intuitively this would be speculated to occur *via* levoglucosan, but this may not be the case because of the huge number of possible intermediates.[63] Nevertheless the process is surprisingly selective, although a char is also produced. This carbonaceous char can be used advantageously to power the Furacell™ process, resulting in an overall (slight) net gain in renewable energy.

The Furacell™ process requires the feedstock to be shredded to millimetre scale dimensions, and the cellulose must be swollen by using a solvent. Although the application of ionic liquids for this purpose is covered in the patent,[59] sulpholane is preferred. The concentration of phosphoric acid needed is typically 2–3% by weight of solvent. To distribute the catalyst and adequately swell the entirety of the raw material, temperatures of 150–170 °C are used when the catalyst solution is applied. Mechanical processes crush and pulp the swollen biomass material. The actual reaction occurs in an extruder at 430 °C, over a duration of 5 minutes. The cellulose component of the feedstock produces levoglucosenone in up to 40% of the theoretical molar yield, along with traces of HMF and levulinic acid. The hemicellulose decomposes into furfural, but the major by-product is the aforementioned char, to which lignin decomposition is the major contributor. The volatile products of the reaction are separated from the solid char, and fractional distillation isolates the levoglucosenone (>90% technical grade or greater).[59]

The relevance of levoglucosenone to solvents is not obvious, given its unusual structure. Levoglucosenone is a high value product, previously only available in very limited quantities. The interesting combination of functionality and fused rings opens up many possibilities in the fine chemical market. At the same time the larger and more stable demand provided by the solvent sector is an advantageous market to access given the production scale is available. Because levoglucosenone can be synthesised from low value feedstocks such as sawdust, it is possible to create novel solvents on a price scale that is appropriate for this type of product.

Circa produce two high value speciality chemicals from levoglucosenone, dairy lactone and 5-hydroxymethyl-2(5H)-furanone. A third product in their portfolio has the brand name Cyrene™. This is a bio-based solvent, and is the hydrogenated equivalent of levoglucosenone (Scheme 4.6). Levoglucosenone is not marketed as a solvent because of its reactive double bond, which is conveniently removed by hydrogenation in the procedure to give dihydrolevoglucosenone (Cyrene™). The first reports of dihydrolevoglucosenone being synthesised from levoglucosenone using elemental hydrogen for the reduction did not appear until the 1990's,[64] despite a strong precedent for the chemistry of levoglucosenone established in the 1970's.[65] Previously diphenyl silane (Ph_2SiH_2) had been used for the hydrogenation of



Scheme 4.6 The synthesis of Cyrene™.

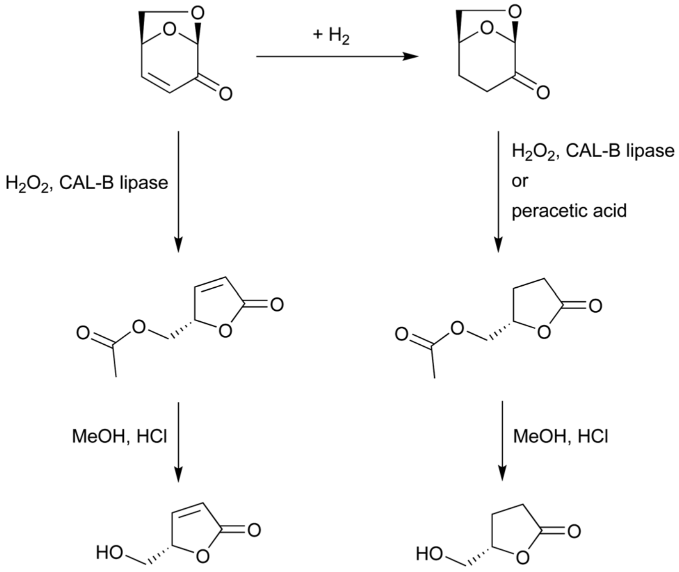
levoglucosenone.[66] The catalyst is generally palladium, either supported (*e.g.* palladium on carbon) or in a homogeneous form. Recent methods have used ethyl acetate as a solvent,[67,68] although the solvent-less reaction is equally viable at elevated hydrogen pressures.[69]

It is most important that the sustainability of the manufacturing process of Cyrene™ is scrutinised, and improvements made to achieve a sustainable process. The Furacell™ process is designed to operate using different feedstocks, including wastes, depending on what is available. The sulpholane solvent is recycled and used again. Obviously it is not viable to expend a greater volume of solvent than what is ultimately produced in the form of Cyrene™. The char co-product has a calorific value that meets the energy demand for the process. The choice of phosphoric acid was decided on the primary basis that it is a strong, dehydrating acid, but also it means the char can be used as a fertiliser. According to the patent describing the Furacell™ process, use of the char as a carbon sequestering agent is also possible.[59] More information about the cradle-to-gate life cycle of Cyrene™ can be found in Chapter 6. The fact that the demonstration plant is limited in size, and resides in an existing pulp and paper facility neighbouring a managed forest is helpful in limiting its environmental impact and achieving the aims of sustainability. On the other hand, the present 50 tonne annual scale might be an issue for customers, who in any major industry look to the availability of the solvent in terms of volume and the option of alternative suppliers. The supply of levoglucosenone, and therefore its downstream products, is not entirely limited to Circa products, but for the moment this is the most affordable source.

The sustainability of the subsequent hydrogenation of levoglucosenone is more questionable. Petrochemical hydrogen and palladium catalysts are used at present, and also an additional solvent is sometimes used. Of the three, the use of solvent is the most easily rectified. Currently ethyl acetate is favoured as the solvent, at least in academic lab-scale syntheses. It is possible to make bio-based ethyl acetate, but ultimately (unless safety concerns determine otherwise) a solvent-less system is much more preferable. At near-ambient pressures, the solvent mediated hydrogenation of levoglucosenone (Scheme 4.6) proceeds at a greater rate than the solvent-free alternative. The synthesis of Cyrene™ was reported as complete after 4 days (without heating) in a small amount of solvent (the molar ratio of ethyl acetate to levoglucosenone was 3 : 1) requiring 0.5 mol% of palladium (in the form of 10% Pd/C) as a catalyst.[69] The solvent-less equivalent took 8 days. The reason the diluted reaction is faster could be down to two factors. Firstly, the hydrogen gas solubility is quite sensitive to the medium, and ethyl acetate may be a better solvent for hydrogen gas than levoglucosenone. Secondly, the viscosity of levoglucosenone may negatively impact the reaction, which of course involves a heterogeneous catalyst and can be subject to diffusion limited kinetics. Both procedures take too long as batch reactions to be commercially viable. Increasing the hydrogen pressure up to 80 bar results in a faster reaction in the solvent-less system (less than two hours), while the reaction in an ethyl acetate solution can still take as long as 2 days to complete. The catalyst is removed by filtration through Celite®.

Addressing the choice of catalyst, patented procedures for the hydrogenation of levoglucosenone exist from other areas of research and development. In one example from Du Pont, 1,6-hexanediol is made by hydrogenating levoglucosenone.[70] Dihydrolevoglucosenone is a by-product of this process, catalysed by supported platinum/tungsten, nickel/tungsten, rhodium/rhenium, or palladium. In another patent, assigned to Japan Tobacco Inc., the hydrogenation of levoglucosenone as an intermediate in the synthesis of 4-hydroxymethyl-γ-butyrolactone (the saturated equivalent to the olefinic 5-hydroxymethyl-2(5H)-furanone) is described.[71] This transformation is also executed in the enzymatic synthesis by Flourat *et al.* (Scheme 4.7).[68] The hydrogenation uses Pd/C and also requires ethyl acetate as a solvent.[71] Alterative conditions given include platinum oxide in diethyl ether, palladium supported on barium sulphate in 1,4-dioxane, and Raney nickel in ethanol. Nickel and the other metals mentioned are not regarded as any more sustainable than palladium (in terms of consumption *versus* natural reserves remaining),[72] and so a lot remains to be achieved in this deceptively innocent looking hydrogenation.

The future of sustainable hydrogenation is likely to combine solvent-less conditions with hydrogen produced through the electrolysis of water.[73,74] This avoids fossil-derived hydrogen gas, and the need to keep large amounts of H_2 stored on site at any one time. Water is stored instead and split into oxygen and hydrogen as needed. The problem of rapidly depleting catalytic metals is best resolved in the short term by improved systems employing flow chemistry over fixed bed reactors.[75] The woeful recycling rates of many metal catalysts is outside of the scope of this book, but needs to be rectified to sustain chemistry that uses rare metals.



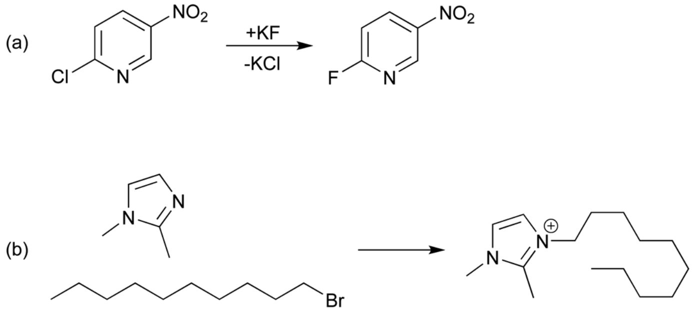
Scheme 4.7 Lactone derivatives of levoglucosenone and dihydrolevoglucosenone.

Dihydrolevoglucosenone, Cyrene™, was first reported as a solvent in 2014.[69] The initial work consisted of a short screening of typical organic chemistry reactions. This was executed in a context that was strongly determined by the properties of Cyrene™, and its limitations of course. Firstly, although the hydrogenation that creates Cyrene™ is performed in order to remove the reactive alkene functionality, the ketone group remains. Carbonyl addition by nucleophiles is a labile reaction, as evidenced by the limited role of ketones and esters as reaction solvents in synthetic organic chemistry. The boiling point of Cyrene™ is very high, above 200 °C. This is extremely limiting for applications where removal by distillation is required, although the product is distilled in the manufacture of Cyrene™, which demonstrates it is possible under vacuum.

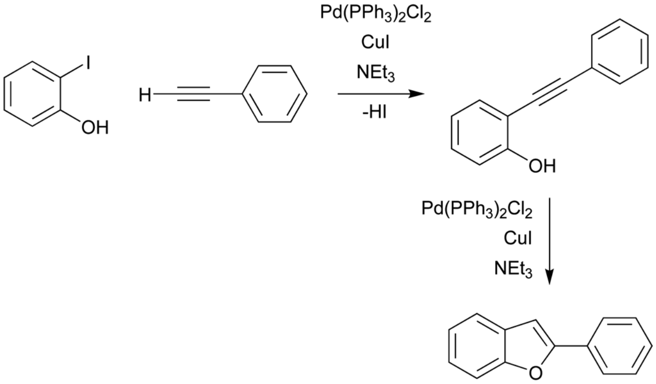
The polarity of Cyrene™ is surprising. If Cyrene™ was as polar as typical ethers or ketones, it would not possess enough advantages to be considered a worthwhile replacement for the reasonably benign solvents of this type, such as acetone or THF. However, the manner in which the acetal and ketone functionalities in Cyrene™ are arranged, and also because of its cyclic structure, Cyrene™ is highly dipolar, more akin to *N*-methyl pyrrolidinone (NMP). It is also considered aprotic, which is again surprising when considering the acidic proton site of the acetal group in Cyrene™. These polarity measurements were derived from the UV response of solvatochromic dyes in solution, and placed on the Kamlet–Abboud–Taft scales of solvent polarity. It is true that the measurement of polarity in this way is potentially susceptible to a bias created by particular solvents, as different solvatochromic dyes lead to different polarity measurements, but generally the Kamlet–Abboud–Taft polarity scales are an excellent basis for describing solvent polarity as expressed in terms of solvent–solute interactions, and also for creating quantitative free energy relationships that describe reaction kinetics as a function of solvent polarity (see Chapter 5, Section 5.3.1.2). When Cyrene™ was first reported as a solvent, it was exactly this sort of linear solvation energy relationship that the authors used to demonstrate the effectiveness of Cyrene™ compared to conventional solvents.

Cyrene™ has been classed as a dipolar aprotic solvent of the sort typically represented by reprotoxic amide solvents. Here lies the opportunity for Cyrene™ and other new solvent products to access key markets in the short term, replacing solvents that have caught the attention of regulatory agencies. Cyrene™ is an ether, but as illustrative of many new ether solvents, its peroxide forming potential is much less than the classic ether solvents (*e.g.* THF and diethyl ether: both possess the European Hazard Statement EUH019 indicating a risk of peroxide formation). A more immediate problem with conventional ether solvents is a low flash point. Conversely, the flash point of Cyrene™ is 108 °C.

Cyrene™ has been tested in two types of nucleophilic substitution reaction, a typical application of NMP and other highly dipolar aprotic solvents (Scheme 4.8).[69] The studies also help to pinpoint the stability of Cyrene™, which is susceptible to degradation in the presence of nucleophiles.



Scheme 4.8 Model reactions for Cyrene™ solvent screening. (a) Nucleophilic fluorination of 2-chloro-5-nitropyridine; (b) the Menschutkin reaction of 1,2-dimethylimidazole and 1-bromodecane.



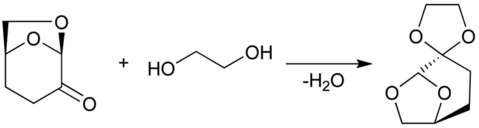
Scheme 4.9 Extended Sonogashira cross-coupling with Cacchi-type annulation.

A fluorination case study was not a success for Cyrene™. Although the solvent seemed to resist the attack of fluoride in the transformation of the activated substrate 2-chloro-5-nitropyridine into 2-fluoro-5-nitropyridine, the rate of reaction was slow. Admittedly the result in NMP was similarly poor, with only DMSO excelling under the conditions used. Nucleophilic fluorination remains a challenging case study for the demonstration of new, polar solvents. The other reaction was the alkylation of 1,2-dimethylimidazole, a weak nucleophile. Cyrene™ facilitated the synthesis of 1-decyl-2,3-dimethylimidazolium bromide, with rates of reaction comparable to the established solvents for this type of reaction. These two reactions are excellent benchmarks for the testing of new dipolar aprotic solvents, given their highly demanding and sensitive dependence on solvent dipolarity.

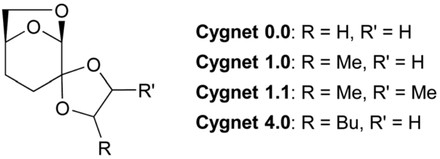
Wilson *et al.* have also explored the potential of Cyrene™ as a solvent in Sonogashira cross-coupling reactions, also modified to additionally perform a Cacchi-type annulation (Scheme 4.9).[76] The yield of the example in Scheme 4.9 was 89% in Cyrene™. The yields for the transformation were similar when compared to *N*,*N*-dimethyl formamide (DMF) as a solvent. This study also contains a helpful demonstration of the stability of Cyrene™ in the presence of a base. Amine bases like diisopropyl ethyl amine and triethyl amine are inert to reaction with Cyrene™, but mineral bases in particular cause decomposition.[76] This is a welcome investigation that contributes towards defining the operational scope of Cyrene™ when applied as a replacement for amide solvents. It reaffirms the need for a number of replacement dipolar aprotic solvents to cover the range of requirements currently served by DMF and other reprotoxic solvents.

Although the full potential of Cyrene™ in organic synthesis is yet to be fully realised, it is probably more advanced processes that will find the greatest mutual benefit. A recent patent includes Cyrene™ as a potential co-solvent for the preparation of polymers where replacements for NMP are sought.[77] Also in the recent literature is an example of Cyrene™ being used as a solvent to synthesise metal–organic frameworks (MOFs).[78] Once again it is DMF that is being replaced. Five MOFs were made. One issue occurred due to the heating of basic solutions of Cyrene™. As reported previously,[76] bases have the potential to decompose Cyrene™. In this instance an aldol condensation product was isolated, proving that the base initiated the dimerisation of Cyrene™.[78]

There is potential to expand the class of levoglucosenone-derived solvents through simple, high yielding reactions. One example converts the ketone moiety of Cyrene™ into a ketal by reaction with ethylene glycol (Scheme 4.10).[79] The resulting solvent signifies a new class of molecules, identified by the informal name ‘Cygnet’. Each Cygnet has a numerical designation based on the [4,5] substitution pattern of the dioxolane ring, which depends on the choice of glycol reactant (Scheme 4.11). Cygnet 0.0 provides superior results compared to Cyrene™ in the fluorination reaction shown in Scheme 4.8, as well as a model Heck cross-coupling reaction between iodobenzene and methyl acrylate.



Scheme 4.10 The synthesis of Cygnet 0.0 from Cyrene™.



Scheme 4.11 The nomenclature of the levoglucosenone-derived Cygnet molecules.

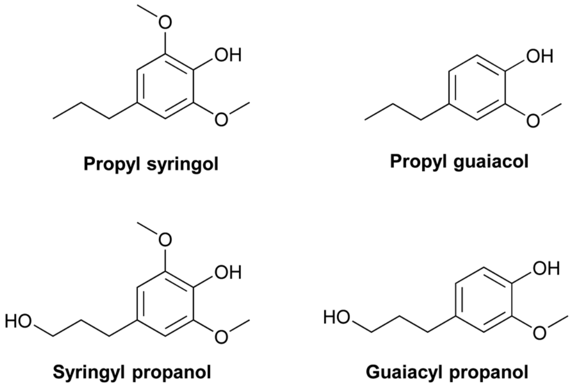
4.1.3 Lignin-Derived Solvents

Although it is possible to make bio-based aromatic hydrocarbons by synthetic routes,[43,45] the more obvious option is to depolymerise the lignin in woody biomass, which is already rich in aromatic structures. Aqueous hydrogenolysis causes depolymerisation of lignin, yielding 4 aromatic small molecules with 60% efficiency based on the maximum feasible output.[80] Syringyl propanol and guaiacyl propanol are water soluble and can be extracted to leave behind a 4 : 1 mixture of propyl syringol and propyl guaiacol (Scheme 4.12). The final binary solvent system was able to act as an extraction solvent for processing of the carbohydrate fraction of the biomass.[80]

Alternatively, lignin can be pyrolysed, and the resulting oil subject to methylation with dimethyl carbonate and purified using supercritical carbon dioxide.[81] The resulting “lignin pyrolysis oil methyl ethers” (LOME) consists of various anisole (methoxybenzene) and veratrole (1,2-dimethoxybenzene) compounds, and can be used as a solvent. Mudraboyina *et al.* reported excellent yields for a model Menschutkin reaction performed in LOME. Non-aromatic solvents made from lignin have also been reported. 1,3-Dioxolane is produced from lignin by deconstructing the linkages between the aromatic lignin monomers.[82] The deformylation of the lignin is elaborated on by trapping the liberated formaldehyde with an excess of ethylene glycol, thus resulting in 1,3-dioxolane. For such a process to be viable for the production of a solvent in a biorefinery, other high value products would need to be synthesised from the lignin simultaneously.

4.1.4 Triglyceride-Derived Solvents

Biodiesel is produced from vegetable oils by means of transesterification. It is a mixture of the methyl esters of long chain fatty acids. It would be perfectly feasible to use biodiesel, otherwise called fatty acid methyl esters (FAMEs), as a solvent but there has been surprisingly little interest in this



Scheme 4.12 Lignin-derived aromatic solvents.

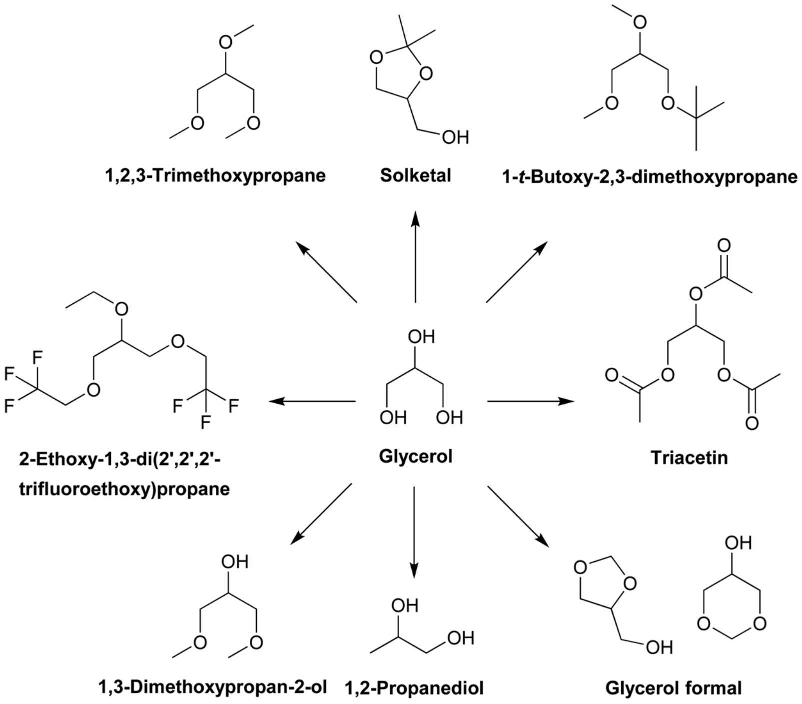
opportunity. To date FAME solvents have been used sparingly as reaction solvents for the modification of olefins,[83,84] and extractions from water,[85] and as solvents for resins.[86,87] The presence of alkene and ester functional groups in biodiesel means reactivity might be an issue. On the other hand, this can be advantageous in coating applications where the solvent is cured to harden the coating, rather than achieving the same effect by allowing a VOC solvent to evaporate to dryness.[88]

The by-product of biodiesel production is glycerol.[89] Possible applications of glycerol as a solvent are numerous,[90,91] with increasing interest in glycerol derivatives as well.[92] The motivation to use glycerol as a solvent comes from its availability and low toxicity. However, crude glycerol is not suitable for many solvent applications.[93] Also, it is not ideal as a solvent for reaction chemistry because of its high viscosity and lack of volatility. Room temperature reactions are possible but higher temperatures are preferable for improved mass transfer.[94] Where glycerol finds most use within its 2 million tonne annual market is as a sweetener and humectant, in animal feed, as a chemical intermediate, as a viscosity modifier in cosmetic formulations, replacing ethylene glycol in antifreeze,[89] and increasingly in e-cigarette liquids. The last two applications are also fulfilled by propylene glycol, which can be made from glycerol.[95]

Other chemical modifications of glycerol can be useful to create superior solvent properties, which can mean lower viscosity, a lower boiling point, or aproticity, for example. Glycerol is also a component in some deep eutectic solvents,[96] as explained in Section 4.6. The acetals and ketals of glycerol are an example of a commercially available class of glycerol-derived bio-based solvents.[97] Solketal (1,2-isopropylidene glycerol) is the product of acetone reacting with glycerol.[98] An equivalent reaction with formaldehyde produces glycerol formal, which is obtained as a mixture of the dioxolane and dioxane forms (Scheme 4.13). To form an aprotic solvent, triple methylation of glycerol results in 1,2,3-trimethoxypropane. Examples of its synthesis and use are limited, but its potential has been shown.[99,100] The triester of glycerol, triacetin, is another available aprotic solvent. Finally, elaborate ethers of glycerol have been synthesised and characterised by García *et al.*[101,102] The complexity of the chemistry used allows selective alkylation of the three glycerol alcohols (Scheme 4.13), but in doing so limits applications to no more than very specific and high value applications, probably with solvent recovery needed to justify the lengths gone to in making the solvent.

4.1.5 Terpene-Derived Solvents

Essential oils are a naturally occurring source of lipophilic solvents. Citrus fruits and citrus oils are a major industry, and limonene is the major component of these oils. Applications of limonene include a long established role in degreasing,[103] and newer extraction procedures.[104,105] Only limited examples of the use of limonene in synthetic chemistry exist.[106] Limonene is conventionally produced by the extraction of orange oil by steam distillation, or



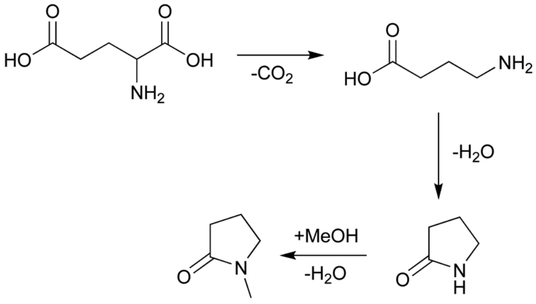
Scheme 4.13 Glycerol-derived solvents.

by cold-pressing waste orange peel. Essential oil yields of 3% or more based on the dry orange peel mass can be expected, with increasing research efforts dedicated to isolating limonene as part of a multi-product biorefinery operation.[107] The annual scale of waste orange peel is in the multi-millions of tonnes range,[108] making this a viable process for competing in the solvent market.

The sap of pine trees is a historically important source of turpentine, and hence pinenes. α-Pinene and then β-pinene are the major components.[109] Turpentine oil is not a major solvent product because petroleum cuts with similar cleaning and formulating performance are less expensive, and if a bio-based solvent is desirable, limonene has a more pleasing odour.[110] Like limonene, the unsaturation of pinenes means they can be reactive, which limits their use. One solution is to hydrogenate the pinenes in turpentine oil to pinane. The resulting aliphatic hydrocarbon can be used for the extraction of natural compounds.[111]

4.1.6 Amino Acid-Derived Solvents

Glutamic acid has been proposed as a platform molecule for chemical synthesis because it is relatively abundant amongst the amino acids in plant proteins.[112] At present glutamic acid is produced industrially by fermentation,[113]



Scheme 4.14 The synthesis of NMP from glutamic acid.

but opportunities exist for the valorisation of bio-economy wastes instead as a means to obtain amino acids. Dried distillers grains with solubles (DDGS), a by-product of bio-ethanol production, could provide a voluminous and reliable source of glutamic acid for this and other chemical processes. DDGS consists of 20–30 wt% protein, and glutamic acid is the most prevalent amino acid in this waste stream.[114,115] For solvent synthesis purposes, glutamic acid can be decarboxylated enzymatically to give 4-aminobutyric acid, then cyclised to pyrrolidinone, and reacted with a methylhalide (made from methanol *in situ*).[116,117] The product is bio-based *N*-methyl pyrrolidinone (NMP), a common dipolar aprotic solvent (Scheme 4.14).[118] Regardless of its origin, NMP possesses serious health issues as a reprotoxin and is considered a substance of very high concern (SVHC).[119] Undoubtedly it is better to design alternative amide solvents without chronic toxicity issues, even if they are not bio-based.[120]

4.1.7 Summary of Commercially Available Bio-Based Solvents

In Chapter 6, there are data sheets documenting the sustainability attributes of 40 representative bio-based solvents. The selection should not be considered as an exhaustive list of products, but the most significant and interesting examples are included, from pre-commercial demonstrator plant stage to market. It is helpful to know under what circumstances these bio-based solvents can be used, and what new products are needed to fully serve the solvent needs of all the chemistry sectors. Polarity and volatility are two of the key attributes of a solvent, and in Figure 4.1 these properties are represented. This is achieved using the Hansen solubility parameters and by grouping solvents into the boiling point ranges specified in the CHEM21 solvent selection guide criteria.[121] This data set is weighted towards highly protic solvents because of a relative abundance of bio-based polyol solvents, and depleted in highly dipolar aprotic solvents (large δ_D, modest δ_H) as is representative of available products. About 60% of the bio-based solvents summarised here have a boiling point in excess of 140 °C. This is expected of the strong hydrogen bonding solvents, but poses a limitation to the function

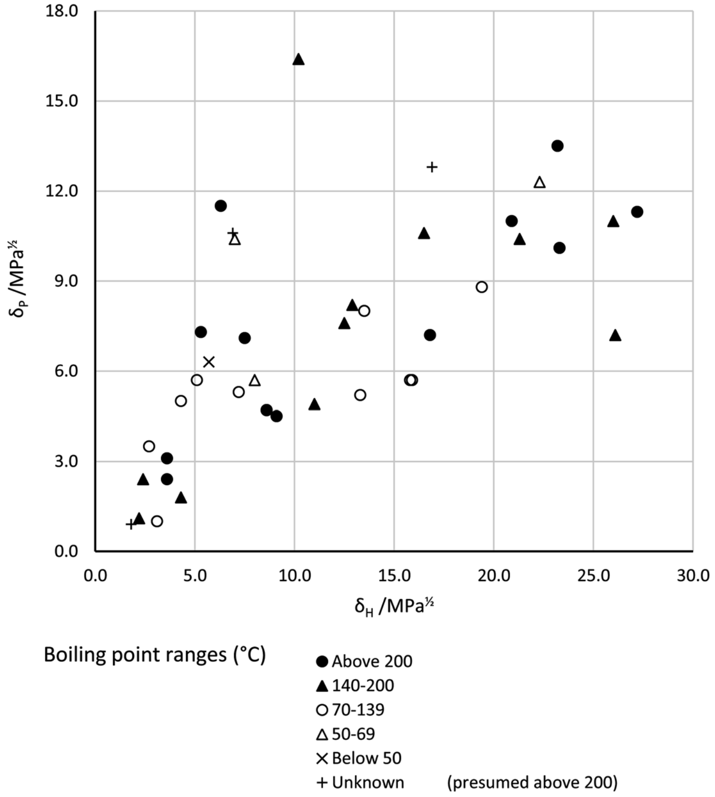


Figure 4.1 A Hansen polarity map of the featured bio-based solvents, with volatility ranges indicated.

of the low polarity solvents. *p*-Xylene and *t*-butyl ethyl ether are the only two low polarity solvents with boiling points in the ideal range (70–139 °C), but they are not yet produced from biomass for solvent purposes. Instead, the intended use of bio-based *p*-xylene is as a chemical intermediate, and *t*-butyl ethyl ether is marketed as a fuel additive. In total, a quarter of the solvents have a boiling point between 70 °C and 139 °C and these are reasonably well distributed throughout Figure 4.1.

In terms of safety, the bio-based solvents considered here mostly perform well. Twenty-one (more than half) have flash points above 60 °C meaning they are not considered as flammable liquids. Two can form peroxides: tetrahydrofuran (THF) and 2-methyltetrahydrofuran (2-MeTHF). The health hazards posed by bio-based solvents vary. Major health hazards are posed by 9 solvents, with a further 14 possessing minor health hazards. This has been evaluated according to the ranking of UN GHS Hazard Statements used in the CHEM21 solvent selection guide (a health score of 6 or more indicates a major health hazard).[121] There were 5 solvents that do not possess any health hazards within the scope of the CHEM21 solvent evaluation criteria, these being glycerol, dimethyl sulphoxide (DMSO), 1,2-propanediol, methyl soyate, and carbon dioxide. There are also 12 more solvents without sufficient data to be sure no hazards are present. Care must be taken to understand whether an absence of hazard statements means the solvent is safe or not understood. European REACH regulation ((EC) No 1907/2006) registration dossiers indicate if substance property data is missing or if it is complete, and this is made clear in the data sheets found in Chapter 6.

Beyond the standardised reporting of hazards, some solvents may be both prevalent and hazardous enough to be placed on lists of undesirable chemicals in need of substitution. Many types of organisation make such lists. It is not to say that a chemical not featured is safe, or those featured are exceedingly worrying, but those included are certainly problematic because of the frequency in which they are used. Greater rates of use mean a higher risk of exposure and that the consequence of any adverse effects is more likely to occur. Of the 40 featured bio-based solvents, methanol, 1-butanol, isobutanol, ethylene glycol, 1,4-butanediol, tetrahydrofurfuryl alcohol, ethyl acetate, acetone, acetic acid, THF, DMSO, turpentine oil, *d*-limonene, and *p*-xylene feature on the SUBSPORT compendium of hazardous substances lists.[122] This online resource contains data from 34 official lists of restricted and priority substances in need of phasing out. The sources of these lists are legislation featuring restrictions of substances, environment agencies, non-government organisations and company lists of restricted substances.

The bio-based content of the featured solvents is generally high. Most (30 of 40) are class A bio-based solvents, and just 3 are class C: 2-ethylhexyl lactate, triacetin and *t*-butyl ethyl ether. This is not unexpected, but a high bio-based content does not mean the solvent is environmentally benign, as hopefully has been made clear in the data sheets provided in Chapter 6 and throughout the discussion in Chapter 3 and elsewhere. It is also possible to reduce environmental health and safety hazards with non-bio-based solvents, and overall the impact of solvent use might be improved by using the right fossil-derived solvent instead of what bio-based solvent is currently available. Bear this in mind when reading the next section dedicated to petrochemical solvents. In time, successful products that are not currently made from renewable resources may become available as bio-based products, should the technoeconomic argument to do so satisfy the expectations of the producer and the customer(s).

4.2 Promotion of Bio-Based Solvents by Standards and Certification

4.2.1 European Standard EN 16766

Whereas academic research is driven by innovation, commercially speaking the use of new solvents and solvent substitution must be justified on a more practical basis. Matters such as reliable sources of solvents with a consistent and well-defined specification are important, as is the price and the stability of that price. Adherence to regulations and polices dictating best practice, emissions, storage, safety, waste management and other considerations are necessary, with issues becoming magnified in importance with increasing scale. In industry, standards provide a means of defining practices in a way that is agreed and understood by producers, suppliers, customers, and regulators. Standards are technical documents that set out requirements for a particular aspect of a product, organisation or service. They are issued by a number of professional international and national bodies, as well as industry groups. Although standards are devoted to a broad spectrum of businesses, for chemicals the most common standards relate to test methods, and the communication of results (including labels and test reports).

If you are purchasing a chemical, or you wish to market a chemical product, you may be interested in its flash point for example. As the flash point determines the flammability of a liquid substance, a supplier must know the flash point in order to report its hazards (as defined by the United Nations (UN) Globally Harmonised System (GHS) of classifications for hazard labelling, and made compulsory for the distribution of safety datasheets). There are a number of different ways a flash point could be determined, and so if tasked with the determination of a flash point, the test method must be standardised, and the way of reporting the result must be standardised. In fact, there are a number of methods by which flash point determination can be conducted, with the following all standardised by the International Organization for Standardization (ISO):

- ISO 1516 Determination of flash/no flash–Closed cup equilibrium method
- ISO 1523 Determination of flash point–Closed cup equilibrium method
- ISO 2719 Determination of flash point–Pensky–Martens closed cup method
- ISO 3679 Determination of flash/no flash and flash point–Rapid equilibrium closed cup method
- ISO 13736 Determination of flash point–Abel closed cup method

When a flash point is reported, a reference to the standard that was followed should be provided. Analytical test laboratories will be certified to carry out procedures defined in standards. Without standards, chemical safety data would not be obtained in a way that is comparable to other tests and other substances. So standards help to improve reliability, reduce errors and misunderstandings, establish a level playing field, and therefore encourage trade and sustainable business relationships.

Bio-based products are an area of interest to the European Commission, where they see potential to boost the economy in a sustainable way. The European Committee for Standardization (CEN) is one standards agency of the European Union, and they have been tasked with the development of standards to describe bio-based products.[123] An obvious area to address is the determination of bio-based content. A series of European standards

(EN 16640, EN 16785-1, EN 16785-2) have been developed to provide recognised test methods for the determination of bio-based carbon content using radiocarbon analysis, and calculation methods for total bio-based content (considering all elements) where direct analysis is not feasible. The sustainability of bio-based products is another area of importance, and EN 16751 provides sustainability criteria to assist sustainability assessments (see Chapter 3, Section 3.2.3).[124]

Bio-based solvents are addressed specifically through their own European standard, EN 16766 (previously published as CEN/TS 16766, which, as a technical specification, is a precursor to a full standard).[125] It is important to understand the requirements set out in EN 16766, as these define the attributes of a bio-based solvent in the eyes of industry, both manufacturers and users. In research and development sectors, knowing what requirements and data are needed to define bio-based solvents for the market place is valuable information. Although the remit of EN 16766 only extends to the European Union, its contents should be of interest to non-Europeans involved in bio-based solvent research and application, especially companies wishing to import bio-based solvents into Europe.

'Bio-based Solvents–Requirements and Test Methods' (EN 16766) addresses performance properties, environmental health and safety, bio-based content, sustainability, and the reporting of these characteristics. With regards to performance properties, it is not suitable to implement minimum or maximum requirements. The necessary boiling point of a (bio-based) solvent is completely dependent on the application. Therefore, EN 16766 lists appropriate test methods found in other standards for the determination of performance properties, not limiting what their values should be. In addition to boiling point, the vapour pressure, colour, density, viscosity, and polarity are required. The determination of polarity lacks a standard test method, and so an annex within EN 16766 describes an approach for the determination of the Hansen solubility parameters.[125]

As the purpose of standards is to encourage market confidence and trade, no restrictions on the environmental, health and safety attributes of bio-based solvents are imposed beyond legal requirements. REACH registration is required, and the communication of hazards with a safety datasheet is compulsory anyway. An additional clause states that the composition of the bio-based solvent product should be provided, meaning all components present in amounts greater than 0.1% should be listed in the documentation that accompanies the solvent when it is purchased. As a note on the language of standards, "shall" always denotes a compulsory requirement, but "should" means something is recommended (either an action, or a way of achieving a compulsory action). The terminology is precise and universally consistent. This means that it is not actually compulsory to report the exact composition of a bio-based solvent product, which may otherwise reveal a confidential formulation. This of course only applies to the EN 16766 reporting template, where information regarding the characteristics of the bio-based solvent in question should be provided. In terms of the legal requirement to supply a separate safety datasheet, any toxic (CMR) or environmentally damaging (PBT, vPvB) substances present in amounts greater than 0.1% must be reported according to the European REACH regulation (in force at the time of writing).[126] This regulation is discussed in Chapter 2.

The attributes of a bio-based solvent outside the scope of a safety datasheet are, crucially, the bio-based content and the sustainability of the solvent. The sustainability of the biomass used to produce the bio-based solvent shall be proven with certification or adherence to EN 16751 (which contains sustainability criteria, refer to Chapter 3, Section 3.2.3). The sustainability of that biomass, as it is converted into a solvent, should be justified with EN 16751. As such, a sustainability assessment does not consider any part of a bio-based solvent that is petrochemical in origin (the assumption being that it is not sustainable). The existence of partially bio-based solvents requires that bio-based content is defined and able to be measured (or at least calculated).

As was covered in Chapter 3, because sustainability is an abstract term not linked to a physical property of a substance, the allocation of sustainable biomass certification to batches of materials such as palm oil after the mixing of sustainable and non-sustainable sources is allowed. This of course applies to a single type of substance (*e.g.* palm oil), and many different types of biomass have their own individual certification schemes. There are two major differences between producing sustainable biomass and producing bio-based chemicals that highlight why bio-based content cannot be treated the same as sustainability. Firstly, one process can create multiple products, and so allocation of bio-based content with a mass balance technique becomes difficult without a common means of deriving the allocation. Even with such means, a mass balance method can lead to claims of bio-based content that actually harm market confidence rather than improve it.[127] Allocation of sustainability on the other hand is resolved in EN 16766 by only allowing sustainable biomass into the process. It is not the case that only 100% bio-based solvents qualify. Secondly, there are recognised and accepted methods for the analytical determination of bio-based content. As such, allocation of bio-based content to a particular batch could be contradicted and therefore undermined by analysis. There has never been any indication or desire that the standardised methods of bio-based content determination (first produced by the American-based standards organisation ASTM) should be revoked, and therefore mass balance is not an appropriate tool for making a claim of bio-based content. Instead, CEN produced its own standards for bio-based carbon content determination, analogous to ASTM D6866,[128] as well as developing new approaches for total bio-based content determination.

Bio-based carbon content is determined analytically from the proportion of ^{14}C present in a sample. All contemporary materials such as biomass, and products made from biomass, have a quantity of ^{14}C present within their overall carbon content (at the level of parts per trillion) that matches modern day atmospheric levels. Accelerator mass spectrometry (AMS) is one method of performing analysis on carbon isotopes, which directly obtains the ratio between ^{14}C and ^{12}C. Otherwise the abundance of ^{14}C can be indirectly measured through its radioactive decay (the half-life of ^{14}C is longer than 5700 years). Whereas radiocarbon dating uses the proportion of ^{14}C to gauge the age of samples, in bio-based carbon content determination, it is assumed that the sample is recent and not historical. Therefore, the ratio of ^{14}C to ^{12}C indicates what combination of new (*i.e.* biomass) and old (*i.e.* petrochemical) material is in the sample.

The elements other than carbon do not have an equivalent marker that allows the proportion of biomass and petrochemical feedstocks incorporated in a sample to be determined. Stable isotopes vary too much to be useful in this regard. However, it remains a helpful approach, despite non-carbon atoms being excluded, because of the emphasis on carbon in legislation and society (*e.g.* measurement of emissions and emissions targets, carbon footprints, replacement of fossil hydrocarbons that are mostly made of carbon). In ASTM standard D6866, only organic carbon is measured, and so in their preparation, radiocarbon analysis samples are treated with acid to remove carbonates. This is not the case in the equivalent European standard EN 16640,[129] but regardless it is not relevant to bio-based solvents. Indeed, the determination of bio-based carbon content for solvents is quite routine compared to other (heterogeneous) samples. As liquids, they have a uniform composition and so representative sampling is not an issue. Before applying AMS, a sample is combusted to carbon dioxide, and then reduced to graphite. As most solvents are carbon rich and flammable, ignition of the sample is not a problem (as it can be for aqueous emulsions such as paints, and materials with flame retardant properties). Because of the way most bio-based solvents are produced, using distinct intermediate chemicals and transforming them in a linear fashion using well understood chemistry, it is possible to anticipate the result of a bio-based carbon analysis. Bio-ethanol and glycerol are examples of solvents with 100% bio-based carbon content. A diester made from succinic acid (bio-based) and 2 equivalents of propanol (fossil-derived) will be 40% bio-based (carbon mass basis).

For products where the carbon content is low, or to satisfy a political desire to represent biomass in bio-based products more completely (as is the case in Europe), total bio-based content becomes an appealing descriptor. For the reasons already mentioned, there is no analytical way to determine the total bio-based content. Instead, calculations have been proposed. For bio-based products manufactured using chemical reactions or biological processes, and formulations of these substances, a radiocarbon analysis is elaborated with a calculation governed by a principle known as "atom connectivity" (see Section 4.2.2.4). European standard EN 16785-1 documents a test method for this.[130] Essentially, from the bio-based carbon content, the actual bio-based carbon atoms within the molecular structure of the substance need to be identified. Other types of atoms covalently bonded to these bio-based carbon atoms then adopt the origin of their neighbouring carbon atom. In instances where two or more bonds to carbon atoms are present, the reaction mechanism of the chemical/biological process is required to resolve any ambiguity. The calculation of total bio-based content (on a mass basis) is verified with elemental analysis to confirm the composition of the product (but not the bio-based content).

European standard EN 16785-2 provides another means to determine the total bio-based content of a solvent, using a material balance.[131] This method relies on records of the material inputs (biomass, fossil material, inorganic substances) and outputs (products, emissions, wastes) of a manufacturing process and calculates the bio-based content from this. Without relying on analysis, the material balance calculation acts as a quick and cheap means to keep track of product batches. It does not allow any sort of allocation of bio-based content, as in a typically mass balance, and transferring actual bio-based content between batches with documentation is not permitted. The approach established by EN 16785-2 is advantageous when the amount of biomass entering the manufacturing process fluctuates. In this instance, a minimum bio-based content can be calculated. For solvents, this might occur if ethanol (or any chemical reactant) is purchased as a feedstock purely on price, so sometimes bio-based feedstocks will be preferred, but other times the fossil-derived equivalent will be more economically appealing.

EN 16766 defines categories of bio-based solvent (Table 4.1), which can be met according to bio-based carbon content (EN 16640) or total bio-based content (EN 16785-1 or EN 16785-2). Class A is reserved for completely bio-based solvents. The actual threshold is ≥95% because of experimental error in the determination of the proportion of ^{14}C present by analysis. Class B is for solvents mostly made of biomass, with at least 50% bio-based content. Class C sets a lower threshold of 25% for a bio-based solvent. This value is arbitrary in a sense, chosen to match an equivalent requirement of bio-based lubricants in Europe (according to CEN/TR 16227).

To accompany the legal and safety documentation when a bio-based solvent is purchased, a business consumer can also request that the reporting template of EN 16766 be provided. This contains all the information relating to the requirements of the standard. The necessary information from this template is provided as Table 4.2.

4.2.2 Certification and Labelling

Sustainability certifications and the standards that underlie them are reviewed in Chapter 3. Certification also exists to attribute bio-based content to products, primarily through labelling. Labels are intended to guide consumer choices, whereas standards are used to specify technical documents of greater use to businesses. A label provides limited information, and to be accepted requires

Table 4.1 Classes of bio-based solvent (carbon mass basis or total mass basis may be used).

Class	Bio-based content, B
A	$95\% \leq B$
B	$50\% \leq B < 95\%$
C	$25\% \leq B < 50\%$

Table 4.2 A simplified version of the bio-based solvent reporting template found in EN 16766,[125] with guidance notes added where necessary.

Property	Methods and guidance
Identification	
Product name	No guidance offered
Supplier name	No guidance offered
Intended end uses	No guidance offered
Bio-based solvent class	According to classes defined in Table 4.1
Biomass information	
Origin	By territory or country or water body
Type	By plant species, chemical composition
Bio-based content	
Bio-based carbon content	According to EN 16640 [129]
Total bio-based content	According to EN 16785-1,[130] or EN 16785-2 [131]
Sustainability aspects	
Feedstock	According to EN 16751 (compulsory according to EN 16766)[124]
Process	According to EN 16751 (optional)[124]
Life cycle information	According to EN 16848 [261]
Biodegradability	
Ultimate biodegradability in the environment	Additional requirement, not compulsory
Technical performance properties	
Composition	List chemical components
Polarity	Provide Hansen solubility parameters
Boiling point	Distillation test (according to recognised standards)
Volatility	Vapour pressure or evaporation rate
Colour	*e.g.* Gardner scale
Density	Density test (*e.g.* EN ISO 12185)
Viscosity	Kinematic viscosity at 40 °C

an element of trust from the consumer that it represents something meaningful and good. Of course behind the label are strict requirements that are comprehensively explained in a standard. In the case of labels for the endorsement of bio-based products, the meaning of the label comes primarily from the application of standardised test methods to determine or calculate the bio-based (carbon) content. At that point the label introduces a threshold of the minimum acceptable bio-based content, and can add brackets of bio-based content in the same way that EN 16766 introduces levels of bio-based solvents (Table 4.1). In terms of solvents, the small consumer market for pure solvents means these labels will be more frequently seen on solvent-based formulations.

4.2.2.1 DIN CERTCO

DIN CERTCO is a German certifier. The label they issue for bio-based products requires a bio-based carbon content measurement in accordance with ASTM standard D6866.[132] The DIN CERTO certification sets a minimum bio-based carbon content of 20%. This designation is based on organic carbon only as described in ASTM D6866. Inorganic carbonate carbon is eliminated in the test method with an acid pre-treatment. Three categories are defined by the label: 20–50% bio-based carbon content; 50–85% bio-based carbon content; and >85% bio-based carbon content. These ranges are stated on the label itself.

4.2.2.2 VINÇOTTE

The 'OK biobased' label issued by VINÇOTTE (Belgium) is similar to that provided by DIN CERTCO.[133] Four categories of the label are available, the lowest bio-based carbon content accounted for is in the 20–40% bracket. There are also 40–60%, 60–80%, and over 80% bio-based carbon content labels. An additional requirement is that certified products carrying the 'OK biobased' label must have at least 30% of its carbon content in the form of organic carbon. This ensures the scope of the label is not extended to mineral products.

4.2.2.3 USDA

In the USA, the United States Department of Agriculture (USDA) oversees a mandatory procurement programme to increase bio-based product use by government agencies. 'BioPreferred®' is a legally binding initiative that also provides a labelling scheme for bio-based products.[134] Unlike the certification of DIN CERTCO and VINÇOTTE, different minimum bio-based (carbon) content requirements apply to different types of product. Solvents are not explicitly covered, but end (formulated) products are. Table 4.3 provides a selection of bio-based product categories relevant to solvents and the minimum bio-based content threshold put in place by the 'BioPreferred®' programme.[135] Products outside of the 97 categories shall be at least 25% bio-based to adhere to the procurement requirements.

4.2.2.4 NEN

The Dutch standardisation organisation (NEN) manages a bio-based content certification scheme in which total bio-based content is assessed.[136] European standard EN 16785-1 is used for verification purposes. It is required that radiocarbon analysis for the determination of bio-based carbon content

Table 4.3 USDA BioPreferred® solvent-containing product categories.

Product type	Minimum bio-based carbon content
Paint (latex and waterborne alkyd)	20%
Paint (oil-based and solvent-borne alkyd)	67%
Paint removers	41%
Graffiti and grease removers	34%
Inks	20–67% (depending on speciality)
Ink removers and cleaners	79%
Industrial speciality precision cleaners and solvents	56%
Car care products	75%
De-icer	93%

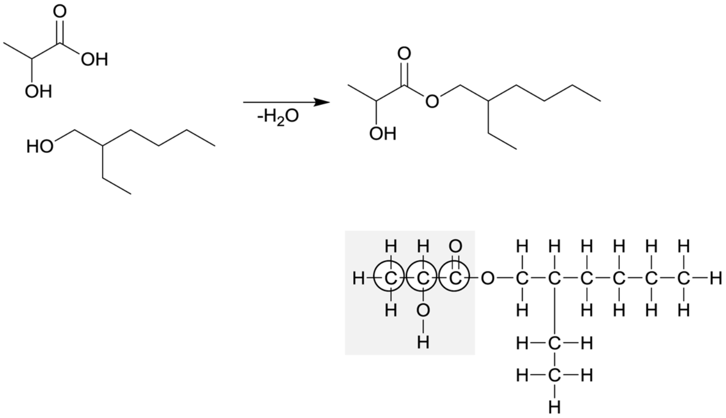


Figure 4.2 An 'atom connectivity' calculation for total bio-based content. Above: reaction schematic for the synthesis of 2-ethylhexyl lactate. Below: assignment of bio-based atoms. The bio-based carbon atoms are shown in circles, and the associated bio-based atoms fall within the grey shaded area.

is supplemented by elemental analysis to (1) confirm the composition of the product, and (2) apply the 'atom connectivity' principle (as mentioned in Section 4.2.1) to produce a value for total bio-based content. Without a direct analytical method for the determination of the origin of atoms other than carbon, the total bio-based content can only be calculated knowing the proportion of each substance within the product. A simple example is given in Figure 4.2. 2-Ethylhexyl lactate is made from lactic acid, a fermentation product, and fossil-derived 2-ethyl-1-hexanol. Radiocarbon analysis of 2-ethylhexyl lactate should indicate a bio-based carbon content of 27% within experimental error. Knowing that the product contains 11 carbon atoms, this analysis should confirm that bio-based lactic acid (with 3 carbon atoms) was used as a reactant. The atoms covalently bonded to the bio-based carbon atoms are also considered bio-based (by application of the "atom connectivity" rule). The bridging oxygen atom of the 2-ethylhexyl lactate ester is considered to be fossil-derived following reaction mechanism ($A_{AC}2$) convention. The proportion of hydrogen and oxygen atoms is confirmed with elemental analysis, and the assignment of total bio-based content is made at 36%. European standard EN 16785-1 provides extra clarification and also contains additional validation steps should the results of the radiocarbon and elemental analysis be inconsistent with declarations.[130]

4.3 Speciality Petrochemical Solvents

The post-second world war chemical industry has achieved a great deal,[137] and mostly without any limitations caused by the availability of suitable solvents. However, it is now widely recognised that some solvents pose a risk so great that they should not be used, or their use confined to essential applications.

Historically this has meant a reduction in chlorinated solvent use (although safe in terms of flammability, they may cause cancer), and the replacement of other chronic toxicants such as benzene for an equivalent solvent, usually toluene. Regulation is now casting scrutiny over these replacement solvents, including toluene for example.[138] This has lead a number of high-profile chemical companies to develop new solvents, sometimes completely original in their molecular structure, with the aim to design solvents that are safe. These are (for the most part) still petrochemical solvents, and so cannot be considered as sustainable, but the social, economic and environmental impact of these products can have a positive influence on processes and formulations presently dependant on more harmful solvents.

In the modern day solvent market, the bespoke petrochemical solvents are found alongside neoteric solvents, named for their novel chemical structures or the unconventional technology needed to harness them.[139] The reason why speciality petrochemical solvents are relevant as viable products is that in terms of technology and cost, it is rarely favourable at this current time to implement a neoteric solvent. Ionic liquids remain expensive, and the apparatus to maintain the supercritical phase of carbon dioxide is an investment only made when economically sensible. Ionic liquid,[140] and supercritical carbon dioxide,[141] industrial processes have been decommissioned in the past because the high operational cost succumbed to fluctuations in the final product market. On the other hand, a safer, low volatility organic solvent is much more appealing to users as a viable solvent substitute. The chemical plant or formulation lab infrastructure does not need modifying, and the cost of speciality petrochemical solvents, although higher than conventional solvents, is not of the order of a typical ionic liquid, and may on balance be justified.

4.3.1 Case Studies

Twenty-five speciality petrochemical solvents are described in the data sheets found in Chapter 6. A summary justifying their inclusion is provided in Table 4.4. Each was chosen because of their prominent market profile as a commercial (branded) product, or because they appear to be very beneficial according to solvent selection guides, yet do not have a dedicated manufacturing process using biomass (bio-based solvent data sheets are also found in Chapter 6). Detailed explanations of some of the more prominent branded solvent products as well as academic developments can be found in the remainder of Section 4.3.1.

4.3.1.1 TamiSolve NxG (Eastman)

TamiSolve™ NxG (propriety chemical structure, not in Table 4.4) is a speciality solvent produced firstly by Taminco and then after acquisition in 2014 by Eastman chemical company.[142] Much like Cyrene™ (Section 4.1.2.1) it is a high boiling, dipolar aprotic solvent intended to act as a substitute for

Table 4.4 Speciality petrochemical solvents useful for the substitution of hazardous solvents.

Name	Trade name/Supplier	Benefits
t-Amyl methyl ether	Multiple suppliers	Green characteristics[262]
Anisole	Multiple suppliers	Green characteristics[263]
Benzyl benzoate	Multiple suppliers	Replacement for chlorinated solvents[264]
Butyl 3-hydroybutyrate	Omnia™/Eastman (USA)	High performance cleaner[265]
Cyclopentyl methyl ether	Zeon (Japan)	Green characteristics[262]
Dibasic isopropyl esters (adipate)	Coasol®/Chemoxy (UK)	Green characteristics[263]
Dibasic methyl esters (adipate)	Rhodiasolv® RPDE, Solvay (Belgium), Estasol®/Chemoxy (UK), and Flexisolve®/Invista (USA)	Green characteristics[263]
Dibasic methyl esters (glutarate)	Rhodiasolv® RPDE, Solvay (Belgium), Estasol®/Chemoxy (UK), and Flexisolve®/Invista (USA)	Present in blends with other dibasic esters
Dibasic methyl esters (succinate)	Rhodiasolv® RPDE, Solvay (Belgium), Estasol®/Chemoxy (UK), and Flexisolve®/Invista (USA)	Green characteristics[263]
Dibutyl ether	Multiple suppliers	Green characteristics[263]
Diethylene glycol monobutyl ether	Butyl Carbitol™/Dow (USA)	Green characteristics[263]
Dimethyl carbonate	Multiple suppliers	Green characteristics[262]
N,*N*-Dimethyl decanamide	Rhodiasolv® ADMA 810/Solvay (Belgium)	Green characteristics[263]
Dimethyl 2-methylglutarate	Rhodiasolv® IRIS/Solvay (Belgium)	High performance cleaner[266]
N,*N*-Dimethyl octanamide	Rhodiasolv® ADMA 810/Solvay (Belgium)	Green characteristics[263]
1,3-Dioxolane	Multiple suppliers	Replacement for amide solvents[267,268]
Glycol acetate	Chemoxy (UK)	Green characteristics[262]
Hexamethyldisiloxane	Dow Corning (USA)	Replacement for VOCs and ozone depleting solvents[269,270]
Isoamyl acetate	Chemoxy (UK)	Green characteristics[262]
Isobutyl acetate	Multiple suppliers	Green characteristics[262]
Methyl-5-(dimethylamino)-2-methyl-5-oxopentanoate	Rhodiasolv® Polarclean/Solvay (Belgium)	Speciality agrochemical solvent[271]
1,1,1,3,3-Pentafluorobutane	Solkane® 365/Solvay (Belgium), and HARP® 365 mfc/Harp (UK)	Replacement for ozone depleting solvents[272]
Polydimethylsiloxane	Dow Corning (USA)	Replacement for VOCs and ozone depleting solvents[269,270]
Polyethylene glycols	Multiple suppliers	Green characteristics[273]
Propylene carbonate	JEFFSOL®/Huntsman (USA)	Green characteristics[262]

N-methyl pyrrolidinone (NMP) amongst other solvents. Unlike Cyrene™ it is not bio-based, but much to the credit of its producers, full toxicity testing has been performed. Proven applications for TamiSolve™ NxG include the manufacture of wire enamels and other coatings, inks, paint strippers and agrochemical formulations, and organic synthesis.

TamiSolve™ NxG has been shown through standardised testing to be neither mutagenic nor classifiable in terms of its prenatal toxicity.[143] It is not sensitising, but it is an irritant. The LD_{50} of TamiSolve™ NxG (rat, oral) is between 300 mg kg^{-1} and 2000 mg kg^{-1}, in line with category 4 of the acute toxicity labelling established by CLP regulations. The associated Hazard Statement (H302: harmful if swallowed) suggests that TamiSolve™ NxG is not highly toxic. Furthermore, TamiSolve™ NxG is biodegradable, and does not meet any of the environmental persistency, bioaccumulation and toxicity (PBT) thresholds that would attract attention in Europe under the controls of REACH.[126] The molecular structure of TamiSolve™ NxG is protected, but physical property data has been made available.[143] As is true of NMP, it is fully miscible with water, but has a boiling point somewhat higher than NMP at 241 °C. The flash point of TamiSolve™ NxG is above 100 °C.

It is unreasonable to expect solvent users to make unnecessary changes to a process or formulation (*i.e.* solvent substitution) without the advantages offsetting the economic impact of the disruption and uncertainty caused. If performance is improved or costs reduced, then customers will invite change. Green premiums have no traction for businesses buying low value commodity chemicals such as solvents, so improvements upon solvent substitution must be more tangible. For these reasons, TamiSolve™ NxG is no different to any other new solvent product in that it must demonstrate either that the performance of the application is not reduced in a situation where the conventional solvent is taken out of use, or, that performance is improved sufficiently to justify the solvent substitution without the push of regulation.

Three case studies addressing different types of formulations illustrate the satisfactory performance of TamiSolve™ NxG. The printing sector does use some NMP-based solutions, but alternatively TamiSolve™ NxG has been shown to have benefits for ink formulations, flexographic prints, printed electronics, and overprint varnishes.[144] Several inkjet formulations for printing on different surfaces were made using NMP and then TamiSolve™ NxG. The results were indistinguishable in terms of colour stability, print quality and heat stability.[145] A clear advantage of TamiSolve™ NxG over NMP in half the inks was that the 'decap time' (the time until the spray nozzle clogs up) was significantly increased. Aqueous polyurethane dispersions also require the use NMP, here as a dispersant. TamiSolve™ NxG improves the coalescence of the polyurethane formulations compared to NMP, while also reducing the drying time.[146,147]

Agrochemicals are formulated in concentrated solutions which are later diluted in water before use. *N*-methyl pyrrolidinone (NMP) is a common co-solvent for biologically active compounds,[148] and the resulting formulation is therefore toxic to humans as well as animals.[149,150] In a study of typical agrochemicals, their solubilities in TamiSolve™ NxG were generally about 10% less compared to solutions in NMP.[145] Of the nine substrates, only one was more soluble in TamiSolve™ NxG. Interestingly, this compound, the fungicide epoxiconazole, was poorly soluble in NMP, and so the slight improvement gained by using TamiSolve™ NxG is more significant than it would otherwise have been.

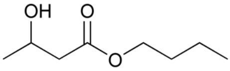
TamiSolve™ NxG has also been tested as a solvent for the Heck reaction, a common carbon–carbon bond forming reaction in the pharmaceutical industry. The synthesis of methyl cinnamate proceeded at a similar rate in DMSO, NMP and TamiSolve™ NxG. Yields for a further nine examples of the Heck reaction demonstrate equal performance between TamiSolve™ NxG and NMP.[145]

4.3.1.2 Omnia: Butyl 3-Hydroxybutyrate (Eastman)

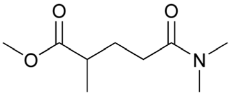
Butyl 3-hydroxybutyrate (Scheme 4.15), sold as Omnia™,[265] is used as a speciality cleaning solvent. It can be formulated as a 3 wt% aqueous solution.[151] For higher concentrations, an additional surfactant is needed. Butyl 3-hydroxybutyrate has no known acute toxicity, chronic toxicity or ecotoxicity within classification boundaries. Various products for industrial and professional cleaning are based on Omnia™ formulations, including degreasers.[152] The cleaning efficacy of Omnia™ is higher than that of equivalent formulations based on glycol ethers or limonene.[153]

4.3.1.3 RhodiaSolv PolarClean: Methyl 5-(dimethylamino)-2-methyl-oxopentanoate (Solvay)

Methyl 5-(dimethylamino)-2-methyl-oxopentanoate (Scheme 4.16) is a solvent for agrochemical formulations.[271] Marketed as RhodiaSolv® PolarClean by Solvay, it has also been demonstrated to be applicable to the production of poly(vinylidene fluoride) membranes.[154]



Scheme 4.15 Butyl 3-hydroxybutyrate, CAS number: 53605-94-0.



Scheme 4.16 Methyl 5-(dimethylamino)-2-methyl-oxopentanoate, CAS number: 1174627-68-9.

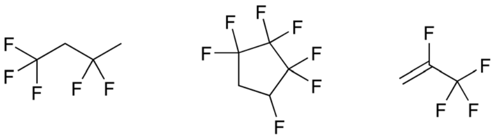
4.3.1.4 Academic Developments

In addition to commercial products, there are a small number of novel petrochemical solvents being investigated by academic research groups. The replacement of dipolar aprotic amide solvents is at the forefront of these efforts. *N*-Butyl pyrrolidinone,[120] and *N*,*N*′-dimethylpropyleneurea (DMPU),[155] have been used recently to replace *N*-methyl pyrrolidinone (NMP) in organic synthesis and materials science applications, respectively. Unfortunately, DMPU is a suspected reprotoxin and therefore does not offer an advantage over NMP as a substitute solvent.[156] At the other end of the solvent spectrum, conventional alkane solvents can be replaced by high molecular weight, non-volatile poly(α-olefin)s in thermomorphic solvent extraction systems with polar solvents.[157]

The use of many halogenated compounds is restricted by the Montreal Protocol.[158] Confirmation that large volume chlorinated solvents such as dichloromethane, not regulated through the Montreal Protocol, can also cause ozone depletion is a concern.[159] The excellent properties of chlorofluorohydrocarbons (CFCs) and hydrochlorofluorocarbons (HCFCs) as refrigerants, blowing agents and aerosols has meant the industry has sought to replicate their performance without the same environmental impact. For example, 1,1,1,3,3-pentafluorobutane is a low boiling point commercial foaming agent with no known ozone depleting potential (Table 4.4).[272] 1,1,2,2,3,3,4-Heptafluorocyclopentane has been claimed by its inventors to be a green solvent.[160] This assertion is severely premature given any sort of environmental health and safety assessment is yet to be conducted. It also requires *N*,*N*-dimethyl formamide (DMF), a reprotoxic solvent, for its synthesis. In another report, 2,3,3,3-tetrafluoropropene has been shown to reduce global warming potential when used in place of ozone depleting extraction solvents.[161] These hydrofluorohydrocarbons are shown in Scheme 4.17.

4.4 Water and Aqueous Solutions

If asked what is the greenest solvent, it is tempting to answer with water. Definitely in terms of production (purification), and environmental health and safety, water is obviously superior to any organic solvent. However, what we have learnt through the case studies in this book is that context is everything. We must also broaden our perspective to consider social and technoeconomic factors, as well as downstream environmental impacts.

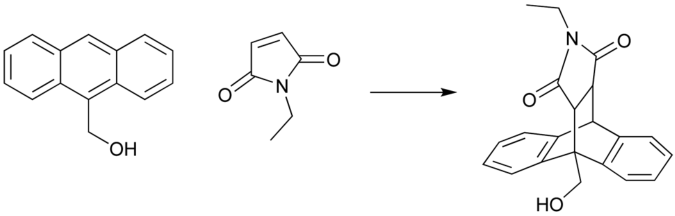


Scheme 4.17 Left: 1,1,1,3,3-pentafluorobutane; middle: 1,1,2,2,3,3,4-heptafluorocyclopentane; right: 2,3,3,3-tetrafluoropropene.

Water will not be a suitable solvent for many applications. This may be an issue of solubility, but that can be addressed by modifying the system. Other times substrate stability and catalyst deactivation will be a problem. Again, a redesign of the process or product can sometimes resolve this. That is not to say that water can replace all organic solvents, because water resistance may be a desirable function that cannot be delivered with an aqueous solvent system. Nevertheless, water is no longer simply dismissed as a solvent as it might have been in the past, and many successful examples of water-based chemistry are described in the literature.[162] Waterborne paints and coatings have already displaced many formulations previously based on organic solvents (see Chapter 2, Section 2.5).

The reason why we perceive water as a benign solvent is because it is naturally occurring in great abundance, bio-compatible, non-toxic, *etc.* For formulations these are perfect attributes, given that application performance is maintained. However, when water is taken into the 'unnatural' environment of the chemical process industry, its use in this way is at odds with its intrinsic and pervasive role in nature. Industrial waste water spreads contamination throughout natural water bodies as it re-joins the water cycle. To prevent this, biological waste water treatments are used to break-down organic contaminants that might arise by using water as a reaction solvent. This is the only way water can be recognised as a 'green' solvent,[163] and is an obligatory step towards sustainability. Water used for cooling systems does not contaminate the water, but it should not be reintroduced to natural water bodies while still warm. Oxygen solubility in water decreases with increasing temperature, which has obvious consequences to any organisms inhabiting the aquatic environment near a chemical plant.[164] The volume in which process water is needed is also important if located in an area of water scarcity. This will far exceed the volume of water needed as the reaction solvent. Consequently, responsible water use practices must be upheld, and the water use rights of local people must not be compromised, now or in the future.

One way to minimise organic contamination of water during reaction chemistry is to practice 'on-water' chemistry.[165] This is where a reaction is not occurring as an aqueous solution, but rather the reactants form a hydrophobic phase of their own. The presence of water is thought to assist through hydrogen bonding, thereby accelerating reactions beyond what is achieved in a solvent-less system.[166] The Diels–Alder reaction is a classic example of on-water chemistry.[167] The rate acceleration of this type of cycloaddition in water is extremely high. The observed solvent effect has been broadened by Myers and Kumar who have shown that a fluorophobic effect exists as well as a hydrophobic effect (Scheme 4.18 and Figure 4.3).[168] Later, it was shown that despite growing interest in ionic liquid solvents, water remains the superior choice.[169] Even so, synthetic chemists follow the "like-dissolves-like" principle and continue to use aromatic and chlorinated solvents for their Diels–Alder reactions,[170] showing that an intuitive feeling towards solvent selection still exists. In terms of industrial applications of water as a solvent, aqueous hydroformylation processes have been successfully established.[171]



Scheme 4.18 The Diels–Alder reaction of *N*-ethylmaleimide and 9-hydroxymethylanthracene.

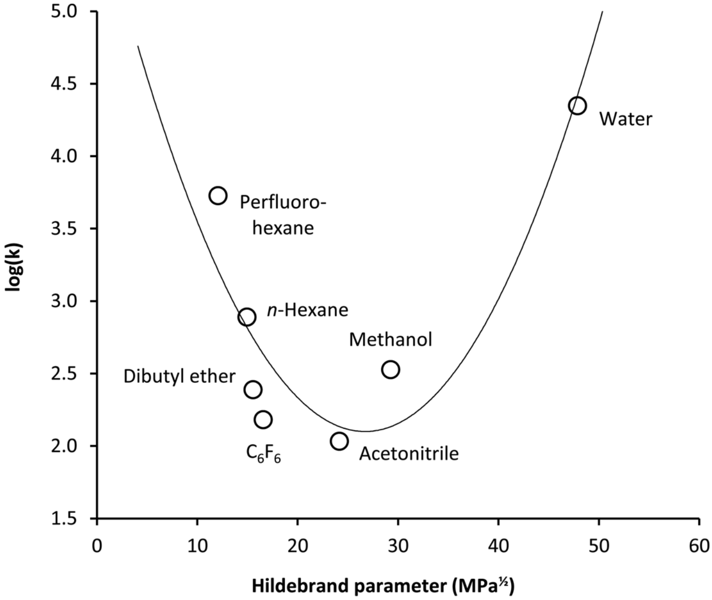
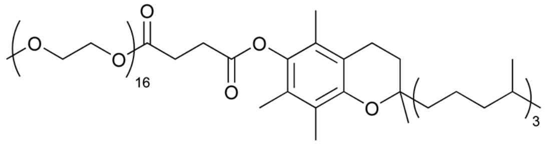
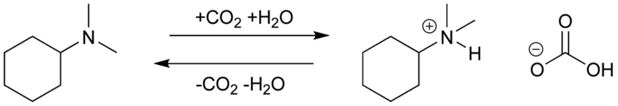


Figure 4.3 The influence of solvent polarity on the rate of the Diels–Alder reaction shown in Scheme 4.18.

The alternative approach to 'on-water' chemistry is to facilitate the solubility of the reactants into the aqueous medium with the use of surfactants. Without the careful design of such a process, the risk is that it becomes even easier to create downstream pollution issues, and also complicate isolation of the products. Lipshutz has pioneered the use of specialised non-ionic surfactants that permit catalysed organic reactions to occur at room temperature in an aqueous medium (Scheme 4.19).[172] The concept of emulsions as reaction media has great promise given that the products can be extracted efficiently, the solvent system can be reused,[173] and the surfactants are biodegradable.[174] Note that organic solvents are still used for product extraction and purification by column chromatography.[175,176]

Quite recently it has become vogue to introduce fruit juices into reactions. The water is able to act as a solvent, and any compounds present in the juice





Scheme 4.19 A biodegradable surfactant suitable for micellar reactions in water.[172]

may be catalytic under the circumstances (*e.g.* citric acid). Extracts of banana peel ashes,[177,178] cucumber juice,[179] and lemon juice have all been used.[180] It is unlikely that the latter two solutions will be useful when pursuing sustainable chemistry because of the direct competition with food. The juice of diseased and overripe fruit could open up an avenue for farmers looking to recuperate costs, but diseased fruit is typically smaller and lower in moisture content then usual and does not provide a stable basis for solvent production, or one that should be encouraged on any appreciable industrial scale.

4.5 Supercritical Fluids and Their Use in Tuneable Solvents and Switchable Solvents

Carbon dioxide is the most important supercritical fluid industrially. Waste CO_2 can be obtained cheaply as a by-product of other industries,[181] meaning a use is provided to this abundant waste even if it is still destined to be discharged to the atmosphere at a later date. Supercritical carbon dioxide ($scCO_2$) is created at and above its critical point, which is found at the reasonably mild conditions (given the circumstances) of 31 °C and 73 standard atmospheres of pressure.[182] The low toxicity and non-flammability of carbon dioxide are also benefits that differentiate it from organic solvents.[183] As a gas, depressurisation causes complete removal of the solvent CO_2 from products. It is possible to use $scCO_2$ as a reaction medium,[184] but the investment needed for a production plant based on pressure resistant apparatus, and the energy cost of operating the process under pressure brings the economic sustainability of this type of enterprise into doubt.[185]

Two areas where $scCO_2$ can offer advantages as a solvent are advanced materials,[186,187] where the cost of buying and maintaining the solvent system has less impact relatively speaking, and secondly renewable material/natural product pre-processing,[188] and extraction.[189] The iconic application of $scCO_2$ extraction is the decaffeination of coffee (replacing dichloromethane or ethyl acetate).[190] Food applications benefit from carbon dioxide extractions because residual solvent is not left behind as contamination.

More generally, carbon dioxide can be considered a substitute for hydrocarbon solvents,[191] given their similar polarity. It follows that extraction of vegetable oils and plant waxes (currently achieved with *n*-hexane or equivalent solvents) are suited to $scCO_2$ technology. The environmental impact of soybean oil extraction can be improved by substituting *n*-hexane for $scCO_2$, but only after the plant is reengineered according to feedback obtained from life cycle assessment (LCA) results.[192] Process optimisation to reduce the running costs of oil extractions has also been attempted.[193] A techno-economic analysis of supercritical fluid technologies within the concept of a complete biorefinery has shown that it can be favourable to move away from conventional liquid solvent processes.[194] Still, the investment in infrastructure remains a barrier to the adoption of supercritical fluid solvents for low value applications (*e.g.* extractions).[195]

There is another role for supercritical fluids in combination with organic solvents. Many of the perceived "greener" solvents are not very volatile. This direction of progress necessitates a change in recovery technologies, replacing distillation as a method of separation. There is a desire to move away from energy intensive distillation as a means of solvent recovery anyway and so there is no conflict between the development of new solvents and new technologies as they are currently progressing. Solvent recovery by distillation can also be dangerous,[196,197] as well as expensive.[198] One way to make non-volatile solvents more practical is to combine them with a gas to modify the medium, thus changing the solubility of the substrates and even precipitating them from solution. Alternatively, supercritical carbon dioxide is a potential extraction solvent, and has been shown to be capable of removing organic products from both aqueous and organic reaction media.[199–201]

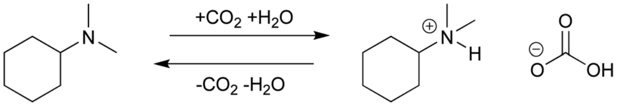
A tuneable solvent is categorised as a medium with variable properties under the control of the user. Carbon dioxide provides ample opportunity to create significant changes in solvent polarity. The gas expanded liquids,[202–206] formed by compressing carbon dioxide in organic solvents can reach ten times the original liquid volume.[203,207] One can imagine that the properties of the gas expanded liquid (GXL) are then markedly different to the organic solvent without the addition of carbon dioxide.[208,209] One advantage of a gas expanded liquid is the improved solubility of gas reactants (*e.g.* hydrogen, carbon monoxide).[210,211] The choice and quantity of organic co-solvent is very important to optimise the polarity of the medium and the solubility of gaseous reactants.[212] After the reaction, the change in polarity achieved by modifying the solvent with carbon dioxide may precipitate the solutes.[213,214] This principle also works to change water miscible solvents (*e.g.* tetrahydrofuran, THF) into biphasic systems upon CO_2 gas expansion.[215] Despite the opportunity to use high boiling point solvents as part of a GXL,[216] common volatile solvents that could be recovered by distillation anyway are still preferred.[217]

Whereas water is able to support hydroformylation of short chain olefins,[171] greasier long chain alkenes require a less polar medium. Jin *et al.* described a process whereby, in CO_2 expanded acetone, 1-octene is reacted, aided by the increased solubility of syngas (hydrogen and carbon monoxide) in the gas expanded medium.[218] The economic and environmental impacts of hydroformylations in gas expanded liquids have been modelled, with the result that potentially both economic and environmental benefits can be achieved if the conventional process were to be superseded.[219] Milder reaction conditions, greater catalyst recovery, and higher product selectivity to linear aldehydes are key reasons why the gas expanded solvent option imparts capital investment and operating cost savings, and reduces emissions. A formal life cycle analysis of 1-octene hydroformylation in CO_2 expanded toluene, and an equivalent process without auxiliary organic solvent, has also been conducted.[220] Without toluene, the associated energy demand of solvent production and recovery is eliminated, and this makes a clear difference to the overall emissions associated with the process. Especially with liquid reactants, the option to exclude any auxiliary solvents should always be considered.

A GXL offers the potential to subtly tune solvent polarity, but in reality the ability to swap between a polar and a non-polar state is what provides a real advantage, and one that could be not achieved otherwise simply through a solvent substitution. Switchable solvents convert lipophilic amines (or amidines) into hydrophilic ammonium carbonate salts (Scheme 4.20).[221] Amines are strongly hydrogen bonding, but share the low dipolarity of hydrocarbon solvents. For this reason, some amines can be used in place of *n*-hexane to extract oils for example,[222] after which addition of water and carbon dioxide allows the solvent to be recovered and the oil purified in one step. The switchable solvent process is reversible upon release of the CO_2 pressure.

4.6 Ionic Liquids and Deep Eutectic Solvents

Ionic liquids are probably the premier neoteric solvents, having grown into a vast area of research in a short period of time.[223,224] Interesting applications of ionic liquids include electroplating,[225] and biomass processing.[226] Research has shown that processes that require cellulose to be dissolved might benefit from 1-butyl-3-methylimidazolium chloride, which has a similar environmental impact to the currently used *N*-methylmorpholine-*N*-oxide.[227]At the turn of the century the prevailing sentiment was one of optimism regarding the greenness of liquid liquids. Earle and Seddon titled their 2000 review "*Ionic liquids. Green solvents for the future*",[228] but now a more cautious path is followed.[229] The environmental impact of ionic liquids is now more well-known,[230] with few authors still assuming that ionic liquids are green just because of their negligible volatility (see Chapter 3, Section 3.3.1). In fact, the volume of organic



Scheme 4.20 An example of a tertiary amine capable of forming a deep eutectic solvent.

solvent used in the synthesis of typical ionic liquids is much more than what they can replace in a single use. Therefore, an ionic liquid needs to be reused many times to suppress the impact of solvent use in its synthesis. It is the lengthy synthesis of typical ionic liquids that also makes them expensive. For some applications, cheaper alternatives are available.[231,232]

Zhang *et al.* have evaluated the environmental impact of the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate, or [bmim][BF_4], using LCA.[233] The life cycle inventory (LCI) requires a synthesis tree, which is drawn in Figure 4.4. Compared to other solvents (water, acetone, lithium perchlorate in diethyl ether (LPDE), and benzene), the use of [bmim][BF_4] as a solvent causes greater environmental damage in all impact categories except ozone depletion, where benzene is worse, and photochemical oxidation potential, where LPDE is worse. As shown in Figure 4.5, the cradle-to-gate life cycle emissions of [bmim][BF_4] production tend to be distinctly higher than those of other solvents. The full list of impact categories is as follows: abiotic depletion potential (ADP), global warming potential (GWP), ozone layer depletion potential (ODP), human toxicity potential (HTP), freshwater aquatic ecotoxicity potential (FAETP), marine aquatic ecotoxicity potential

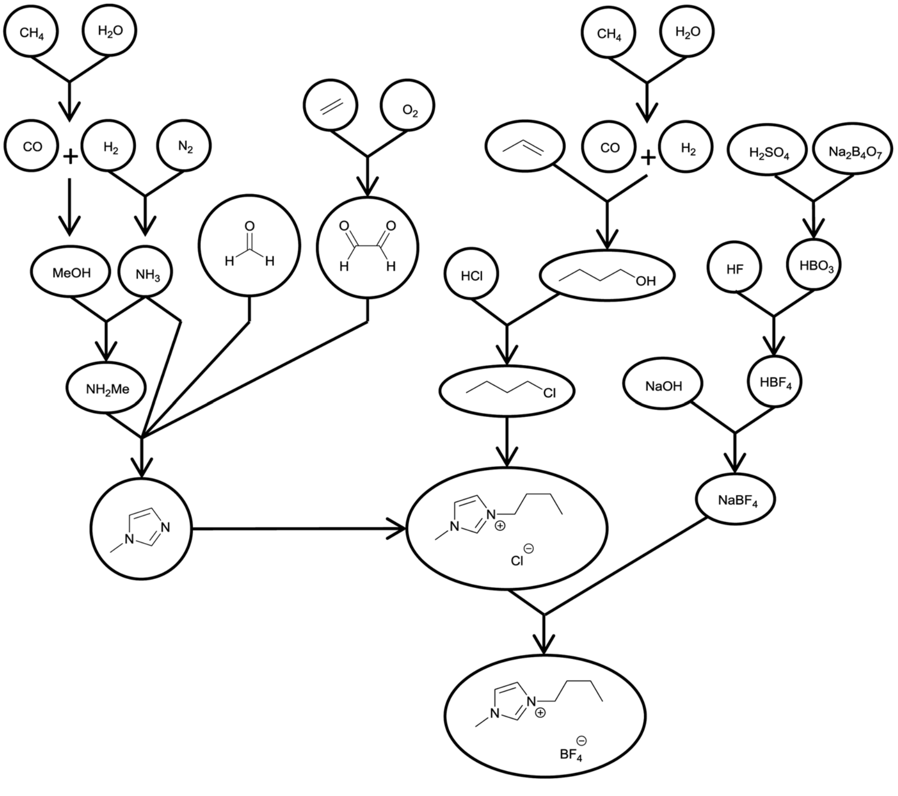


Figure 4.4 A synthesis tree for [bmim][BF_4].[233]

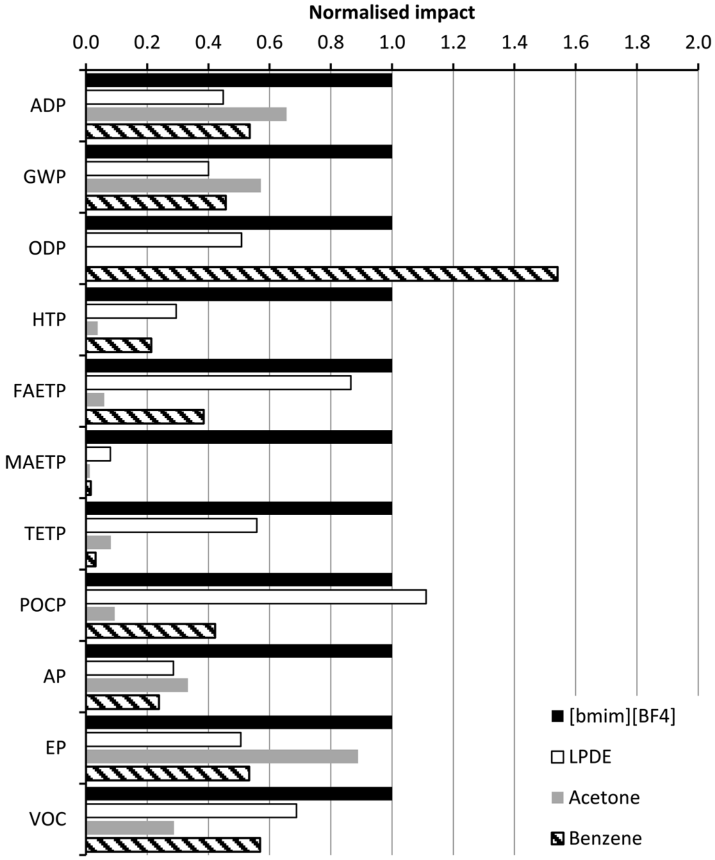


Figure 4.5 Environmental impact category scores normalised against the result for $[bmim][BF_4]$.[226]

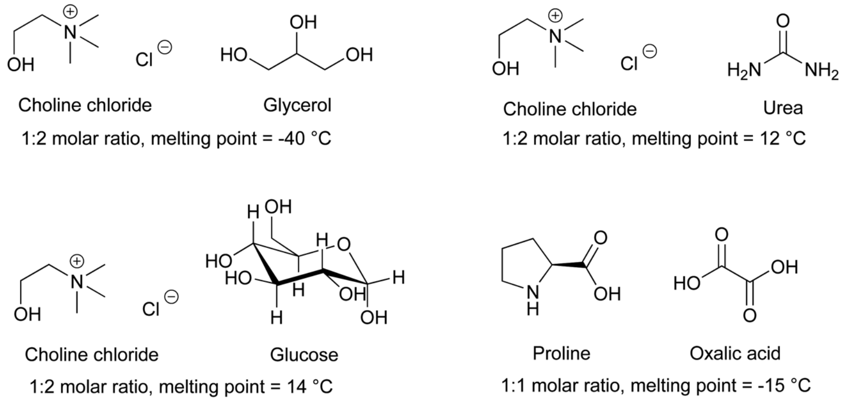
(MAETP), terrestrial ecotoxicity potential (TETP), photochemical oxidation potential (PCOP), acidification potential (AP), eutrophication potential (EP) and volatile organic compound (VOC) emissions.

The boundary of this LCA incorporates applications: the hydrogenation of benzene or an example of the Diels–Alder reaction.[233] What this shows is that a solvent, be it an ionic liquid or otherwise, should not be chosen for a reaction only on the basis of its inherent properties. What it does in the context of an application will determine the impact the solvent has, for better or worse. The environmental impact of the ionic liquid-mediated hydrogenation was extremely poor, but $[bmim][BF_4]$ applied in the Diels–Alder reaction was competitive with water or LPDE. The reason was due to the improved selectivity of the reaction achieved in the ionic liquid, meaning less waste. Products are extracted with diethyl ether, probably allowing $[bmim][BF_4]$ to be reused, further reducing the environmental impacts due to the original synthesis of the ionic liquid.

The sheer breadth of cations and anions available to make ionic liquids means that there is a true possibility to design ionic liquids to be environmentally benign, high performance solvents in their respective niches. The design of a bespoke ionic liquid for carbon dioxide capture, trihexyltetradecylphosphonium 1,2,4-triazolide, was undertaken to resolve the issues presented by the toxic carbon dioxide capture agent monoethanolamine. Although the ionic liquid is less toxic to humans, a life cycle assessment showed that in all other respects monoethanolamine was superior.[234] Greater use of structure–activity relationships,[235] and pursuing the functionalisation of anions in preference to cations,[236] have been suggested as approaches to consider in order to finally create sustainable ionic liquids. Bio-based ionic liquids might be a step in the right direction,[237] or perhaps deep eutectic solvents which lend themselves more readily to renewable platform molecule precursors.

A deep eutectic solvent is formed of two or more components that create a highly polar hydrogen bonded medium.[96] The original components are often high melting point compounds or salts, which if combined in the correct ratio become a eutectic mixture exhibiting a eutectic point (Scheme 4.21). The resulting melting point suppression means room temperature liquid mixtures can be formed. A popular component in deep eutectic solvents is the salt choline chloride.[238] Bio-based molecules are often suited to the formation of eutectic mixtures given their extensive hydrogen bonding ability (sugars, amino acids, glycerol, urea, *etc.*).[239] It is unsurprising therefore that eutectic systems are speculated to contribute to the physiological processes occurring in the cells of living organisms.[240,241]

As highly polar, non-volatile liquids, deep eutectic solvents are thought of in much the same way as ionic liquids. Therefore, it is no surprise that research interest in deep eutectic solvents is cutting into the territory of ionic liquids, including for ionometallurgy,[242] biocatalysis,[243] biomass processing,[244] carbon dioxide capture,[245] and synthesis.[246] Leather processing



Scheme 4.21 Selected deep eutectic solvent systems.[260]

(see Chapter 2, Section 2.10) is also possible in a deep eutectic solvent.[247] Enthusiasm is high regarding the potential of deep eutectic solvents, with bold claims in the literature, reminiscent of the early days of ionic liquid research, being made about the sustainability of these solvents.[248,249,260] However, we are yet to see this translate into actual sustainability assessments proving the social, economic and environmental benefits of deep eutectic solvents.

Unlike the evolution of ionic liquid research, since Abbott's description of deep eutectic solvents in 2003,[250] toxicological studies have advanced rapidly and are now quite comprehensive (if somewhat contradictory in some cases). Taking a very general view, deep eutectic solvents are usually presented as being less toxic than ionic liquids,[251] but this is disputed for ecotoxicity.[252] If a deep eutectic solvent is made of benign compounds, such as choline chloride,[96] and glycerol for example, the resultant mixture might also be assumed to be equally non-toxic. However, research has shown that a synergism between the components of a deep eutectic solvent enhances what (little) toxicity is exhibited by the individual components. This is true of the cytotoxicity of ammonium,[253] and phosphonium,[254] deep eutectic solvents for example. Conversely in some organisms the reverse is true (*e.g.* fish EC_{50} of choline chloride–malonic acid).[255] We cannot assume combinations of compounds will only act as the sum of their parts.[256] One must also be careful not to treat all deep eutectic solvents as if they were the same because they are an extremely diverse collection of substances. This is also demonstrated by the range of biodegradability results determined for common deep eutectic solvents in the hands of different scientists using different test methods.[257–259] Given time to mature, it is possible that the field of deep eutectic solvent research will eventually demonstrate significant advantages over conventional solvents across the whole spectrum of sustainability indicators.

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CHAPTER 5

Green Chemistry Concepts and Metrics for Solvent Selection

5.1 Solvents and the Green Chemistry Philosophy

Green chemistry was established in the context of risk assessment, hazard avoidance, and the design of inherently benign chemical products in order to achieve this. Implementing green chemistry practices does not necessarily result in sustainable chemistry, because the latter is measured by achieving certain agreed objectives that minimise negative social, economic and environmental impacts. Green chemistry is limited to the application of experimental principles and product/process design (without necessarily involving quantification) that direct progress towards environmentally benign, low risk chemistry. This may not go so far as to fulfil all the far reaching aims of sustainable development.[1] This chapter provides stronger links between green solvents and the ultimate objective of using solvents in a sustainable way (Section 5.1). Also offered is a comprehensive interpretation of what a green solvent is, or must do, and how this relates to the aforementioned criteria of sustainable development (Section 5.2). It is not only environmental health and safety issues that are important. It is crucial that the correct solvent is chosen and used appropriately. Solvent selection procedures and tools exist in order to achieve this, as explained in Section 5.3. If no suitable solvents are available, which might be on the basis of combined requirements of performance and greenness, a new solvent needs to be designed (Section 5.4). As more and more solvents come under regulatory control, demand for solvent design and ultimately the realisation of new solvent products is set to increase.

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The topic of green chemistry is not a precise science, but an interpretation of best practice for environmental protection. That being the case, it is not surprising that the concept of green chemistry has been subject to lengthy philosophical debate.[2] To understand green chemistry, it is first helpful to review the 12 principles of green chemistry,[3,4] the guidelines that direct chemistry on the way towards potential sustainability.[5] Armed with a dozen principles with which to evaluate alternative chemical value chains, the greenest option can be judged in much the same way that a LCA can be used for comparisons between process options. The way in which an LCA is different to green chemistry is that impact categories show what happens in terms of emissions, resource use, *etc.* Green chemistry is a means to avoid chemical risks in the first place. The 12 principles of green chemistry do not provide thresholds, and so using these principles alone, a definitive indication that a process or product is green is not achievable. However suitable thresholds could be imagined. For example, regarding the prevention of waste (principle 1), no waste would obviously be a satisfactory outcome. In some instances, the definition of waste is important because some materials can be recovered and recycled. There is a difference between inherent waste, such as the loss of chemical groups substituted in a reaction, and auxiliary waste, such as solvents. Some waste is benign while others consist of toxic or environmentally damaging substances. The design of a process holds the key to reducing waste, and this includes the choice of solvent, and in what amounts, and how it is recovered (if at all).

Table 5.1 lists the 12 principles of green chemistry, also noting their relevance to solvents. The emphasis is very much on synthetic chemistry. The three pillars of sustainability are not sufficiently represented. Green chemistry is advantageous to workers and consumers for health and safety reasons, and clearly another benefit is the preservation of the environment. However economic and most social concerns are not included, and other methods must be used alongside the guidance of the 12 principles of green chemistry to have a complete framework in place to evaluate whether a sustainable outcome is reached.

Green chemistry principle number 5 is the most provocative in a book dedicated to solvents, but it is important to question solvent use. Why are organic solvents used, and why given the large choice of available solvents are toxic and environmentally damaging solvents in widespread use? To answer these questions we must appreciate the problems that solvents solve. Essentially the reactivity of chemicals requires them to be mobile. As a solution, individual molecules are free to orientate and interact, giving rise to chemical reactions under the correct conditions. Formulations use solvents to modify viscosity but mainly to create a homogeneous distribution of ingredients and produce a stable dispersion. Sometimes a solvent does not contribute to the desired performance of a product but the application of the formulation relies heavily on a solvent to maintain a solution. This is true of paints and coatings, which must be fluid initially, but to act as a paint or coating must be dry and free of solvent. The reason why so many of our necessary solvents

Table 5.1 The 12 principles of green chemistry according to Anastas and Warner.[3]

	Principle	Solvent impact
1	*It is better to prevent waste than to treat or clean up waste after it has been created*	Solvents are unchanged during a reaction or as a medium for formulation, only contaminated. They then become a major source of waste in chemical manufacturing. Some solvents can be recovered by distillation. If resorting to the fact that the solvent is an unrecoverable waste, many solvents are biodegradable and can be treated in appropriate facilities
2	*Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product*	Solvents are auxiliary to the reactants in chemical synthesis. When producing solvents, the reactions used are typically highly efficient
3	*Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment*	Some solvents have high toxicity. Solvent substitution should be applied to avoid the most toxic solvents
4	*Chemical products should be designed to affect their desired function while minimizing their toxicity*	Beyond solvent substitution selecting from the present day catalogue of solvents, new bespoke solvents can be designed for specific applications to eliminate intolerable toxicity issues
5	*The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used*	Solvents are the most abundant auxiliary substances in reaction chemistry and formulations. All possible attempts to reduce solvent use should be made
6	*Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure*	The use of solvents is closely linked to energy. As the major component of most processes, the energy of heating is mostly being used to raise the temperature of the solvent. Then distillation to recover the solvent is also energy intensive. Greater availability of catalysts active at ambient temperature and solvents with alternative methods of recovery are needed
7	*A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable*	Bio-based solvents are available and offer advantages documented throughout this book
8	*Unnecessary derivatization (use of blocking groups, protection/deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste*	Not relevant to the synthesis of solvents. Any extra reaction chemistry will lead to increased solvent use with the highlighted issues of waste and energy requirements exacerbated

9	*Catalytic reagents (as selective as possible) are superior to stoichiometric reagents*	Not relevant to solvents, although solvents influence reaction kinetics in the same way as catalysts, but additionally also modify equilibria. There are examples where the partnership of solvent and catalyst is synergetic in improving the reaction[142,143]
10	*Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment*	Most solvents are readily biodegradable in effluent treatment plants. Ultimate biodegradability in the environment is a higher standard required of solvents used outside of (controlled) laboratory or plant conditions. Solvents are typically volatile and therefore their end-of-life is ultimately dictated by atmospheric chemical (radical) processes
11	*Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances*	Not relevant to solvent use, but can be applied to solvent production
12	*Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires*	Solvents are helpful as heat sinks, controlling exothermic reactions to a degree. Solvents present their own risks, including flammability and volatility, and ethers oxidise to peroxides

are toxic or environmentally damaging is because this was never part of the specification. Availability, fluidity and volatility have always been the leading priorities.

To replace organic solvents, formulations can use water as the solvent in many cases, and cleaning solvents can be replaced by aqueous surfactants. Reaction chemistry is where solvent-less conditions have been most successful. Liquid organic reactants are able to mix of their own accord, but solids pose a problem. If the mixing of solids can be made effective, then many reactions will in fact proceed without an additional solvent being required. Mechanochemistry is the discipline of grinding solid reactants together, usually with a ball mill, to initiate solvent-less reactions.[6,7] However the dependence on a solution is not shaken off completely, because the heat generated in a ball mill can potentially cause localised hot spots that cause the melting of the reactants and thereby better (liquid) mixing. Also, moisture present will act as a solvent. The term “solvent-less chemistry” is convenient but can only be taken to mean a lack of purposefully added auxiliary solvent(s). Liquid reactants act as a solvent if no auxiliary solvent is added.[8] Care must be taken to devise a means of removing the product from a ball mill and purifying it without the excessive use of solvent. Otherwise the modest volume of reaction solvent saved makes little or no impact.

5.2 Principles of Green Solvents

In 2013, Gu and Jérôme collaborated to produce the first definitive review of bio-based solvents.[9] In this work they outline principles that define a green solvent. The final criterion concerns the renewability of the feedstock, and hence a specific link to bio-based solvents is made. The 12 rules are listed here as they appear in the original publication (Table 5.2), and later will be considered in greater detail.

Of course others have also attempted to define a 'green solvent' through formal criteria. Most notably Jessop presented four 'grand challenges' for green solvents: preparing sufficient replacements for ungreen solvents (guided through polarity mapping), recognising green solvents in the first place, finding removable dipolar aprotic solvents, and the development of solvents that do not require distillation.[10] With respect to the second challenge, Jessop's own answer is a list of 9 indicators that act as a quick guide,

Table 5.2 The 12 criteria of Gu and Jérôme that define green solvents.[9]

	Criteria	Description
1	Availability	*A green solvent needs to be available on a large scale, and the production capacity should not greatly fluctuate in order to ensure a constant availability of the solvent on the market*
2	Price	*Green solvents have to be not only competitive in terms of price but also their price should not be volatile during time in order to ensure sustainability of the chemical process*
3	Recyclability	*In all chemical processes, a green solvent has to be fully recycled, of course using eco-efficient procedures*
4	Grade	*Technical grade solvents are preferred in order to avoid energy-consuming purification processes required to obtain highly pure solvents*
5	Synthesis	*Green solvents should be prepared through an energy-saving process and the synthetic reactions should have high atom-economy*
6	Toxicity	*Green solvents have to exhibit negligible toxicity in order to reduce all risks when manipulated by humans or released in nature when used for personal and home care, paints, etc.*
7	Biodegradability	*Green solvents should be biodegradable and should not produce toxic metabolites*
8	Performance	*To be eligible, a green solvent should exhibit similar and even superior performances (viscosity, polarity, density, etc.) compared to currently employed solvents*
9	Stability	*For use in a chemical process, a green solvent has to be thermally and (electro)chemically stable*
10	Flammability	*For safety reasons during manipulation, a green solvent should not be flammable*
11	Storage	*A green solvent should be easy to store and should fulfil all legislations to be safely transported either by road, train, boat or plane*
12	Renewability	*The use of renewable raw materials for the production of green solvents should be favored with respect to the carbon footprint*

enabling the user to speedily rule out certain solvents that may have otherwise been mistakenly considered as a greener alternative. These questions are presented in Table 5.3, and are unmodified from the original publication.[10] Any questions to which the answer is 'yes' is indicative of an ungreen solvent.

Jessop recommends preparing a synthesis tree to show how many chemical transformations are required to manufacture a solvent, and what chemicals are required, in order to answer his questions (with the exception of question (f)) (Figure 5.1). This is crucial to this approach, which is almost entirely devoted to the critique of solvent production and does not address solvent application or disposal. The number of reactions increases rapidly with every modification because even a routine transformation (such as the esterification of a carboxylic acid for example) is not necessarily just one reaction. All the processes that are required beforehand to make a given reactant are equally important to consider in the context of a synthesis tree. There are limitations to this approach. In practice it is unwieldy to produce correct synthesis trees to describe a complete synthesis beginning at raw materials. To produce an LCA, the synthesis tree only needs to go back as far as the materials contained in life cycle inventory databases anyway. Furthermore, challenging and energy intensive reactions are given an equal footing alongside energy efficient processes to produce commodity substances such as carbon monoxide and hydrogen (syngas) with little waste.

With respect to question (a) in particular (Table 5.3), as with several of the other stipulations posed by Jessop, the subjective nature of the assessment makes conclusive decisions difficult to reach, and the answer inferior to a quantitative calculation of cumulative energy demand (CED) for instance (see Section 5.2.1.1). The length of a conventional solvent synthesis chosen

Table 5.3 Jessop's rules for the synthesis of green solvents.[10]

Rule	Question
(a)	Does the family tree have many more steps than is the case with other solvents?
(b)	Are there any phosphorus compounds in the synthesis tree (eutrophication risk)?
(c)	Are there any highly dangerous compounds (*e.g.* HCN, HF)?
(d)	Are there any volatile compounds of N, S, Cl, Br, F (acid rain formation)?
(e)	Are there any compounds that are very hydrophobic, having a log $K_{OW} > 4.3$ (bioaccumulation risk)?
(f)	Does the solvent have an LD_{50} (rat, oral) between 50 and 500 mg kg^{-1} (moderate toxicity) or <50 mg kg^{-1} (high toxicity)?
(g)	Are there any volatile halogenated organics (global warming and ozone depletion risks)?
(h)	Does the synthesis (or any of the catalysts in the synthesis) require any elements at risk of depletion? They are, in order of decreasing risk: Xe >> He > Au > Ir, Rh, Ru > Kr, Os > Pt, Sb, Re, Hg, Se, Cd, Ne, Pd, Sn
(i)	Are there any volatile organic C_2–C_7 compounds, especially unsaturated molecules (smog formation risk)?

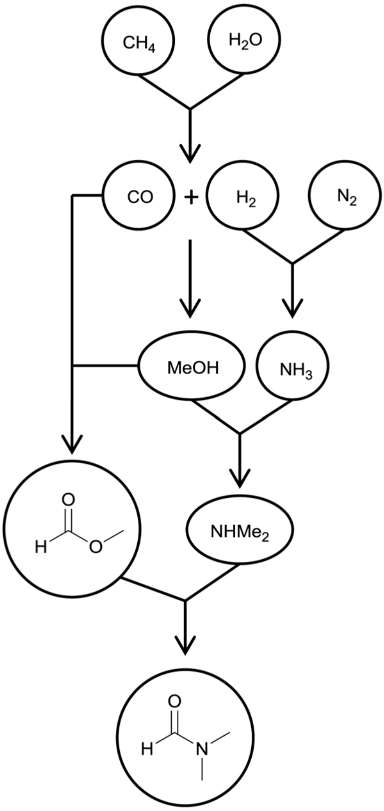


Figure 5.1 A synthesis tree for *N*,*N*-dimethyl formamide.[10]

for comparison may already be too long: the shorter the synthesis, the less energy and materials it can consume. We propose a rule of thumb that no more than 2 reactions are used from a recognised bio-based platform molecule (not starting from the raw biomass) in order to produce a solvent. This reduces the complexity of the synthesis tree, and the use of more routine transformations (*e.g.* hydrogenation) does not reflect badly on the synthesis (we consider hydrogenation to be one step, whereas in the full synthesis tree an additional step is needed to convert natural gas into syngas). As described in Chapter 3, Section 3.1.3.1, methanol is considered as a feedstock not an intermediate in this approach. The same applies to bio-ethanol, 5-(hydroxymethyl)furfural (HMF), and other platform molecules.

It is preferable to have reasonable benchmarks and thresholds (taken from regulation where possible), as the basis of an assessment. Eutrophication (question (b), Table 5.3), acidification (d), global warming potential (g) and low level ozone (smog) creation (i) can be measured in a life cycle assessment (LCA). Safety (question (c)), toxicity (f) and ecotoxicity (e) requirements should be aligned with regulated limits prescribed in the United Nations (UN) Globally Harmonised System (GHS) of classification

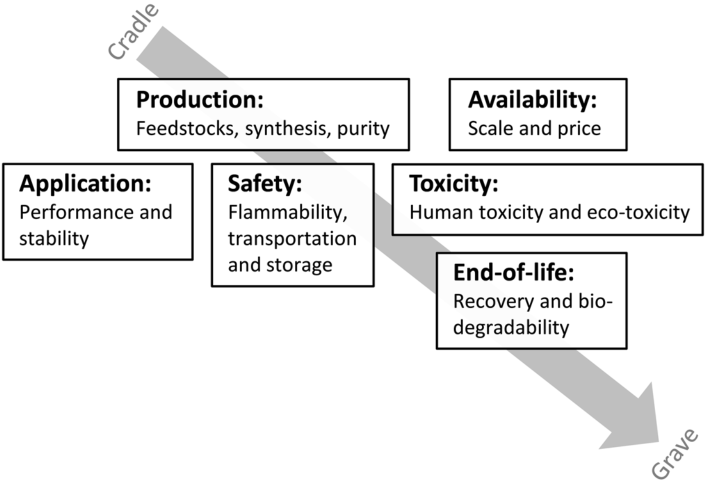


Figure 5.2 Cradle-to-grave categories of green solvents.

and labelling of chemicals,[11] and European REACH Regulation ((EC) No 1907/2006) documentation, for example.[12] The sustainability of elements is more precisely related to reserves and recycling rates elsewhere by Dodson *et al.* (question (h)).[13]

Using the work of Jessop,[10] and Gu and Jérôme,[9] some general principles to guide sustainable solvent design, production and application can be formulated. To discuss these concepts in more detail, six categories have been created from the proposals of the aforementioned authors (Figure 5.2). With reference to Gu and Jérôme's numbered rules, these are solvent production (principle 4, 5, and 12), availability (1 and 2), performance and stability (8 and 9), toxicity (6), safety and storage (10 and 11), and end-of-life (3 and 7) (Figure 5.2). Our intention here is to make the intuitive rulings posed by Jessop, Gu, and Jérôme more easily transferable towards the understanding of the sustainability of solvent production, use, and end-of-life management.

5.2.1 Production

Firstly, we consider the feedstock, the synthesis, and the resultant purity of the solvent. Gu and Jérôme stated that "*the use of renewable raw materials for the production of green solvents should be favored with respect to the carbon footprint*" in their final principle.[9] We can infer from this an assumption that the carbon footprint is improved by replacing fossil feedstocks with biomass or various wastes (including recyclates and carbon dioxide) to make solvents. This is not automatically true in every case, but potential benefits are created with a renewable feedstock, primarily the displacement of carbon from the long-term carbon cycle. What was an assumption proposed by Gu and Jérôme can be elaborated into an unconditional requirement that the feedstock for solvent production is sustainable, meaning certified biomass, excluding virgin fossil resources by definition.

The availability and cost of suitable feedstocks is a crucial challenge for a sustainable chemical industry. We are, at the time of writing, in a period of relatively cheap oil but also one in which the price is volatile and unpredictable. In 2010, the price of a barrel of crude oil was $80–120.[14] However, by the end of 2014, this had reduced by half, with a further price drop down to $30 per barrel at the beginning of 2016. Since then the price has recovered to $50+ per barrel. Fracking has also created low cost methane.[15] In truth, the low oil price is indicative of the price volatility of fossil fuels, dictated by the rate of production set by a few prominent oil producing countries. This luxury cannot last indefinitely, as fossil fuel is not a sustainable commodity in the sense that there is only a finite supply.

To successfully replace crude oil and natural gas resources for chemical production, the type of biomass and its source is crucial. Biomass is predominately grown for food (animal and human).[16] With demand for food and feed projected to double this century, growth in the renewable chemical industry is not compatible with unrestricted use of food for non-food purposes.[17] In this respect more needs to be done to advance cellulosic feedstock transformations towards economic sustainability to in turn fulfil our social and environmental obligations.

Additionally, secondary fossil materials (waste petrochemicals and materials) are already in circulation, and should not automatically be excluded as a sustainable precursor for solvent production. In fact, if a use is found for these waste articles rather than landfill or incineration, the carbon is locked away for longer, and in the form of an organic solvent it also provides a beneficial service. It is surely preferable to do that than resort to other pollution mitigation practices such as the sequestering of carbon dioxide underground. Solvents made of CO_2 are in theory complimentary to carbon reduction policy, but in practice the energy required to make them (carbonates for example) is responsible for greater carbon emissions than what is captured within the solvent.[1] Standardised requirements demonstrating the sustainability of wastes repurposed as chemical feedstocks were discussed in Chapter 3.[18]

That said, biomass is the most promising feedstock for sustainable solvents. Primary biomass in the form of dedicated crops offers the most flexibility and opportunity for bio-based products. It is a renewable feedstock and the scale of production is market driven according to downstream product demand, but meanwhile limited by the availability of land. The harvest volumes achieved will be subject to variability year by year due to weather conditions and disease, creating fluctuations to supply. This means that we will not break free of price volatility by moving increasingly towards renewable feedstocks. Where at all possible, the availability of agricultural residues and wastes instead should be examined and contemplated as a feedstock. However, the quantities of these so-called residues available for use in symbiotic industries depends on the success of the processes that create these wastes. It is not always the case that these are true wastes, but might be surplus, and it must be appreciated that their price and availability can fluctuate for this reason also. To secure the required scale to produce bio-based solvents, primary biomass will have to be used to a large extent for the foreseeable future, as is true in the case of biofuels (*e.g.* first generation bio-ethanol).

To copy the business model established by the petrochemical industry, dedicated manufacturing processes are necessarily only reserved for high value products and the most vital of those products. Otherwise, from the network of commodity chemicals that are produced to serve a multitude of other markets, solvent products and their immediate precursors can be filtered away from the primary production chain. Another way solvents are obtained is as by-products and minor product streams.[19] The bio-based economy needs to expand so that a stable network of renewable chemical production is established, sufficient to provide a mixture of small-scale high-value products and also serve the larger chemical commodities market. From this, a few speciality solvents might be made, but more commonly solvent production will rely on products for other markets, which stabilises production scale and cost. The polylactic acid (PLA) market for instance means bio-based lactic acid is available on the market and can be applied in secondary uses, directly as a solvent or modified to an ester solvent. If isosorbide is produced as a precursor for surfactants, dimethyl isosorbide becomes much more viable as a bio-based solvent. Bio-ethanol production exists to create fuel, but also facilitates an industry based on the dehydration of ethanol to ethylene for the production of plastics, *i.e.* polyethylene,[20] and PET from ethylene glycol.[21] Ethylene glycol also has applications as a solvent, whether it is derived from bio-ethanol or otherwise (Figure 5.3). Therefore, the economics controlling the conversion of bio-ethanol into glycols

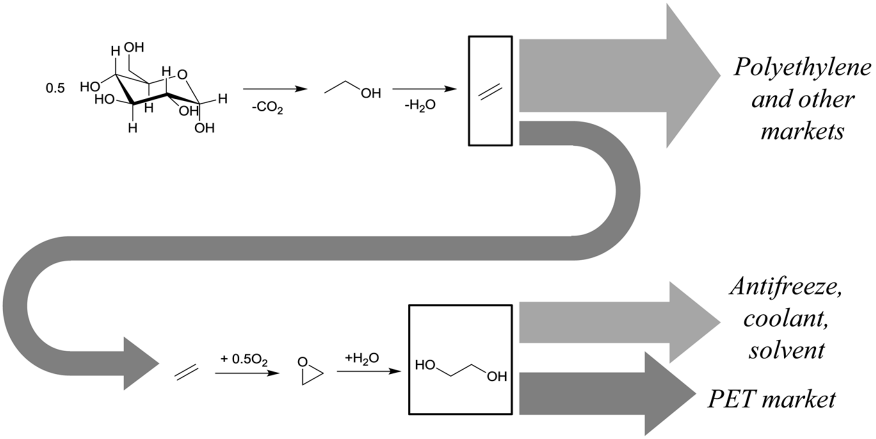


Figure 5.3 Indicative value chain of bio-ethylene produced by carbohydrate (sugars or starch) fermentation.

Table 5.4 A selection of green chemistry metrics.

Metric	Calculation
Atom economy[144]	$\frac{\text{Molecular mass of product / kg}}{\text{Combined molecular mass of reactants / kg}}$
Reaction mass efficiency	$\frac{\text{Mass of product / kg}}{\text{Mass of reactants / kg}}$
Process mass intensity	$\frac{\text{Total mass input / kg}}{\text{Mass of product / kg}}$
Renewables intensity[23]	$\frac{\text{Mass of renewable materials used / kg}}{\text{Mass of product / kg}}$
Waste intensity[23]	$\frac{\text{Mass of waste / kg}}{\text{Total mass input / kg}}$

and glycol ether solvents (all *via* ethylene oxide) relies on a market pull for fuels and bio-based polymers, as well as demand for antifreeze, cooling fluids, and other solvent products, in what is a complex scenario involving many interconnected value chains.

Green solvent principle number 5 is that "*green solvents should be prepared through an energy-saving process and the synthetic reactions should have high atom-economy*" (Table 5.2).[9] Jessop's rules (Table 5.3) provide an elaboration of this when it comes to the types of substance employed and what to avoid.[10] As for metrics to report the energy and mass efficiency of reaction chemistry, and therefore facilitate a decision making process regarding the choice of synthesis, various calculations exist (Table 5.4).[22,23] Gu and Jérôme allude to atom economy, which is just one of many metrics used to quantify the (inherent) efficiency of chemical reactions.[24] A metrics toolkit developed by the European CHEM21 project (a public–private partnership established under the Innovative Medicines Initiative,[25] consisting of pharmaceutical companies and research centres) unifies the application of metrics and introduces new calculations by which to evaluate the efficiency of reaction chemistry.[23]

The purity of a solvent is a consequence of its synthesis. It must be well defined and establish a consistent specification that consumers find acceptable and reliable. Gu and Jérôme favour a technical grade specification (>90% purity) but this would be unacceptable to many solvent users. It is true that if an unnecessarily arduous and energy intensive purification is routinely performed to complete the synthesis of a solvent, then the increased energy demand will be reflected in the sale price. This has an impact on the environmental and economic sustainability of the solvent product. Where possible, different specifications should be made available to suit different markets where they exist.

5.2.1.1 Cumulative Energy Demand of Bio-Based Solvent Production

The production of solvents has been studied in detail, and the cumulative energy demand (CED) for the synthesis of conventional petrochemical solvents has been modelled extensively (see Chapter 3, Section 3.1.3.1).[26] It is not a straightforward task to obtain equivalent data for new routes to solvents, but a few examples can be found in the literature for certain bio-based chemicals. It is important to consider that new technologies operating on a smaller scale than petrochemical solvent production will likely benefit from increased energy efficiencies in the future. Nevertheless, it is important that renewable feedstocks are competitive with the petrochemical industry, even in their infancy (and when crude oil is cheap). The same solvent, but prepared from different raw materials, and also perhaps by different processes, can be compared directly to the conventional product using CED. For instance, the production of petrochemical ethanol and bio-ethanol from fermentation can be compared like-for-like on energy terms, cradle-to-gate. This also offers a reasonable indication of the economic viability of different routes to the same product, with the cost of higher energy consumption during production necessarily being offset by higher end-product prices. The CED of a chemical synthesis is proportional to the degree of different environmental impacts too.[27]

Bio-ethanol is a key product in the bio-based economy. The production of bio-ethanol by fermentation requires more energy than the hydration of petrochemical ethylene,[19] although this has not prevented commercialisation on a huge scale. The fact that bio-ethanol is bio-based is the reason that it exists (as a fuel). Most bio-based solvents cannot command a higher price tag than their petrochemical counterparts simply because they are renewable. Other benefits need to be proven to establish a market for more expensive solvent products. In Figure 5.4, the CED for each step in the synthesis of ethanol is plotted as a function of the degree of oxidation achieved. This is extended to bio-based ethylene to emphasise the contrasting situations of the oil refinery and the biorefinery. Petrochemical ethylene is oxidised to ethanol with a reduction of CED (mass basis). The biorefinery moves in the opposite direction, requiring energy to decrease oxygen content, and necessarily converting bio-ethanol to ethylene rather than the other way around. The implication is that the production of bio-based ethylene glycol and glycol ethers from bio-ethylene would require a very high amount of energy. Therefore, these bio-based products become less economically appealing and will find it harder to compete in the solvent market.

Similarly, producing acetic acid from bio-ethanol by oxidative fermentation will carry a high CED. Instead, acetogenic microorganisms can produce acetic acid directly under anaerobic conditions, reducing the number of reaction steps. Another advantage is the inherent carbon efficiency. Fermentation to give ethanol co-produces an equal molar amount of carbon dioxide, but this is not the case for direct acetic acid formation.[28] There are even life

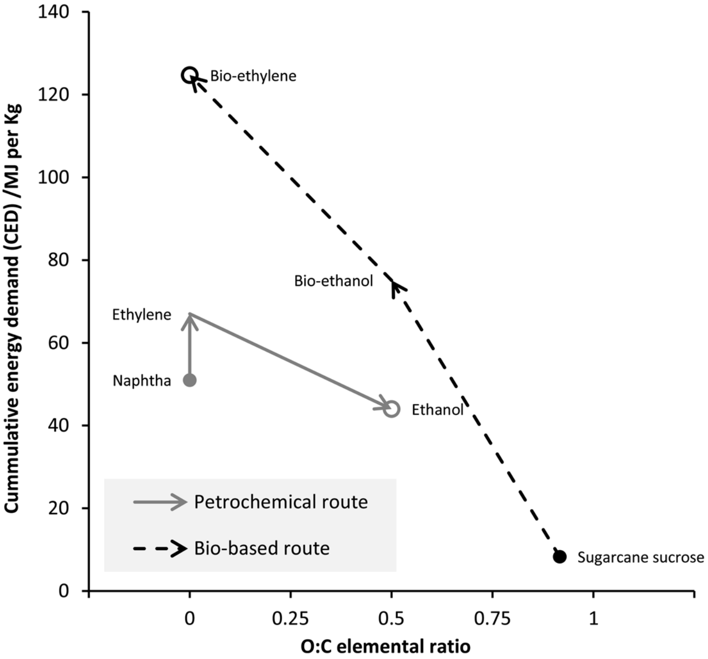


Figure 5.4 A comparison between petrochemical and bio-based ethanol and ethylene production energy.[26,139–141]

cycle benefits to producing bio-ethanol *via* the seemingly longer route from acetic acid.[29] The CED graph for acetic acid shows a very energy intensive fermentation process (Figure 5.5). Future advances in continuous fermentation technology are predicted to bring bio-based acetic acid production more in line with the expectations for energy consumption established by the petrochemical industry.[140]

Given the high CED of bio-ethanol and bio-based acetic acid production, the conditions for renewable ethyl acetate manufacturing do not seem not terribly favourable. However, ethyl acetate does not need to be made by Fischer esterification of its respective carboxylic acid and alcohol. Dehydrogenative coupling of ethanol (as in the Tishchenko reaction) is also viable as a means of producing ethyl acetate.[30] This process provides an opportunity for bio-based ethyl acetate that is competitive with the conventional product, and in fact the CED of the renewable route to ethyl acetate is reported as being comparable to the conventional Fischer esterification of petrochemical ethanol and acetic acid.[31] Two calculated values of the CED for petrochemical ethyl acetate of 84 MJ kg^{-1},[26] and 96 MJ kg^{-1},[32] are available. Using literature data, the CED of bio-based ethyl acetate made by ethanol dehydrogenation is also 96 MJ kg^{-1}.[33] This is shown in Figure 5.6, where the arrow between acetic acid and the higher estimate of fossil-derived ethyl acetate has been omitted for clarity. Production of ethyl acetate from renewable feedstocks has been

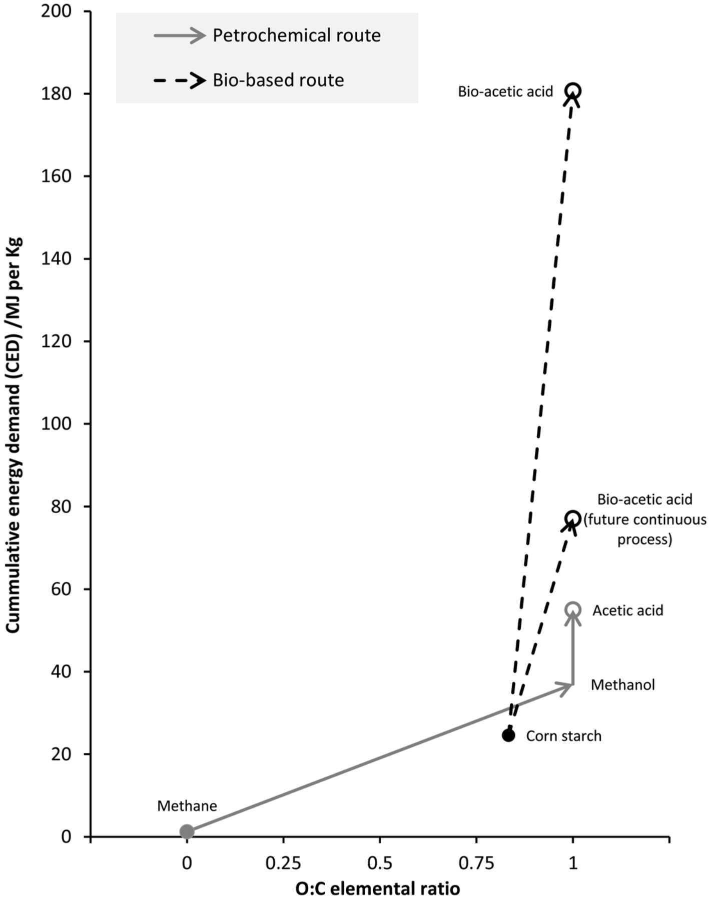


Figure 5.5 A comparison between petrochemical and bio-based acetic acid production energy.[19,26,140]

on the cusp of becoming an established process for some time,[34] but feedstock economics and limited markets due to the product purity achieved have dampened success up to now (see Appendix).

5.2.2 Availability

It is imperative that greener solvents, as alternatives to the less desirable conventional solvents, are available to purchase in suitable quantities, and at a competitive price. This is not true of the subjects of many academic studies involving the discovery and development of new applications for neoteric solvents. In the majority of published examples there is no aspiration to translate these proof-of-concept studies into manufacturing scale solvent production, and equally it is not warranted on the available evidence of performance, toxicity, *etc.* anyway. Some neoteric solvents have been

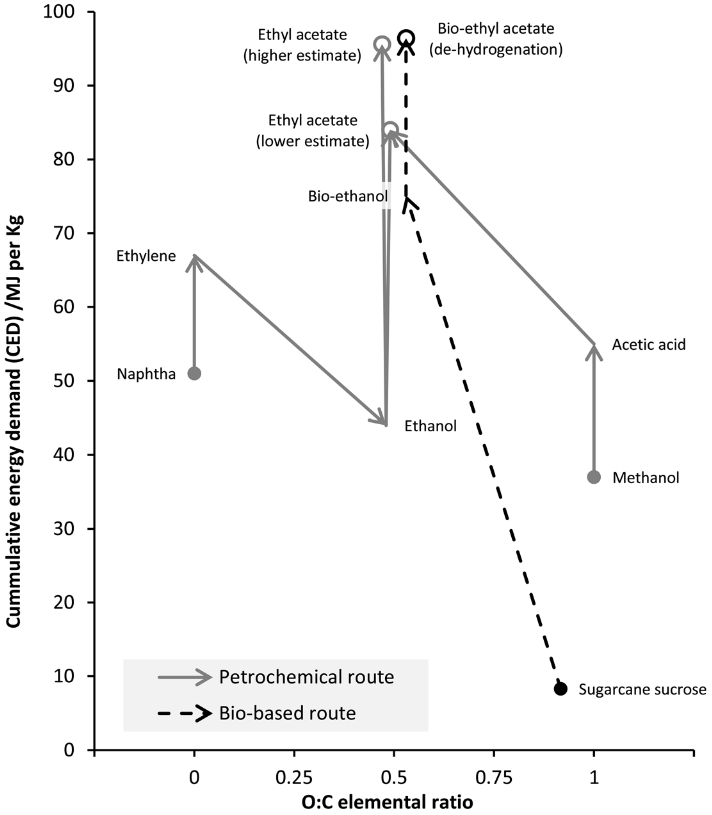


Figure 5.6 A comparison between petrochemical and bio-based ethyl acetate production energy.

commercialised, and a few ionic liquids are an example of this. However, ionic liquids remain expensive and applications that suit an ionic liquid solvent are rarely justified by sufficient benefits to initiate a change in solvent.[35] In one rare example, Chevron recently announced that it will be changing to an ionic liquid system for catalysed alkylation chemistry.[36,37] Here, the role of the ionic liquid is primarily catalysis not solvation. Alternative options are acid-base ionic liquids (which are not true ionic liquids but rather the result of a hugely favourable equilibrium position between a base (*e.g.* a tertiary amine, methylimidazole), and an acid (*e.g.* sulphuric acid, sulphonic acids)), which have been shown to be affordable.[38,39]

The connection between solvent availability and its sustainability is perhaps not the most obvious, but it is important. Industrial and commercial sector solvent users are right to be wary of products with only one supplier. The longevity of a process dependant on a solvent with a single supply source is vulnerable, and with that comes economic sustainability issues. Further upstream, the sources and types of biomass required for bio-based solvent production are best if they are non-specific. Whereas a medicinal product may completely rely on a specific biomass source from which it is extracted, a solvent should ideally not have a chemical structure that is only realistically achievable from a niche feedstock. Solvents derived from carbohydrate or lignin will be more appealing to participants downstream in the supply chain than extracts from a major crop (*e.g.* limonene from citrus fruits), which are themselves preferable to specific extracts from less common crops (of which no commercially relevant solvents exist for these reasons). The price of limonene is related to its availability, which in 2012 peaked because of disease and weather conditions curtailing citrus crops in the Americas (Brazil and Florida specifically as the two major producing regions).[40] Citrus fruit production is also seasonal, which introduces a natural variation to supply across the year. This is why there is a market for limonene replacements with a stable price.[41]

The cost of the solvent will always be a key deciding factor for customers. Solvents are a mostly low value, high volume market. It is difficult to justify using greener solvents if they are a more expensive option for the same performance. Gu and Jérôme state in their second principle of green solvents that "*green solvents have to be not only competitive in terms of price but also their price should not be volatile during time in order to ensure sustainability of the chemical process*". Having said that, higher performance or more facile recovery can lead to overall economic benefits, and so there is a route to commercialise 'premium' solvents (expensive at the point of purchase) if the market is there.

5.2.3 Application

Rules 8 and 9 within Gu and Jérôme's principles of green solvents have been combined into this single category to consider performance and stability together as 'application'. Stability is a universal performance criterion, relevant to every application. It is absolutely essential, but not usually granted special attention as a characteristic of a solvent. Gu and Jérôme state that "*for use in a chemical process, a green solvent has to be thermally and (electro) chemically stable*".[9] This is true of all solvents, but it will be application specific depending on the chemical functionality present. In particular, reactivity limits the use of alcohols, ketones and esters for reaction chemistry more than any other type of popular solvent. These classes of solvent are common in cosmetic and cleaning formulations, demonstrating that they are powerful solvents nonetheless in non-reactive circumstances.

As will be described in Section 5.3, the performance of a solvent candidate can be established using a comparison to the conventional solvents used in that product or process. Better still, a set of criteria that define the requirements of the solvent in terms of physical properties (and environmental properties as relevant) can be used for solvent selection purposes. This reduces the workload compared to 'trial-and-error' investigations. It is clear that green solvent substitutes that replace a conventional solvent in all of their applications with equal performance will never exist. More likely, there will be a range of candidates with increasing specialism because of differences in boiling point, functionality, viscosity *etc.* Limonene is a high performance degreaser to replace petrochemical hydrocarbons, but cannot be used in place of *n*-hexane for extractions because its high boiling point typically prevents recovery. Limonene also has reactive alkene functionality and so is not broadly speaking a solvent for reaction chemistry. Therefore, other alternative solvents need to be proven to perform well across the applications of *n*-hexane to work towards a justified phase-out of this ecotoxic solvent with serious health hazards.

5.2.4 Toxicity

Gu and Jérôme demand negligible toxicity of their green solvents: "*Green solvents have to exhibit negligible toxicity in order to reduce all risks when manipulated by humans or released in nature when used for personal and home care, paints, etc.*" (principle 6).[9] Although the ambition is laudable, an argument can be made against this position. To be pedantic, any substance is toxic if the necessary dose or exposure level is reached. The large number of solvents needed for all purposes probably means that, in a best case scenario, mildly toxic solvents will still have to be used on occasion in appropriate circumstances. For the foreseeable future, solvents will remain an integral part of the chemical industry, and toxicity will have to be managed like any other chemical hazard. So the question becomes one of acceptability. Based on the direction of evolving regulations, chronic toxicity is definitely unacceptable. From the UN GHS,[11] we have formally defined ranges of acute toxicity. For instance, an LD_{50} (rat, oral) below 300 mg kg^{-1} is considered toxic (or even fatal below 50 mg kg^{-1}), and harmful between 300 mg kg^{-1} and 2000 mg kg^{-1}. This is a wider and therefore stricter range than that offered by Jessop (Table 5.3).[10]

One of the biggest problems with toxicity is the misunderstanding of the many different potential modes of human toxicity and how animal tests relate to human effects, and consequently gathering the resources in order to determine them all. The toxicity of solvents has historically been assumed to be low until scientific data confirms otherwise, but by then irreversible damage has already been done. The use of carcinogenic benzene as a solvent in the 20th century was phased out in favour of toluene, another toxic solvent. An early report on *N*-methyl pyrrolidinone (NMP) claimed that it was non-toxic,[42] but we now know that this is not the case. Although NMP is a SVHC because of its reprotoxicity,[43] it has a high LD_{50} (rat, oral) of 4150 mg kg^{-1}, indicating that it is not (acutely) toxic. This is an important illustration of the need to acquire comprehensive toxicological data to understand the hazards of solvents as early as possible in their development.

Substance toxicity and risk management are certainly within the scope of green chemistry, and only indirectly consequential in environmental sustainability assessments. Application of the 12 principles of green chemistry (Table 5.1),[3] will reduce toxicological hazards, which may in turn reflect well in life cycle assessment (LCA). Human toxicity is a common mid-point indicator used in LCA. Respect shall also be given to workers' rights; whether this means maintaining jobs, particularly in developing countries, that are reliant on toxic chemicals by improving working conditions (by reducing exposure), or possibly losing those jobs is a debate that needs to be had. In terms of sustainability, the threat of regulation putting a stop to the sale of products and the operation of processes using seriously (*i.e.* chronically) toxic solvents requires an immediate evaluation of alternative options. If a product or process is not legally viable it cannot be considered sustainable, and just the same applies in biomass certification, all of which require adherence to the law (see Chapter 3). The European REACH Regulation ((EC) No 1907/2006) restricts what substances can be included in consumer items intended for the general public, effectively banning chemicals with chronic toxicity hazards.[12] In the USA, the 'Toxic Substances Control Act' (TSCA) serves a similar purpose, imposing limitations on the manufacturing, processing and use of hazardous chemicals.[44]

5.2.5 Safety

The safety hazards posed by solvents are in some ways more important to consider than toxicity, because if an explosion or fire occurs, the risk of exposure to the solvent (and other chemicals in the vicinity, and their decomposition products) is greatly increased, for workers and the neighbouring environment and its inhabitants. Gu and Jérôme suggest that a green solvent is one that is not flammable. We can define this more precisely with the international UN GHS of classification and labelling of chemicals.[11] The relevant thresholds for categories of flammability are repeated in the European Classification, Labelling and Packaging (CLP) Regulation ((EC) No 1272/2008), for example,[45] which defines a flammable liquid as a liquid with a flash point of 60 °C or less. Furthermore, three categories of flammable liquid exist for labelling reasons: 'extremely flammable', 'highly flammable', and 'flammable' (Table 5.5). The exact classification depends on the boiling point as well as the flash point.

Extremely flammable solvents certainly cannot be considered as green solvents, with the added concern that the very low boiling point (≤35 °C) limits how much can be done to control solvent emissions. Many solvents that fit the perception of green solvents (*e.g.* ethanol, ethyl acetate) are categorised as highly flammable (Table 5.6), and therefore the ruling of Gu and Jérôme that

Table 5.5 Criteria for categories of flammable liquids.

Category	Hazard statement	Flash point/°C	Boiling point/°C
1	H224: Extremely flammable	<23	≤35
2	H225: Highly flammable	<23	>35
3	H226: Flammable	≤60	Any

Table 5.6 Flammable solvents.

Solvent	Hazard statement	Flash point/°C	Boiling point/°C
Acetone	Highly flammable	−20	56
Cyrene™	Not flammable	108	227
Diethyl ether	Extremely flammable	−40	35
Ethanol	Highly flammable	12	78
Ethyl acetate	Highly flammable	−4	77
Ethyl lactate	Flammable	53	153
Glycerol	Not flammable	160	290
n-Hexane	Highly flammable	−26	69
Limonene	Flammable	48	178
2-MeTHF	Highly flammable	−11	80
Solketal	Not flammable	90	192
THF	Highly flammable	−21	65

green solvents should be non-flammable is unrealistic. The current European standard for bio-based solvents (many of which are regarded as green solvents) does not place any additional burden on demonstrating the safety of the product beyond what is required by law for all solvent products.[46] This relaxed approach was implemented so as not to place an additional market barrier on producers and support growth in the bio-based solvent sector. The purpose of the UN GHS is to communicate hazards, and so long as this is done, appropriate management of the risks presented by flammable liquids can be achieved. Indeed, flammable liquids (green or otherwise) are widely used, but their use in large volumes creates a risk that should be avoided where practical to do so. Auto-ignition temperatures of solvents should also be considered and appropriate solvent selection measures should include flash point, auto-ignition point, potential for peroxide formation, conductivity, *etc.* with thresholds suitable for the application.

According to Gu and Jérôme, "*a green solvent should be easy to store and should fulfil all legislations to be safely transported either by road, train, boat or plane*".[9] The hazards posed by a solvent determine how it can be handled and transported. Long standing international rules stipulate the conditions for safe chemical transportation.[47] Furthermore, if a choice of transportation is available, the impact of each should be considered. Shipment by boat has a lower global warming potential (CO_2 equivalents per kilometre) than transport by air, while for regional transport of goods, rail has lower emissions than road transport, weight for weight.[48]

5.2.6 End-of-Life

There is a slight contradiction between requirements 3 and 7 for green solvents as proposed by Gu and Jérôme. Principle 3 (recyclability) states that "*in all chemical processes, a green solvent has to be fully recycled, of course using eco-efficient procedures*", while principle 7 (biodegradability) requires that "*green solvents should be biodegradable and should not produce toxic* *metabolites*".[9] If the solvent is fully recycled there is no need for a process solvent to be biodegradable (except as a sort of fail-safe in case of inadvertent release), and actually the labile functionality required for a substance to be biodegradable could sometimes limit the thermal stability and impair solvent recovery through distillation. To overcome this issue, careful design of the solvent and appropriate validation testing is required. Biodegradability becomes important when solvents are disposed of into waste water treatment facilities, perhaps the end-of-pipe biological treatments of municipal facilities. For other environmental releases of solvents, most are unlikely to reside in an environment that allows for biodegradation. Instead, evaporation is likely to be rapid, and so decomposition through atmospheric hydroxyl radical chemistry will be the likely final end-of-life scenario. However, less volatile solvents may in fact reside in the environment for some time. The most obvious environmental destination of high boiling point hydrophilic solvents like glycerol is water. Hydrophobic solvents will have a stronger affinity for soils and suspended organic matter in waterways. Partition coefficients (measured or calculated) can indicate the environmental fate of a solvent, whether that is air, water, or soil. Estimations of this sort are compiled in the TOXNET 'Hazardous Substances Data Base' (HSDB), for example, which is a free to access database.[49] A selection of solvents and their environmental fate are summarised in Table 5.7. Briefer descriptions are given for more solvents within the appendix data sheets.

Table 5.7 provides environmental data for six solvents. The soil adsorption coefficient (K_{OC}) indicates a tendency for substances to adsorb into soils and water sediments. Limonene has a high affinity for soils. For volatile solvents with lower K_{OC} values, it is likely that they will evaporate from the water bodies they migrate to. A high Henry's law constant, expressed in Table 5.7 as vapour pressure over aqueous molar concentration, indicates that the solvent will evaporate from water. If the solvent does not evaporate or biodegrade readily, it may present a bioaccumulation hazard. Bioconcentration factor (BCF) is used to assess the ratio of concentrations in a model organism compared to in water. Toxic metabolites of solvents are mentioned by Gu and Jérôme (principle 7).[9] The BCF values reported in Table 5.7 fall some way short of legislative thresholds.[50] In relation to the European REACH Regulation ((EC) No 1907/2006),[12] the biodegradability of substances is required for all registrations, while the degradation products need to be known for products made in, or imported into, Europe in excess of 100 tonnes per year.

Ecotoxicity is also a part of the REACH persistent (non-biodegrading), bioaccumulating and toxic (PBT) regime. Substances eligible for restrictions are those expressing either chronic toxicity, or a long-term no-observed effect concentration (NOEC) below 0.01 mg L^{-1}, or similarly an EC_{10} for freshwater or marine organisms below 0.01 mg L^{-1}.[12] Study of the ecotoxicity of solvents is already an established area of research.[51,52] In one example, two neoteric solvents with similar physical properties were compared in a variety of ecotoxicity tests.[53] The ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate, [bmim][PF_6], was found to be more hazardous to aquatic

Table 5.7 The environmental fate of selected solvents.[49]

Solvent	Soil/water partition (K_{OC})	Air/Water partition[a]	Bioconcentration factor (BCF)	Biodegradability	Destination and lifespan
Ethanol	2.75	5.0×10^{-6}	3 (estimated)	Readily	Air. Estimated $t_{1/2}$ of photochemical degradation is approximately 36 hours
Glycerol	1 (estimated)	1.73×10^{-8}	3 (estimated)	Readily	Water. Near complete biodegradation within 24 hours
n-Hexane	130 (estimated)	1.80	170 (estimated)	Readily	Air. Estimated $t_{1/2}$ of photochemical degradation is approximately 24 hours
d-Limonene	1100 (estimated)	0.032	480 (estimated)	Readily	Soil and sediment, slowly evaporating. Estimated $t_{1/2}$ of photochemical degradation is in minutes-hours range
THF	18–23	7.05×10^{-5}	3 (estimated)	Inherently	Air. Estimated $t_{1/2}$ of photochemical degradation is approximately 24 hours
p-Xylene	246–540	6.90×10^{-3}	15–19	Slowly	Air. Estimated $t_{1/2}$ of photochemical degradation is approximately 24 hours

[a] Henry's law constant/atm m^3 mol^{-1}.

environments than the glycerol derivative 1,3-*bis*(2,2,2-trifluoroethoxy)propan-2-ol. With a solvent also needing to be persistent and bioaccumulating to acquire PBT status, few are recognised as such.

5.2.6.1 A Solvent Waste Hierarchy

It is important to establish a hierarchy of waste treatment options for solvents, and not to rely on natural decomposition processes, which should be a last resort and only for benign substances. The application of the solvent will determine how high up the waste hierarchy the waste management procedure can be (Figure 5.7).[54] The waste hierarchy comes from the European Waste Framework Directive (2008/98/EC),[55] and is designed with the intention of promoting waste management practices that maximise the value of secondary materials, instead of just disposing of products without thinking about the implications. We will interpret the order of preference when it comes to dealing with waste solvents within the framework of a circular economy. In a circular economy, the value of resources is maintained through considerate product design that allows the materials contained in articles to be reused and recycled.[56] Promoted by the European Commission, a circular economy is key to the future of (European) industries and their supply chains, and for economic growth and jobs.[57] For chemicals, the principles of a circular economy are most perceptible when applied to end products with well-known and obvious pollution issues, such as packaging. The impact of a circular economy on how we view solvent use and disposal is perhaps not so outstanding and so must be defined. An ambitious interpretation of a circular economy is that non-renewable virgin feedstocks will no longer be justified, and there will be no need for landfill or waste incineration because products will be made from other products. Articles that cannot be reclaimed will be bio-based, designed to biodegrade and therefore contribute to the production of biomass in a material loop.

Prevention sits at the top of the waste hierarchy (Figure 5.7), and in the context of this book is associated with solvent reduction. Reuse is the second

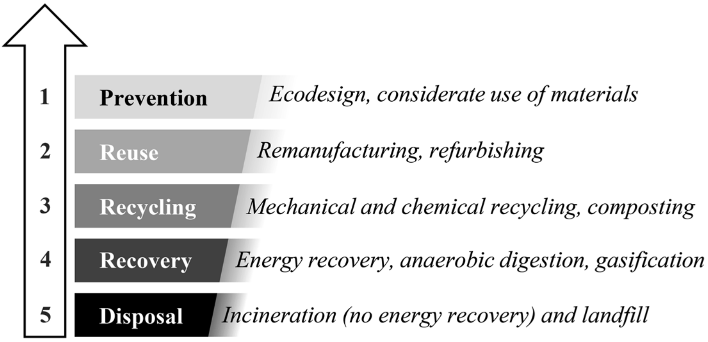


Figure 5.7 The waste hierarchy.[56]

best option, and actually this is the best description of solvent 'recycling' through distillation. The European Waste Framework Directive, bearing in mind that future revisions will adapt the text to reflect circular economy ambitions for Europe,[58] at present seem to associate distillation as a form of recovery (much lower down the waste hierarchy), and the only mention of solvents is in Annex II of this Directive, listing "solvent reclamation/regeneration" as a recovery option.[55] However solvent reclamation by distillation, either in-house or as a service provided by a waste management company, is not equal to 'recovery' options such as anaerobic digestion or incineration, in which the material is sacrificed. Distillation allows the solvent to be purified and reused, without additional resource demand or waste (other than distillation residues and discarded cuts). The best available techniques for industrial waste treatments dictate that solvents shall be reconditioned for reuse by distillation if at all possible. Guidance for the waste treatment industry in the form of a European reference document states that unmixed solvents that can be distilled economically with 60% material recovery fulfil the requirements for reconditioning in this way.[59]

Recycling is the next option after reuse to consider. Mechanical recycling is not appropriate for solvents, but chemical recycling is. Chemical recycling deconstructs a product back to its chemical precursors. For example, *n*-butyl acetate could be hydrolysed to 1-butanol and acetic acid. It is not foreseeable to have a situation where solvent waste pure enough for chemical recycling would economically produce chemical intermediates compared to reconditioning through distillation. The role of chemical recycling, if any, is more likely to be for the generation of solvents from other sources. In a variation of chemical recycling, feedstock recycling takes a waste material (*e.g.* a polyester plastic) and chemically modifies it into a new substance for the manufacture of other products. It would be possible to take bio-based polymers such as polylactic acid (PLA) and obtain solvents such as lactic acid and ethyl lactate in this way.[60] For this purpose, PLA is particularly suited because mechanical recycling does not produce a high quality recyclate and can contaminate other recyclates.[61,62] Feedstock recycling can also be used to convert waste into more general chemical commodities, or a mixture of base chemicals. Gasification would be an example, but now we are talking about recovery, a step down again from recycling on the waste hierarchy.

Recovery also consists of anaerobic digestion to produce methane (typically for fuel) and incineration with energy recovery. If solvents must be incinerated, energy recovery is the only satisfactory way to execute this less than desirable end-of-life option. However, the solvent is then contributing to net greenhouse gas (GHG) emissions. The waste management industry must get to the stage where only products made from renewable materials, and therefore short-cycle carbon, are incinerated with energy recovery. This would mean only bio-based solvents, and solvents made from captured CO_2 without fossil-derived chemical moieties would be considered as suitable. This is not achievable without upstream feedstock suppliers and solvent manufacturers working towards a global, circular economy. At present there are industries that embrace incineration of waste solvents (waste management companies, cement kiln operators) and economically profit from it. In a circular economy, where materials and their function are valued and waste reduced, these business models would need to be re-evaluated for a more sustainable outlook.[56]

Biodegradation is in some ways less preferable to incineration on the basis that the oxidation products emitted to the atmosphere are ultimately the same, but biodegradation does not allow for the added bonus of energy recovery, whether it is occurring in the environment or an industrial composting facility. Biodegradation used for the purpose of composting is often considered as 'organic recycling', and of course this has broad benefits towards improving soil quality and the consequences that arise from that. Ultimately, an LCA must be conducted to establish the relative benefits of different end-of-life scenarios with more certainty. Waste solvent is not an obvious candidate for composting, partly because it is (often a volatile) liquid and partly because of (eco)toxicity concerns. Glycerol can be added to compost as a source of carbon rich energy,[63] but it will be used directly out of bio-diesel production plants without an intermediate use as a solvent. In theory, using the glycerol by-product of bio-diesel production firstly as a solvent and then adding it to compost is a nice idea, but the inevitable contamination of the solvent will have an impact on compost quality and may introduce traces of unacceptably ecotoxic substances. Biodegradation only becomes an appealing option for solvent waste management in instances where it cannot be recovered and is dissipated into the environment as part of its function. It is also a last resort for solvents that cannot be economically recovered, and therefore must be discharged into a waste water effluent plant.

Thus, a hierarchy of solvent end-of-life treatments can be summarised, with priority given to maintaining the value of the material the solvent is made of (Figure 5.8). The first priority is to minimise solvent use to reduce waste and environmental impact. Process solvents can be distilled in many cases in order to reuse the solvent. Mechanical recycling is not viable, but chemical recycling offers an opportunity to provide secondary uses of

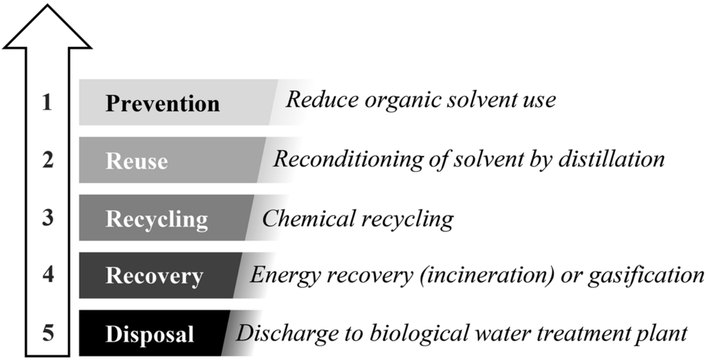


Figure 5.8 Solvent treatments prioritised according to retained (material) value within the waste hierarchy.

solvents in the form of chemical intermediates, and similarly the production of solvents from other chemical recyclates becomes possible. Incineration at least reclaims some energy, but should not be encouraged for petrochemical solvents. If nothing can be done to generate value from solvent waste, it should be disposed of in a way that rapidly breaks down any hazardous substances (*e.g.* biological waste water treatments).

5.3 Solvent Selection

Solvent selection is the process of choosing a solvent for an application based on a set of requirements. It is increasingly necessary to implement changes away from hazardous substances and towards green chemicals, and not least for solvents. A life cycle perspective to these efforts is gaining popularity.[64] Solvent selection requirements can be performance (physical property) driven, or based on how green the solvent is, or ideally both. There are a number of different ways in which a solvent can be identified as a suitable candidate for an application, which is entirely down to preference. What is important is that the limitations of the approach chosen do not prevent the selection of solvents ideally placed to serve the application of interest.

5.3.1 Performance Basis

Replacing hazardous solvents with green, renewable alternatives is the ultimate goal, but fundamentally the substitute solvent must offer performance that is at least comparable to the original solvent. Actually the real scenario is tougher than this, because to offset what is often going to be a more expensive speciality solvent, users will expect higher performance a lot of the time. Without a definitive improvement to be gained, there will not be a sufficient stimulus to encourage a change of solvent. The cost of adapting a production plant or formulation to a new solvent is enough of a deterrent without commanding legislation in place to force the change.

Generally speaking, polarity governs the solvent interactions that are chiefly fundamental to the action of the solvent. Whether the solvent is used for cleaning, reaction chemistry, extraction, separation, or formulation, the polarity is the primary property of the solvent that determines its effectiveness. In a solvent replacement strategy, it may be that to achieve the desired polarity, the boiling point of a substitute solvent is higher than that of the original solvent, or that it is more viscous. Any number of physical properties can impact, for better or worse, the performance of the solvent. The amount of flexibility given towards these attributes must be taken case by case, but overall a measure of success, be it reaction yield or performance in a standardised test for cleaning ability for example, is needed to indicate that a specified level of performance has been reached. Unsatisfactory consequences of the physical properties of the solvent, such as the viscosity being too high to operate the process, will act as ‘no-go’ indicators in the solvent selection process.

When performance criteria are defined based on physical properties (and polarity), solvent selection can be performed in a systematic way by screening solvents, either by looking up data to match requirements or by practical application testing. When defining performance criteria, instead of requesting that a solvent is removable by distillation and can be pumped using the equipment present in the existing plant infrastructure for example, rephrasing this to define a minimum vapour pressure and maximum viscosity is much more helpful.

It is not always possible to define solvent performance criteria in a precise enough manner because the required information is just not available. One way to begin to develop an understanding is to screen a small number of solvents and measure the outcome. In certain cases, performance data has already been compiled for this purpose, and this acts as a tool for solvent selection. The two interpretations of solvent selection discussed here are solvent selection tables (Section 5.3.1.1) and the linear solvation energy relationship (LSER, Section 5.3.1.2).

5.3.1.1 Solvent Selection Tables Based on Conditions and Results

The work of Watson and co-workers introduced the concept of solvent selection tables documenting reaction conditions and yields. In a grid format, the optimum combinations of solvents and reactants, catalysts or reagents are highlighted. In one example, five amide coupling agents were investigated in four reactions each using eight solvents.[65] The solvent selection table for the reaction of phenylacetic acid and aniline is given as Table 5.8. The chosen coupling agents were *N*-[(dimethylamino)-1*H*-1,2,3-triazolo-[4,5-*b*]pyridin-1-ylmethylene]-*N*-methylmethanaminium hexafluorophosphate *N*-oxide (HATU), (1-cyano-2-ethoxy-2-oxoethylidenaminooxy)dimethylamino-morpholino-carbenium hexafluorophosphate (COMU), *N*,*N*′-diisopropylcarbodiimide/hydroxybenzotriazole (DIC/HOBt), (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP), and *n*-propylphosphonic anhydride (T3P®). The solvents included the common choices of dichloromethane (DCM) and *N*,*N*-dimethyl formamide (DMF). The procedure does not require heating, and so boiling point is not a factor in solvent selection. The solvating power

Table 5.8 Amidation solvent selection table (for the reaction of phenylacetic acid and aniline).

	HATU	COMU	DIC HOBt	PyBOP	T3P®
MTBE	>70%[c]	<50%[a]	<50%[a]	<50%[a]	<50%[a]
CPME	<50%[a]	<50%[a]	<50%[a]	50–70%[b]	<50%[a]
DCM	100%[e]	100%[e]	100%[d]	100%[d]	50–70%[b]
DMC	100%[d]	100%[d]	>70%[c]	>70%[c]	50–70%[b]
DMF	100%[e]	100%[e]	100%[d]	100%[d]	<50%[a]
EtOAc	100%[d]	100%[e]	100%[d]	>70%[c]	50–70%[b]
IPA	100%[d]	100%[d]	<50%[a]	<50%[a]	<50%[a]
2-MeTHF	100%[d]	100%[e]	100%[d]	100%[d]	<50%[a]

[a] Poor (<50% yield).
[b] Reasonable (50–70% yield).
[c] Good (>70%).
[d] Complete after less than 4 hours.
[e] Complete after less than 1 hour.

of DCM and DMF makes them popular solvents despite their chronic toxicity hazards. The alternative solvents used were methyl *t*-butyl ether (MTBE), cyclopentyl methyl ether (CPME), dimethyl carbonate (DMC), ethyl acetate (EtOAc), isopropanol (IPA), and 2-methyltetrahydrofuran (2-MeTHF).

A solvent selection table specifies the success of the reaction according to yield.[65] As shown in Table 5.8, a five tiered classification places the result as poor (<50% yield), reasonable (50–70%), good (>70%), and complete in either 4 hours or even 1 hour. Also considering the results of the other reactions not shown,[65] it transpires that DCM and DMF can be replaced quite comprehensively by more benign solvents, even esters (ethyl acetate) and carbonates (dimethyl carbonate) that one might have expected to decompose under the reaction conditions that promote carbonyl addition. 2-Methyltetrahydrofuran, a cyclic ether, was another excellent solvent choice. The acyclic ethers are less dipolar and were not suited to the amidation. In terms of the coupling agent, COMU was preferred as a substitute for HATU.

In a second solvent selection table by Watson and co-workers, reductive amination was addressed in a yet more extensive study.[66] A reducing agent is required to convert an imine (formed by the reaction of an aldehyde and a primary or secondary amine) into an alkylated amine. Three reducing agents were studied across 12 reactions. These were sodium cyanoborohydride (SCB), sodium triacetoxyborohydride (STAB) and a picoline–borane complex (pic-B). The solvent set was expanded from the previous amidation case study to also include 1,2-dichloroethane (DCE) and tetrahydrofuran (THF). Chlorinated solvents are a common solvent option for this transformation. The results of two reactions are shown in Table 5.9. The stand out result is that STAB is particularly effective regardless of the solvent. In other types of

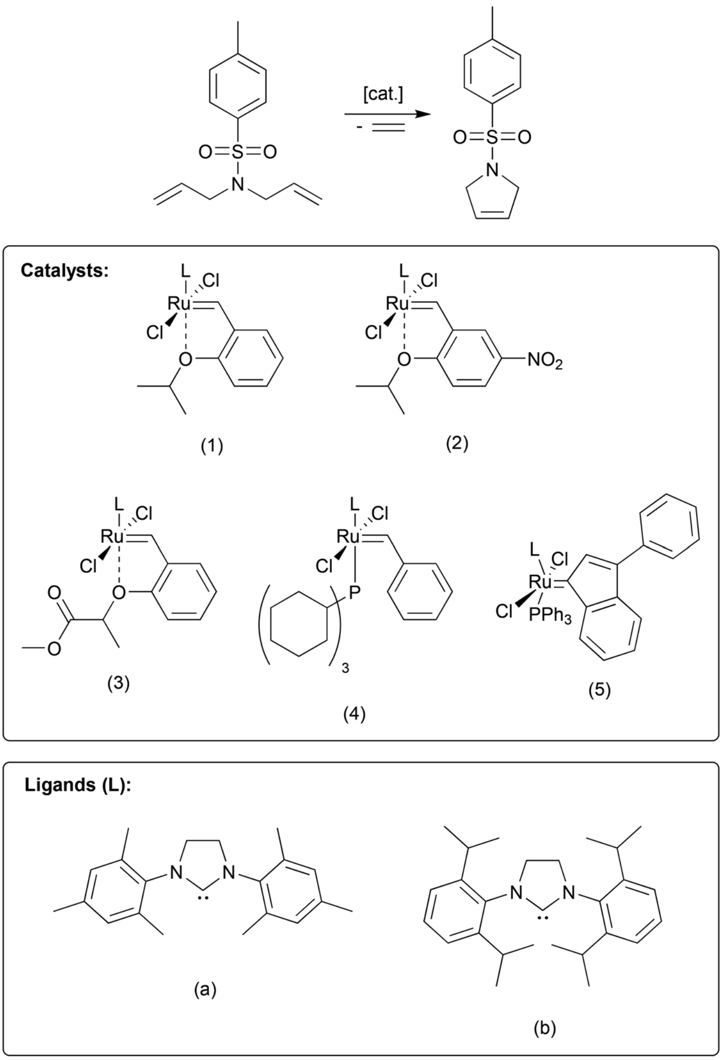
Table 5.9 Reductive amination solvent selection table (for the reaction of 3-phenyl-1-propylamine or *N*-methyl 2-methyoxybenzylamine with benzaldehyde).

	3-Phenyl-1-propylamine			*N*-Methyl 2-methoxybenzylamine		
	SCB	STAB	Pic-B	SCB	STAB	Pic-B
MTBE	<50%[a]	100%[d]	>70%[c]	>70%[c]	100%[e]	50–70%[b]
CPME	>70%[c]	>70%[c]	>70%[c]	50–70%[b]	100%[e]	50–70%[b]
DCM	>70%[c]	100%[d]	>70%[c]	100%[d]	100%[d]	50–70%[b]
DCE	>70%[c]	100%[d]	>70%[c]	100%[e]	100%[d]	50–70%[b]
DMC	100%[d]	100%[e]	>70%[c]	>70%[c]	100%[d]	<50%[a]
DMF	>70%[c]	100%[e]	50–70%[b]	<50%[a]	100%[d]	50–70%
EtOAc	>70%[c]	100%[d]	>70%[c]	<50%[a]	100%[d]	<50%[a]
IPA	100%[d]	100%[d]	>70%[c]	50–70%[b]	100%[e]	>70%[c]
2-MeTHF	>70%[c]	>70%[c]	>70%[c]	<50%[a]	100%[e]	50–70%[b]
THF	>70%[c]	50–70%[b]	>70%[c]	<50%[a]	100%[d]	<50%[a]

[a] Poor (<50% yield).
[b] Reasonable (50–70% yield).
[c] Good (>70%).
[d] Complete after less than 4 hours.
[e] Complete after less than 1 hour.

reductive amidation (*e.g.* where an acyclic secondary arylamine is a reactant), DMF and isopropanol do not provide satisfactory yields, with STAB or other reducing agents. Ethyl acetate was the preferred solvent for general use in reductive amination reactions, replacing DCM and DCE.

The solvent selection table approach also works for catalysis, as shown by Skowerski *et al.*[67] For the ring closing olefin metathesis of *N*,*N*-diallyltoluenesulphonamide, a popular model compound, several second generation Grubbs catalysts and Hoveyda–Grubbs catalysts were tested in seven solvents: methanol (MeOH), IPA, EtOAc, DMC, CPME, 2-MeTHF and DCM (Scheme 5.1). The reaction at 40 °C is shown in Table 5.10. Dichloromethane



Scheme 5.1 A model ring closing metathesis (RCM) reaction, relying on one of five types of ruthenium catalyst (1–5) with a choice of ligand (a or b).

Table 5.10 A solvent selection table for olefin metathesis using 10 catalysts listed according to the designations in Scheme 5.1.

	MeOH	IPA	EtOAc	DMC	CPME	2-MeTHF	DCM
1a	28%	31%	97%	93%	73%	38%	97%
1b	58%	88%	96%	93%	90%	90%	93%
2a	9%	11%[a]	94%	85%	79%	49%	96%
2b	45%	85%	96%	99%	97%	97%	88%[a]
3a	8%	9%	66%	79%	20%	37%	95%
3b	57%	86%	98%	99%	97%	97%	91%
4a	15%	16%	97%	98%	80%	35%	92%
4b	19%	31%	88%	97%	85%	84%	91%
5a	3%[a]	15%[a]	96%	98%	69%	38%	93%
5b	8%[a]	51%	92%	98%	89%	93%	95%

[a] Undesired isomers observed.

is frequently used for olefin metathesis reactions and generally the results were excellent in this solvent. Of the alternative non-chlorinated solvents tested, dimethyl carbonate and ethyl acetate provided good yields, especially for catalysts with the isopropyl functionalised ligand ('b', Scheme 5.1). Alcohol solvents are not suitable, even at higher temperature. At 70 °C the ethers CPME and 2-MeTHF become more broadly applicable as solvents.[67]

Although the more toxic solvents tend to find use in reaction chemistry, which is a problem in need of addressing, after the transformation is complete the work-up requires far greater volumes of solvent. Chromatography is solvent intensive, and is routinely used in small scale preparations of compounds. Two common combinations of solvent mixtures used in preparative chromatography for the purification of organic compounds are ethyl acetate and a hydrocarbon (*n*-hexane, cyclohexane, or *n*-heptane), and secondly a mixture of dichloromethane and methanol for polar compounds. Ideally the use of dichloromethane in particular should be eliminated, and in that respect cyclopentyl methyl ether (CPME) has been shown to be an ample replacement.[68] Moreover, a comprehensive solvent substitution guide has been created by Taygerly *et al.*, who have designed a series of scales that match the eluting strength of different binary solvent mixtures.[69] The guide for neutral compounds is shown in Figure 5.9. Vertical lines up from the DCM–methanol system show the ratio of alternative solvents needed to recreate the eluting strength required. If for example you had been using 10% methanol in DCM as a solvent system, methyl *t*-butyl ether (MTBE) with 23% methanol would be worth investigating.

5.3.1.2 Linear Solvation Energy Relationships

The aforementioned solvent selection tables are an excellent resource if the case study is applicable to your work. If not, you would need to conduct your own study to reach the same level of understanding. Also, the reason why some solvents are superior to others is not apparent through a solvent

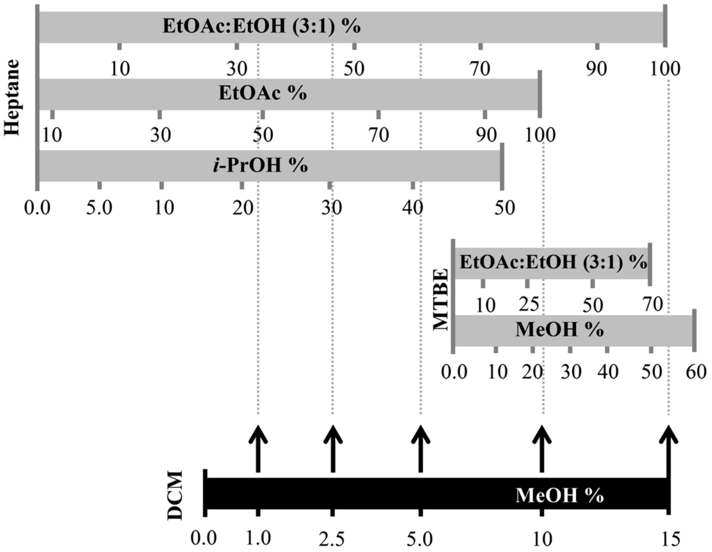


Figure 5.9 Solvent selection scale for chromatographic purification applications.

selection table. Therefore, speculation is the only way additional high performance solvents from outside the original data set can be identified. Another way to produce a tool for solvent selection is through physical organic chemistry principles linking the properties of the solvent to a measured outcome. This could be the rate of reaction, and in so doing a linear free energy relationship is formed. Specific to solvents is the linear solvation energy relationship (LSER).[70] The key to these relationships is the polarity of the solvent. If a reaction or extraction is conducted in a number of solvents, keeping all other parameters (*e.g.* temperature) constant, it should be possible to relate the observed solvent phenomena to polarity. Being a LSER, the measured outcome should be proportional to energy, typically $\ln(k)$ or $\ln(K)$ depending on whether a kinetic or thermodynamic effect is being measured. Therefore, the expression of solvent polarity used must also be proportional to energy. The Kamlet–Abboud–Taft solvatochromic parameters are derived from the UV absorbance of dyes dissolved in solvents,[71] and accordingly are directly related to the energy between the ground state and the excited state of the dye. Reichardt's dye, nitroaniline and *N*,*N*-diethylnitroaniline are examples of relevant dyes.[72] As an alternative to nitroanilines, nitrophenol and nitroanisole can be used, which are said to have benefits when it comes to the peak shape of the UV response obtained.[73,74]

The Kamlet–Abboud–Taft solvatochromic parameters are together three scales of solvent polarity: hydrogen bond donating ability (α), hydrogen bond accepting ability (β), and dipolarity/polarisability (π^*) (Table 5.11). Each is normalised to sit on a 0 to 1 scale. Dimethyl sulphoxide defines the upper limit of π^*, but a number of more dipolar solvents exist and they will have

Table 5.11 Selected Kamlet–Abboud–Taft solvatochromic parameters.[145] The dyes used as the basis of these values differ.

Solvent	α	β	π^*
Acetone	0.08	0.48	0.71
Cyclopentyl methyl ether	0.00	0.53	0.42
Dimethyl carbonate	0.00	0.38	0.47
Ethanol	0.83	0.75	0.51
Ethyl acetate	0.00	0.45	0.55
Ethyl lactate	0.69	0.52	0.82
Glycerol	1.06	0.66	0.96
Isopropanol	0.76	0.84	0.48
2-Methyltetrahydrofuran	0.00	0.58	0.53
α-Pinene	0.00	0.00	0.11
Propylene carbonate	0.00	0.40	0.83
γ-Valerolactone	0.00	0.60	0.83
Water	1.17	0.14	1.09

a value of π^* greater than 1. The lower limit of the π^* scale is established by cyclohexane. Historically methanol and hexamethylphosphoramide have been used to normalise the upper limit of α and β respectively, but equations now exist to directly transform a UV wavenumber from a dye dissolved in a solvent into these polarity scales. Any combination of the three can form the basis of a LSER. Since their inception, the Kamlet–Abboud–Taft solvatochromic parameters have been used successfully in a great number of linear solvation energy relationships.[75–83,143]

Applied as a LSER, the Kamlet–Abboud–Taft solvatochromic parameters create a powerful tool for solvent selection on the basis of actually understanding what the solvent is doing, and therefore the ideal properties of the solvent become apparent. In a simple example, the amidation of 4-phenylbutyric acid with benzylamine shows that the rate of reaction is inversely proportional to hydrogen bond accepting ability (β) (Figure 5.10).[75] An initial study of seven solvents indicated the trend shown in Figure 5.10, revealing the benefit of low polarity solvents. In order to improve the solvent from a petrochemical aromatic hydrocarbon or chlorohydrocarbon, to a bio-based alternative, targeted solvent selection in favour of terpenes was rationalised. Limonene and *p*-cymene were thus shown to be capable solvents for this reaction. The reason is due to an entropic effect, with hydrogen bonding between the solvent and the activated complex of the reaction creating an ordered complex.[75] This entropic penalty is more significant than the enthalpic benefit of the hydrogen bonds in polar solvents.

If we compare this LSER case study,[75] to the previously described solvent selection table for amidation,[65] we see contrasting conclusions for what is essentially the same type of reaction. The LSER was constructed from data for an uncatalysed reaction without amide coupling agents, at elevated temperature (100 °C). On the other hand, the solvent selection table of MacMillan *et al.* is based on more realistic reaction conditions, at room temperature

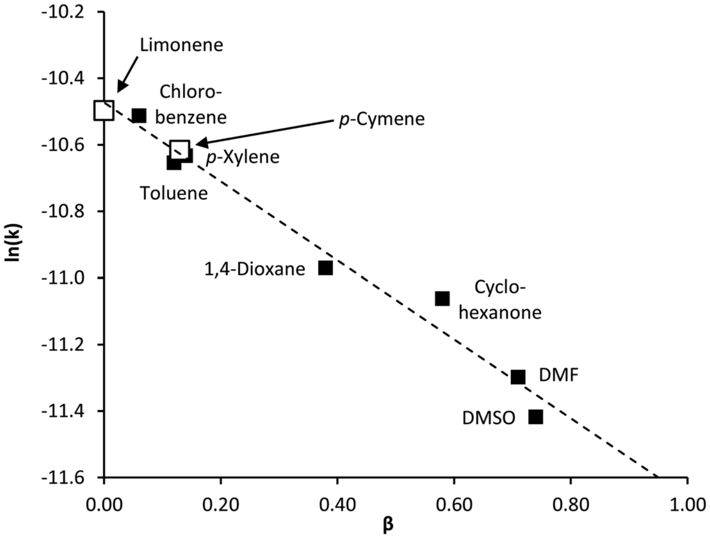


Figure 5.10 A LSER describing the rate of reaction (amidation) as a function of hydrogen bond accepting ability (β). Conventional solvent data is shown in black, and bio-based solvents in white.

with a coupling agent employed. The LSER (Figure 5.10) shows that hydrocarbon solvents are preferable to accelerate the reaction, but the results of the solvent selection table (Table 5.8) indicate that the amidation reaction proceeds fast enough not to rely too much on the choice of solvent in this regard. The solubility of the coupling agent may be more crucial to the success of the reaction, with ethyl acetate, dimethyl carbonate, and 2-methyltetrahydrofuran preferred instead of hydrocarbon solvents. If transferred to the LSER reaction conditions, the appreciable hydrogen bond accepting ability of these solvents would be shown to impede the rate of reaction. Ethyl acetate and dimethyl carbonate would also probably react with the amine under these conditions. Therefore, in a sense the solvent selection table approach is superior, but to make that approach as comprehensive as a LSER the range of solvents included must be large and more diverse in the modes of polarity expressed.

A kinetic study explaining the rate of ring closing olefin metathesis has been completed by Adjiman *et al.*[76] In it, the solvent effect is modelled according to the LSER principle, but for each individual step of the reaction. Overall the greatest rate of product formation is achieved in acetic acid as the solvent. Acetone provides the second fastest initial rate, but deactivation of the ruthenium catalysts curtails the reaction, limiting yields to about 60%. Catalyst deactivation also occurs in acetic acid, but to a lesser extent. In the conventional solvent, dichloromethane (DCM), the catalyst activity is maintained, as it is in cyclohexane. However, the rate of product formation is greater in cyclohexane than in DCM making it a valuable substitute.

Cyclohexane was not included in the solvent selection table of Skowerski *et al.*[67] Combining the information from both types of study (LSER and solvent selection table) provides a valuable insight into the role of the solvent and how to maximise productivity. It is unfortunate that there is a lack of overlap between the datasets, otherwise an even stronger understanding could have been gained.

5.3.2 Green Characteristics

If solvent options are well understood in terms of what physical properties provide the required performance, the next question is one of greenness. It has been the pharmaceutical industries who have most actively taken to green solvent selection guides used to differentiate greenness between solvents, for reaction chemistry and chromatography. Analytical chemistry has also adopted versions of these tools.[84,85] Green solvent selection guides for medicinal chemistry are helpful for simple comparisons, say, if two procedures can be found for a transformation and a chemist wishes to know which allows for the least hazardous solvent. Larger scale chemistry requires more sophisticated information, although the GSK green solvent selection guide[86] actually started as a tool for process development teams.[87] A detailed review of green solvent selection guides for the pharmaceutical industry has been produced by Byrne *et al.*[88] It is an open access publication, and so there is no need to cover all the different green solvent selection guides in great detail here, especially because most rely heavily on colour coding. An earlier survey of green solvent selection guides is also available.[89]

Broadly speaking there are three types of green solvent selection guide. The most basic type groups solvents into categories based on the environmental health and safety policies of a company. An example is the Pfizer green solvent selection guide,[90] and more recently the Sanofi equivalent.[91] Alternatively, numerical scores can be used to allow for more detailed comparisons across different criteria. The GSK green solvent selection guide is the most prominent example.[86] Both these types of green solvent selection guide interpret the physical and environmental properties of solvents by transforming their values into a scale to determine their greenness. Finally, a more sophisticated analysis of solvent properties has recently begun to produce green solvent selection guides and related tools that are less led by human interpretation and instead rely on computational data analysis.[92–94] Now, LCA is being incorporated into computer-assisted solvent selection tools as well.[95,96]

5.3.2.1 CHEM21 Selection Guide of Classical-Solvents and Less Classical-Solvents

A significant limitation of solvent selection guides is that they contain a set number of solvents. New solvents can only be introduced with an update. They also tend to be based on a methodology that is not explained or is unclear to the user,[90] or one that requires undisclosed data. The scoring can be based on a principle of spreading the results evenly across the solvents contained within the guide, normalised through averages and preferred data ranges, for example.[86] As solvent use evolves over time, the solvent set may become less relevant and thus the green solvent selection guide itself becomes less relevant. Alternatively, some tools are based on thresholds established through regulatory limits and classification. One of these is the ETH Zurich system,[32] but unfortunately it uses a now out of date classification system. Similarly, a new solvent selection guide produced by the CHEM21 consortium converts UN GHS Hazard Statements into a ranking.[97] The publication is open access and freely available,[97] and has an accompanying spreadsheet tool for applying the method to any solvent.[98] The approach provides three scores for solvents based on Hazard Statements for health, safety and environmental properties. A detailed explanation of the CHEM21 solvent selection guide is provided here, and its relevance to sustainability indicated. A minor error in the original publication is amended according to the correction issued by the authors.[99]

A safety score is produced primarily by considering the flash point of the solvent. As for all the scores, 1 is the greenest result and 10 the least desirable. To create differentiation between solvents, three possible scores can be achieved under the conditions described by UN GHS Hazard Statements H224 and H225. The best score (1) is given to non-flammable solvents (meaning the flash point exceeds 60 °C). The boiling point of the solvent is not additionally used to form the safety score (Table 5.12). The score is increased by one if the auto-ignition point of the solvent is below 200 °C, the resistivity of the solvent is above 10^8 Ω m, or the solvent forms peroxides (as established by supplementary European Hazard Statement EUH019). Furthermore, the safety score of the solvent is automatically increased to ten if the solvent is explosive, defined by an energy of decomposition exceeding 500 J g^{-1}.

The health score in the CHEM21 consortium green solvent selection guide is more elaborate in its determination.[97] The common approach of using occupational exposure limits to signify the human health impact of the solvent was

Table 5.12 Flammable liquid classification and its relation to the CHEM21 safety score.

Hazard statement	Criteria	Safety score
H224: Extremely flammable liquid and vapour	Flash point <23 °C and boiling point ≤35 °C	4 (0 °C ≤ flash point ≤ 22 °C); 5 (−1 °C ≤ flash point ≤ −20 °C); 7 (−20 °C > flash point)
H225: Highly flammable liquid and vapour	Flash point <23 °C and boiling point >35 °C	4 (0 °C ≤ flash point ≤ 22 °C); 5 (−1 °C ≤ flash point ≤ −20 °C); 7 (−20 °C > flash point)
H226: Flammable liquid and vapour	23 °C ≤ flash point ≤ 60 °C	3
Not applicable	Flash point >60 °C.	1

rejected as a possible means of scoring. This was because these thresholds are not internationally agreed, and they are not derived exactly from physical properties, meaning the approach would not translate to new solvents until an occupational exposure limit is legislated. Instead, the health score of the solvent is increased by 1 if the boiling point of the solvent is lower than 85 °C (signifying a high risk of exposure). The final health score is decided according to the UNGHS Hazard Statements summarised in Table 5.13.

Meeting the requirements of irritation Hazard Statements is only achieved through standardised animal testing. It cannot be predicted with sufficient certainty, but unlike occupational exposure limits it is within the power of the solvent producer to obtain this data, as would be routine in preparing a safety datasheet (SDS) or applying for REACH registration. The same applies for specific target organ toxicity and chronic toxicity, which should be investigated for high tonnage products. Acute toxicity Hazard Statements are defined by the LD_{50} values (or equivalent).

The authors of the CHEM21 solvent selection guide admit themselves that the methodology behind the environmental score is incomplete.[97] It is also clear that the chosen indicators are not necessarily measuring environmental impact, but instead a preference for continuing to use established technologies seems to have been introduced. What is meant by this is that the boiling point of the solvent has a strong role in deciding the environmental score. The ideal boiling point range of 70–139 °C was proposed, and justified because low boiling point solvents more readily and easily contribute to VOC emissions, while high boiling point solvents cannot easily be distilled in recovery operations. This approach is behind thinking in academic research that is seeking alternatives to distillation and volatile organic solvents generally, although the notion that the most difficult solvents to capture and recover, as embodied by the choice of boiling point criteria thresholds, should be penalised, is a satisfactory stopgap. It also reaffirms the scope of the solvent selection guide, intended for pharmaceutical research and development, not formulation for example. Otherwise various environmental UN GHS Hazard Statements define the environmental score (Table 5.14). The worst applicable characteristic decides the environmental score, as is true of the safety and health scores. Water is reserved the ideal score of 1.

The methodology is equally applicable to conventional solvents and new solvent products providing sufficient data is available. Scores for selected solvents of interest have been provided in Table 5.15. In the original guide, colour-coding divides the scores into three levels. Green is used to highlight scores of 1, 2, and 3. Yellow denotes scores between 4 and 6. Higher scores are coloured red in the original CHEM21 consortium green solvent selection guide.[97] The colour-coding is not reproduced in this book. The ‘traffic-light’ designation is widely used in solvent selection guides, but purposely creates a bias through the emotional response we have towards certain colours, which furthermore has its own differing cultural associations. The safety (S), health (H), and environmental (E) categories are then supplemented by a worded message, either ‘Recommended’, ‘Problematic’, or ‘Hazardous’.

Table 5.13 Derivatisation of the CHEM21 health score from Hazard Statements.

Irritation	Acute toxicity	Single target organ toxicity	Chronic toxicity (CMR)	Health score
Not applicable at this health score	H300: Fatal if swallowed; H310: Fatal in contact with skin; H330: Fatal if inhaled	Not applicable at this health score	H340: May cause genetic defects; H350: May cause cancer; H360: May damage fertility or the unborn child	9
H314: Causes severe skin burns and eye damage	Not applicable at this health score	Not applicable at this health score	Not applicable at this health score	7
Not applicable at this health score	H301: Toxic if swallowed; H311: Toxic in contact with skin; H331: Toxic if inhaled	H370: Causes damage to organs; H372: Causes damage to organs through prolonged or repeated exposure	H341: Suspected of causing genetic defects; H351: Suspected of causing cancer; H361: Suspected of damaging fertility or the unborn child	6
H318: Causes serious eye damage	Not applicable at this health score	H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled	Not applicable at this health score	4
H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H335: May cause respiratory irritation; EUH066: Repeated exposure may cause skin dryness or cracking	H302: Harmful if swallowed; H312: Harmful in contact with skin. H332: Harmful if inhaled; H336: May cause drowsiness or dizziness; EUH070: Toxic by eye contact	H304: May be fatal if swallowed and enters airways; H371: May cause damage to organs; H373: May cause damage to organs through prolonged or repeated exposure	Not applicable at this health score	2

Table 5.14 Derivatisation of the CHEM21 environment score from solvent boiling point and Hazard Statements.

Boiling point	Environmental hazard	Environment score
Not applicable	H420: Harms public health and the environment by destroying ozone in the upper atmosphere[a]	10
Below 50 °C or above 200 °C	H400: Very toxic to aquatic life; H410: Very toxic to aquatic life with long lasting effects; H411: Toxic to aquatic life with long lasting effects	7
50–69 °C or 140–200 °C	H412: Harmful to aquatic life with long lasting effects; H413: May cause long lasting harmful effects to aquatic life	5
70–139 °C	No hazard statements in the 'H4xx' category	3
Not applicable	Water	1

[a] Not used in European Regulation (EC) No 1272/2008.[45] In its place, EUH059: Hazardous to the ozone layer.

Table 5.15 Selected entries from the CHEM21 solvent selection guide.

Solvent	S	H	E	Summary
Water	1	1	1	Recommended
Methanol	4	7	5	Problematic
Ethanol	4	3	3	Recommended
Ethyl lactate	3	4	5	Problematic
Glycerol	1	1	7	Problematic
Acetone	5	3	5	Problematic
MEK	5	3	3	Recommended
Cyrene	1	2	7	Problematic
Ethyl acetate	5	3	3	Recommended
Propylene carbonate	1	2	7	Problematic
Diethyl ether	10	3	7	Hazardous
CPME	7	2	5	Problematic
THF	6	7	5	Problematic
2-MeTHF	6	5	3	Problematic
n-Hexane	8	7	7	Hazardous
Cyclohexane	6	3	7	Problematic
d-Limonene	4	2	7	Problematic
Toluene	5	6	3	Problematic
p-Cymene	4	5	5	Problematic
DCM	1	7	7	Hazardous
Carbon tetrachloride	2	7	10	Hazardous
DMF	3	9	5	Hazardous
DMSO	1	1	5	Recommended
Nitromethane	10	2	3	Hazardous
Carbon disulphide	9	7	7	Hazardous

The allocation of these summary statements is systemised. Two scores of 7, or one of 8 or higher denotes a hazardous solvent. One score of 7, or any two above 3, indicates the solvent is problematic. Otherwise the solvent is recommended.

Despite the unambiguous (if admittedly subjective) ranking, it was felt necessary to overrule the assessment based on pharmaceutical residual solvent classes or occupational exposure limits. Not only is this not applicable to anyone wishing to apply the approach to different solvents outside of the dataset provided, but it undermines the concept of the assessment, maybe even suggesting it is flawed. The adjustments given in the original publication, favourable to methanol, acetone, and anisole, but downgrading 1,4-dioxane, DMSO, and chloroform, are not given in Table 5.15.

5.4 Computational Solvent Design

Many of the chemical sectors producing high value products will have to accept the possibility that designing new solvents from scratch might be the only way to deliver the required performance and greenness in their processes.[100–102] This is an ambitious goal, but professional solvent design and selection services are available,[103,104] and a number of manufacturers are already producing new solvents to meet this challenge (as covered in Chapter 4). This demonstrates that the commercialisation of new solvents is a viable business strategy, and hopefully one that is economically sustainable.

Gani has developed a system for designing solvents based on the physical property requirements of the user. The 'ProCamd' (professional computer aided molecular design) software is able to generate molecules and their isomers based on user defined ranges of acceptable melting point, boiling point, density and polarity.[105–107] Additionally, certain functional groups can be included or excluded, and phase behaviour modelled to confirm the miscibility status of each solvent candidate in the application of interest. The relevance of the molecules produced can be ascertained with a scoring system that acts as a form of solvent selection.[105] This is achieved by indicating a target value for all the different solvent properties. Proximity to the target is rewarded with a favourable score. Both the bespoke solvents generated *in silico* and a database of common solvents can be assessed to find the most suitable option. The novel solvent candidates are pieced together in 'ProCamd' from molecular fragments and the properties of the resultant molecule estimated with group contribution models.[108,109] This approach relies on experimental data to develop the model, and considers a molecule to be (more or less) the sum of its parts with respect to how each functional group increases or decreases the value of a physical property (*e.g.* boiling point). The user must then discern between realistic molecules (those that could actually be synthesised) and less viable solvent candidates, as the software does not differentiate between the two. Recent developments by Gani have sought to model ionic liquids,[110] and solvent mixtures,[111] and introduce a greater emphasis on azeotropes and distillation characteristics for solvent recovery.[112]

Unlike 'ProCamd', GRASS ('GeneratoR of Agro-based Sustainable Solvents') designs solvents from known (bio-based) platform molecules using pre-programmed achievable chemical transformations.[113,114] The GRASS software has been tasked with the *in silico* synthesis of itaconic acid derivatives,[113] as well as solvents for nitrocellulose made from glycerol.[114] In the latter example, Moity *et al.* found diacetin to be a high performance solvent.

It is prudent to validate the solvents suggested by computer programmes by some other means before committing to synthesising them. Moity *et al.* used COSMO-RS ('COnductor-like Screening MOdel for Realistic Solvation') to interpret the polarity of their theoretical itaconic acid-derived solvents.[113] COSMO-RS is an application of statistical thermodynamics using the polarisation charge densities of the surfaces of molecules to define their properties and as a consequence their interactions.[115] Moity *et al.* took the solvent descriptions made in COSMO-RS and reinterpreted classes of solvent defined by their polarity.[116] This allows potential solvents to be assessed through comparison to existing solvents with known properties. Being able to do this with computer software makes it easy to screen a great number of solvent candidates. Targeting solvents with more particular polarity (chlorinated solvents for instance) is assisted by this methodology in particular. Acetals of glycerol have been modelled with COSMO-RS,[117] and COSMO-RS results have been incorporated into other solvent selection tools as well.[118]

In the context of reaction chemistry, the computer aided molecular design (CAMD) approach (and COSMO-RS) is suited to the calculation of equilibria using the ability of the proposed solvent(s) to interact with reactants and products.[119] An understanding of kinetics is a step more difficult as it involves transient activated complexes, whose interaction with the solvent is crucial to the rate of reaction. Either the activated complex found at the transition state of the reaction must be modelled with a dedicated approach needing a sophisticated understanding of the reaction,[120,121] or a proxy for this precise level understanding employed. As described previously, linear solvation energy relationships are a robust empirical tool for the understanding of solvent effects and the prediction of high performance solvents (Section 5.3.1.2). If the solvent properties that define the LSER can be calculated from proposed solvent structures *in silico*, then a rate constant can be predicted. This approach has been used by Folić *et al.* for a model reaction of the solvolysis of *t*-butyl chloride.[122] They found glycerol to be the ideal solvent, a prediction that was vindicated experimentally. More industrially relevant case studies are also appropriate of course. Amine solvents for carbon dioxide capture have also be studied, for example.[123,124]

The design of solvents *in silico* requires that the properties of chemicals can be adequately calculated based only on a molecular structure.[125] This is possible through a variety of computer models with increasing sophistication.[126,127] For physical properties, such as boiling point, polarity, flash point, partition coefficients *etc.* the state of the art is quite capable.[128] However, estimating toxicity remains troublesome. Despite several models for the different modes of toxicity,[129–133] there remains a need for the experimental determination of toxicological effects to remove the uncertainty of the computer models. Software is available for the prediction of toxicity in addition to physical properties. The US Environmental Protection Agency (EPA) offers the 'Toxicity Estimation Software Tool' (TEST) to download from its website.[134] The Royal Society of Chemistry's National Chemical Database Service (CDS),[135] contains 'ACD/I-Lab' which is available *via* registered UK academic networks.[136] Both software packages derive estimated toxicity and physical property data from the molecular structure provided. Toxicity models are limited by the training sets of experimental data, and particularly for toxicity data the development of novel solvents with uncommon chemical structures limits the usefulness of *in silico* predictions.

In addition to toxicity, environmental fate is an important consideration when designing bespoke solvents. Linking to the European REACH Regulation ((EC) No 1907/2006),[12] persistency, bioaccumulation, and aquatic toxicity (PBT) define the minimum acceptable standard. A substance must possess all three to be a concern. As with mammalian toxicity, actual test data is preferable to computational estimates. To this end, biodegradability (to establish environmental persistence) and aquatic toxicity are relatively straightforward and inexpensive experimental tests to conduct. Most solvents are biodegradable anyway, but incorporating esters and other functionalities vulnerable to hydrolysis can go some way to ensuring this at the solvent design stage. Avoiding functionalities that are resistant to biodegradation (*e.g.* highly branched alkyl chains) is also advantageous, and this we can learn from the history of surfactants.[137] The prediction of ecotoxicity and bioaccumulation can be performed in a crude way through estimating $\log K_{\mathrm{OW}}$ values. Substances with a $\log K_{\mathrm{OW}}$ below 4.5 are considered as unlikely to be able to reach hazardous levels of bioaccumulation. Therefore, the substance is poorly absorbed by aquatic organisms, and cannot exert a dose related toxicological effect. Remember, if a solvent is not bioaccumulating, or if it is biodegradable, it cannot be classified as PBT. Exact guidance regarding REACH requirements (which depend on the market size for the substance in question) can be found online.[138]

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CHAPTER 6

An Appendix of Solvent Data Sheets

6.1 Bio-Based Solvent Data Sheets

The following bio-based solvent data is provided in the format needed to fulfil the requirements of EN 16766,[1] as well as the CHEM21 solvent selection guide,[2] and the 12 principles of green solvents as proposed by Gu and Jérôme.[3] The numerical value of physical properties and the consequential hazard statements are provided, but not a conclusion as to whether a solvent is "green", "ungreen", "sustainable" or "unsustainable". This depends on the context of the application, whether a solvent is being substituted for another, and the implementation of sustainability (or greenness) thresholds. After the key (Table 6.1), data for 40 bio-based solvents is provided. Some are traditional solvents (*e.g.* ethyl acetate) while others are relatively new inventions. Equivalent data sheets are provided for non-renewable solvents in the final section.

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Table 6.1 Guide to using the data sheets for bio-based solvents.

Entry	Format
1. Identification	Information about the chemical structure and availability of the solvent is provided here
Product name	IUPAC name (brand name(s) in brackets)
Structure	A schematic is provided (skeletal formula)
CAS number	The CAS Registry Number
REACH registration	Information on REACH registered substances was found at https://echa.europa.eu/information-on-chemicals/registered-substances (accessed September 2016). A link to the REACH registration dossier is provided after the superscript letter ([a]) at the end of each data sheet. Registrations can be "full" or "intermediate", referring to whether the substance is a product or an isolated manufacturing intermediate
REACH status	The European Chemical agency (ECHA) provides infocards describing the hazards and uses of REACH registered substances. The infocard also summarises the regulatory status of the substance in the EU. A link to the substance's infocard is found after the superscript letter ([b]) at the end of each data sheet
Supplier	Suppliers are named, with the company location (headquarters) given in brackets. If several suppliers exist, "multiple" is written in the data sheet
Purity grade	The purity of commercial products is provided using technical specifications provided by the manufacturer. The minimum purity is given to 1 decimal place where possible. In cases where a record of the solvent purity is not available, on occasion the purity of the equivalent product supplied by Sigma-Aldrich is quoted. Where this is the case it is clearly stated, but the product may not be bio-based in this instance
Uses	Uses of each solvent are listed from the ECHA infocard or supplier information. "Research and development" is stated if uses are limited to, or are primarily, academic research
2. Biomass information	For the product(s) given in the Identification section, information about the feedstock is provided (if available) in line with the requirements of the reporting template of EN 16766 (see Chapter 4, Section 4.2.1)
Type	The type of biomass may be listed in terms of species, material, or both. Examples include starch, or corn starch
Origin	If available the country or region of origin is given (*e.g.* Brazil, or Europe)
Sustainability	The sustainability of the biomass is usually unknown. Some companies have their own policies, which are indicated. For solvents that also primarily act as fuels (*e.g.* bio-ethanol), sustainable biofuel regulations apply. Occasionally there is a record of the feedstock being certified (*e.g.* FSC for wood, RSPO for palm oil). See Chapter 3 for discussion
3. Manufacturing	Aspects of the manufacturing process are reported. The type of reaction and its environmental, social or economic impact is provided where possible. Information was obtained from supplier statements
Process name	The chemical, biological, or physical process to convert the feedstock into a solvent is provided. Examples include hydrogenation, fermentation, and extraction
Reaction	A stoichiometric reaction scheme is given. The equations are usually balanced, although some of the biological transformations and thermal cracking procedures are not drawn as balanced equations
Atom economy	An atom economy is provided to satisfy the 12 principles of green solvents proposed by Gu and Jérôme. For fermentations a yield may be given instead to better reflect the efficiency of the process

Impact	Sustainability impacts in the form of cumulative energy demand and greenhouse gas emissions have been summarised if possible. References to life cycle assessments and technoeconomic assessments are given where available
4. Bio-based content	Bio-based content data (by calculation) is given in an analogous way to the requirements of European standard EN 16776[1]
Bio-based carbon content	The theoretical bio-based carbon content is given according to the rules of EN 16785-2[4]
Total bio-based content	A percentage total bio-based content is given according to the rules of EN 16785-2[4]
Class	The class of bio-based solvent is decided on the basis of bio-based carbon content. The result in each case would have been the same if the total bio-based content had been used. Class A ≥ 95% bio-based; class B ≥ 50% bio-based; class C ≥ 25% bio-based
5. Environmental health and safety	This section of the data sheet is led by UN GHS hazard statements.[5] Information was primarily extracted from REACH dossiers, but also safety datasheets and supplier technical specifications. If no hazard statements apply, but this is due to a lack of data, this is indicated. Only those hazard statements that correspond to requirements of the CHEM21 solvent selection guide are reported here. REACH registration dossiers and safety data sheets will provide full lists of applicable hazard statements. The actual flash point, auto-ignition temperature and resistivity are also provided. Resistivity was calculated from conductivity as found in Smallwood's 'Handbook of Organic Solvent Properties'[6]
Flash point	Reported to the nearest integer value (°C). The flash point (and boiling point) determines the flammability hazard statement of the solvent
Flammability	H224: Extremely flammable liquid and vapour 
	H225: Highly flammable liquid and vapour 
	H226: Flammable liquid and vapour 

(continued)

Table 6.1 *(continued)*

Entry	Format	
Auto-ignition temperature	Reported to the nearest integer value (°C). Auto-ignition temperatures below 200 °C can cause a safety issue in some contexts	
Resistivity	The inverse of conductivity, reported in standard form, with units of Ωm. Solvents with a resistivity above 10^8 Ωm pose a safety hazard	
Other safety hazards	EU019: May form explosive peroxides (from European regulation 1272/2008)[7]	No hazard symbol
Acute toxicity	EUH070: Toxic by eye contact (from European regulation 1272/2008)[7]	No hazard symbol
	H300: Fatal if swallowed	
	H301: Toxic if swallowed	
	H302: Harmful if swallowed	
	H310: Fatal in contact with skin	
	H311: Toxic in contact with skin	
	H312: Harmful in contact with skin	

	H330: Fatal if inhaled	
	H331: Toxic if inhaled	
	H332: Harmful if inhaled	
	H336: May cause drowsiness or dizziness	
Chronic toxicity	H304: May be fatal if swallowed and enters airways	
	H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled	
	H340: May cause genetic defects	

(*continued*)

Table 6.1 (*continued*)

Entry	Format
	H341: Suspected of causing genetic defects 
	H350: May cause cancer 
	H351: Suspected of causing cancer 
	H360: May damage fertility or the unborn child 
	H361: Suspected of damaging fertility or the unborn child 
	H370: Causes damage to organs 
	H371: May cause damage to organs 

	H372: Causes damage to organs through prolonged or repeated exposure	
	H373: May cause damage to organs through prolonged or repeated exposure	
Other health hazards	EUH066: Repeated exposure may cause skin dryness or cracking (from European regulation 1272/2008)[7]	No hazard symbol
	H314: Causes severe skin burns and eye damage	
	H315: Causes skin irritation	
	H317: May cause an allergic skin reaction	
	H318: Causes eye damage	

(*continued*)

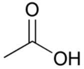
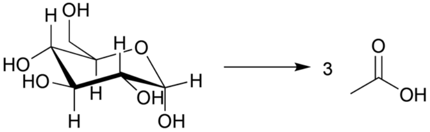
Table 6.1 (*continued*)

Entry	Format	
	H319: Causes serious eye irritation	
	H335: May cause respiratory irritation	
Environmental hazards	H400: Very toxic to aquatic life	
	H410: Very toxic to aquatic life with long lasting effects	
	H411: Toxic to aquatic life with long lasting effects	
	H412: Harmful to aquatic life with long lasting effects	No hazard symbol
	H413: May cause long lasting harmful effects to aquatic life	No hazard symbol
	H420: Harms public health and the environment by destroying the ozone in the upper atmosphere	

6. End-of-life	Statements relating to the feasibility of solvent recovery have been provided, as has guidance on the status of each solvent with respect to European hazardous waste laws (European directive 2008/98/EC).[8] The description of environmental fate is summarised from the information available on the TOXNET hazardous substances databank.[9] Information on ecotoxicity can also be found in REACH registration dossiers
Recovery	The following information may be included: How the use of the solvent impacts the ability to recover it, if distillation is energetically favourable compared to incineration with energy recovery, and any issues with distillation (azeotropes, peroxides)
Waste management	Most solvents are sufficiently hazardous to be considered as hazardous waste. This information can be found in EU region safety datasheets, and is clarified here
Environmental fate	Biodegradability is given. "Readily biodegradable" is a more stringent requirement than "inherently biodegradable". Where a high percentage biodegradability is observed, but over a longer period of time than what is needed to meet "readily biodegradable" status, "slowly biodegradable" is stated. The volatility and water solubility of a solvent will dictate its environmental fate, and its mobility between air, soil, and water. The eventual fate of each solvent is predicted, based on partition coefficients
7. Technical performance	To complete the requirements of European standard EN 16766,[1] some physical properties must be reported. These are given here, as obtained primarily from REACH registration dossiers
Polarity	δ_D, δ_P, and δ_H, are given to 1 decimal place according to the values calculated using HSPiP commercial software (units of $\mathrm{MPa}^{1/2}$)[10]
Boiling point	Reported to the nearest integer value in units of °C (at atmospheric pressure). A decomposition temperature may be reported if this is lower than the normal boiling point
Vapour pressure	Given in units of hPa, with the temperature specified
Density	The density is given in units of $\mathrm{g\ mL^{-1}}$ at 25 °C unless stated otherwise
Viscosity	Kinematic viscosity is reported in units of cSt at 40 °C unless stated otherwise. Note that dynamic viscosity is a common alternative, which can be converted to kinematic viscosity by dividing it by the density of the solvent

6.1.1 Acetic acid

Table 6.2 Acetic acid data sheet.

Identification			
Product name	Acetic acid		
Structure			
CAS number	64-19-7		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Cleaning products, coatings, and anti-freeze products. Solvent for the production of PET		
Biomass information			
Type	Sugars or starch (food grade)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation		
Reaction		Atom economy	100%
Impact	Anaerobic fermentation from corn starch is highly energy intensive[11]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	39 °C	Flammability	H226
Auto-ignition temperature	427 °C		
Resistivity	1.7×10^7 Ωm	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H314	Environmental hazards	n/a
End-of-life			
Recovery	Distillation energetically preferable to energy recovery[12]		
Waste management	Hazardous substance: Flammable and corrosive. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporates from dry soil. High water solubility/high soil mobility directs acetic acid into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	14.5 MPa$^{1/2}$	
	δ_P	8.0 MPa$^{1/2}$	
	δ_H	13.5 MPa$^{1/2}$	
Boiling point	118 °C	Density	1.04 g mL^{-1}
Vapour pressure	20.8 hPa (25 °C)	Viscosity	1.0 cSt (25 °C)

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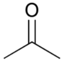
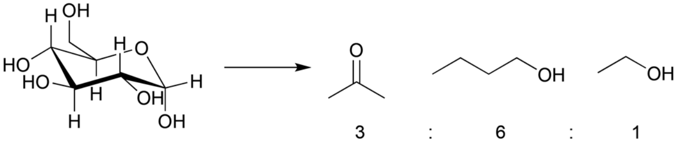
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15549.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.528.

6.1.2 Acetone

Table 6.3 Acetone data sheet.

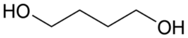
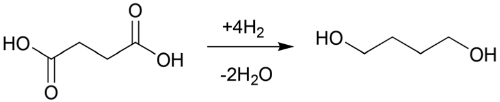
Identification			
Product name	Acetone		
Structure			
CAS number	67-64-1		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Green Biologics (UK), Cathay Industrial Biotech. (China)	Purity grade	Unknown
Uses	Anti-freeze products, coatings, lubricants, adhesives, non-metal surface treatment products, manufacture of fabricated metal products, and various types of formulations		
Biomass information			
Type	Corn starch		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation (co-produced with 1-butanol)		
Reaction		Atom econ.	Product yield typically 30%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	−20 °C	Flammability	H225 (highly)
Auto-ignition temperature	540 °C		
Resistivity	2.0×10^7 Ωm	Other safety hazards	n/a
Acute toxicity	H336	Chronic toxicity	n/a
Other health hazards	EUH066, H319	Environmental hazards	n/a
End-of-life			
Recovery	Distillation energetically preferable to energy recovery.[12] Acetone is exempt from VOC status in the USA[13]		
Waste management	Hazardous substance: Flammable, eye irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.5 $\mathrm{MPa}^{1/2}$	
	δ_P	10.4 $\mathrm{MPa}^{1/2}$	
	δ_H	7.0 $\mathrm{MPa}^{1/2}$	
Boiling point	56 °C	Density	0.79 g mL^{-1} (20 °C)
Vapour pressure	233 hPa (20 °C)	Viscosity	0.34 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15460.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.602.

6.1.3 1,4-Butanediol

Table 6.4 1,4-Butanediol data sheet.

Identification			
Product name	1,4-Butanediol		
Structure			
CAS number	110-63-4		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Genomatica (USA). Technology licensed to several other companies in Europe	Purity grade	Unknown
Uses	Cosmetics and personal care products, reactive coalescing agent for coatings, adhesives, polymers and inks		
Biomass information			
Type	Sugars: sucrose from sugarcane and sugar beet, or dextrose (corn, cassava)		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation (direct or *via* succinic acid)		
Reaction		Atom economy	71%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	121 °C	Flammability	n/a
Auto-ignition temperature	385 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	H302, H336	Chronic toxicity	n/a (inconclusive reprotoxicity tests)
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Hazardous substance: Acutely toxic. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental 1,4-butanediol into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	16.6 MPa$^{1/2}$	
	δ_P	11.0 MPa$^{1/2}$	
	δ_H	20.9 MPa$^{1/2}$	
Boiling point	232 °C	Density	1.02 g mL^{-1} (20 °C)
Vapour pressure	0.019 hPa (25 °C)	Viscosity	83.2 cSt (20 °C)

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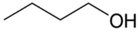
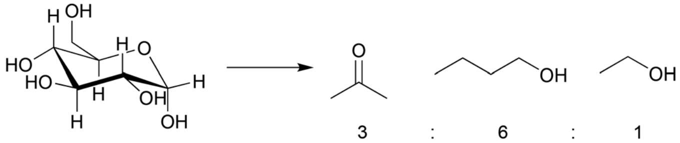
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15496.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.443.

6.1.4 1-Butanol

Table 6.5 1-Butanol data sheet.

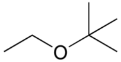
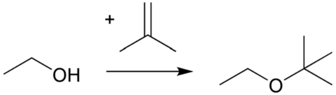
Identification			
Product name	1-Butanol		
Structure			
CAS number	71-36-3		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple pre-commercial operations	Purity grade	Depends on supplier
Uses	Anti-freeze products, adhesives and sealants, polishes and waxes, chemical synthesis		
Biomass information			
Type	Corn starch, sugarcane, sugar beet		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation. Guerbet reaction (ethanol coupling) also possible (Abengoa Bioenergía, Spain)		
Reaction		Atom econ.	Product yield typically 30%
Impact	Use of agricultural lignocellulosic feedstocks is being examined. Process from starch has a reasonably similar cumulative energy demand (116 MJ kg^{-1}) to petrochemical propylene hydration[14]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	35 °C	Flammability	H226
Auto-ignition temperature	355 °C		
Resistivity	1.1×10^7 Ωm	Other safety hazards	n/a
Acute toxicity	H302, H336	Chronic toxicity	n/a
Other health hazards	H315, H318, H335	Environmental hazards	n/a
End-of-life			
Recovery	Distillation energetically preferable to energy recovery[12]		
Waste management	Hazardous substance: Flammable and toxic. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	16.0 MPa$^{1/2}$	
	δ_P	5.7 MPa$^{1/2}$	
	δ_H	15.8 MPa$^{1/2}$	
Boiling point	118 °C	Density	0.81 g mL^{-1} (21 °C)
Vapour pressure	10 hPa (20 °C)	Viscosity	3 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15322.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.683.

6.1.5 *t*-Butyl Ethyl Ether

Table 6.6 *t*-Butyl ethyl ether data sheet.

Identification			
Product name	*t*-Butyl ethyl ether		
Structure			
CAS number	637-92-3		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Braskem (Brazil)	Purity grade	>96.5% (up to 3% ethanol)
Uses	Fuel additive		
Biomass information			
Type	Sugarcane sucrose		
Origin	Brazil		
Sustainability	Information provided by supplier[15]		
Manufacturing			
Process name	Ethanol alkylation by isobutene		
Reaction		Atom economy	100%
Impact	Lower greenhouse gas emissions than *t*-butyl methyl ether (0.783 kg (CO_2 equivalents) per kg of solvent)		
Bio-based content			
Bio-based carbon content	33%	Class	C
Total bio-based content	44%		
Environmental health and safety			
Flash point	−19 °C	Flammability	H225 (highly)
Auto-ignition temperature	392 °C		
Resistivity	Unknown	Other safety hazards	n/a

Acute toxicity	H336	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides)		
Waste management	Hazardous substance: Flammable. Treated as hazardous waste within the EU		
Environmental fate	Very persistent (but not bioaccumulating). Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	14.4 $MPa^{1/2}$	
	δ_P	3.5 $MPa^{1/2}$	
	δ_H	2.7 $MPa^{1/2}$	
Boiling point	73 °C	Density	0.74 g mL^{-1} (20 °C)
Vapour pressure	170 hPa (25 °C)	Viscosity	0.47 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15520.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.010.282.

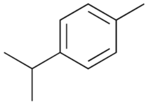
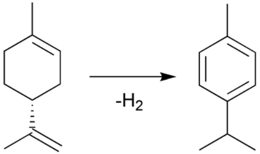
6.1.6 Carbon Dioxide

Table 6.7 Carbon dioxide data sheet.

Identification			
Product name	Carbon dioxide		
Structure	$O=C=O$		
CAS number	124-38-9		
REACH registration	No	REACH status	Exempt
Supplier	Multiple	Purity grade	Ultra-pure grades available
Uses	Food grade extractions		
Biomass information			
Type	Potentially any biomass		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation, combustion, organic recycling (for example)		
Reaction	n/a	Atom economy	n/a
Impact	Carbon dioxide is a waste product of many industries (brewing, Haber process, cement kilns *etc.*)		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	n/a	Flammability	n/a
Auto-ignition temperature	n/a		
Resistivity	n/a	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Can be recycled in supercritical fluid applications		
Waste management	Waste containers are issued with a warning: Vessels may contain gas under pressure that may explode if heated		
Environmental fate	Greenhouse gas		
Technical performance			
Polarity	δ_D	15.7 $MPa^{1/2}$	
	δ_P	6.3 $MPa^{1/2}$	
	δ_H	5.7 $MPa^{1/2}$	
Boiling point	−78.5 °C	Density	n/a
Vapour pressure	57 249 hPa (20 °C)	Viscosity	n/a

6.1.7 *p*-Cymene

Table 6.8 *p*-Cymene data sheet.

Identification			
Product name	*p*-Cymene		
Structure			
CAS number	99-87-6		
REACH registration	Intermediate[a]	REACH status	No action needed[b]
Supplier	Multiple. Vigon (USA) sell bio-based *p*-cymene on a multi-kilogram scale	Purity grade	95% (Axxence, Germany), 97% (Vigon, USA), 97% (Aurochemicals, USA)
Uses	Research and development		
Biomass information			
Type	Terpene oils, including sulphite pulp liquors		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Distillation (pulp liquor feedstock) or dehydrogenation (of limonene)		
Reaction	 $-H_2$	Atom economy	99%
Impact	Environmental and technoeconomic assessments show co-production of pectin and hydrogen gas is a feasible biorefinery operation.[16] Gasification of the residual biomass is appealing in theory but in fact proven to be detrimental		

(*continued*)

Table 6.8 (*continued*)

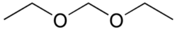
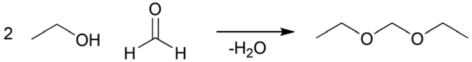
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	47 °C	Flammability	H226
Auto-ignition temperature	436 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	H304
Other health hazards	H315, H319	Environmental hazards	H411
End-of-life			
Recovery	Recoverable by distillation (but liable to oxidation)		
Waste management	Hazardous substance: Flammable, irritant, ecotoxic. Treated as hazardous waste within the EU		
Environmental fate	Slowly biodegradable. High affinity for soils, or if discharged into water suspended solids and sediment. Evaporation is important		
Technical performance			
Polarity	δ_D	17.3 MPa$^{1/2}$	
	δ_P	2.4 MPa$^{1/2}$	
	δ_H	2.4 MPa$^{1/2}$	
Boiling point	177 °C	Density	0.86 g mL^{-1}
Vapour pressure	2.0 hPa (20 °C)	Viscosity	0.8 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/8564.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.002.542.

6.1.8 Diethoxymethane

Table 6.9 Diethoxymethane data sheet.

Identification			
Product name	Diethoxymethane (ethylal)		
Structure			
CAS number	462-95-3		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Lambiotte & Cie (Belgium)	Purity grade	Unknown
Uses	Paints and coatings, anti-freeze products		
Biomass information			
Type	Any bio-ethanol sources (typically sugars or starch)		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Acetalisation of formaldehyde		
Reaction		Atom economy	85%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	80%	Class	B
Total bio-based content	87%		

(continued)

Table 6.9 (*continued*)

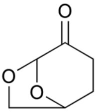
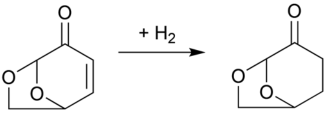
Environmental health and safety			
Flash point	4 °C	Flammability	H225 (highly)
Auto-ignition temperature	240 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H315, H319, H335	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides). Mostly used in formulations, including coatings, and so actually the most likely fate is escape to the air		
Waste management	Hazardous substance: Flammable, irritant. Treated as hazardous waste within the EU		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	15.4 MPa$^{1/2}$	
	δ_P	5.7 MPa$^{1/2}$	
	δ_H	5.1 MPa$^{1/2}$	
Boiling point	88 °C	Density	0.83 g mL^{-1} (20 °C)
Vapour pressure	70 hPa (20 °C)	Viscosity	0.5 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/11805.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.006.665.

6.1.9 Dihydrolevoglucosenone

Table 6.10 Dihydrolevoglucosenone data sheet.

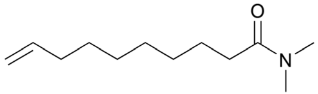
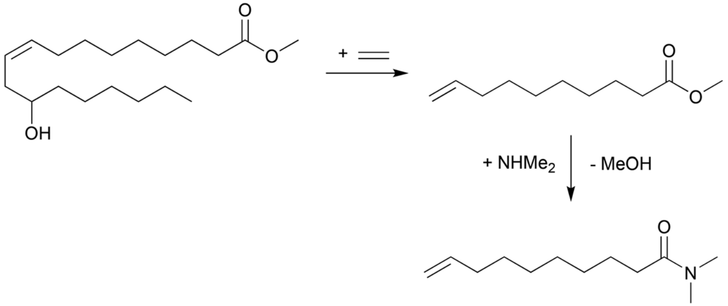
Identification			
Product name	Dihydrolevoglucosenone (Cyrene™)		
Structure			
CAS number	53716-82-8		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Circa (Australia)	Purity grade	>99.5%
Uses	Research and development		
Biomass information			
Type	Softwood lignocellulose		
Origin	Australia		
Sustainability	FSC certified plantation		
Manufacturing			
Process name	Hydrogenation of levoglucosenone		
Reaction		Atom economy	100%
Impact	Global warming potential lower than NMP synthesis[17]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	108 °C	Flammability	n/a
Auto-ignition temperature	296 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H319	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Vacuum distillation. Decomposes during distillation at normal atmospheric pressure		
Waste management	Hazardous substance: Eye irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	18.8 MPa$^{1/2}$	
	δ_P	10.6 MPa$^{1/2}$	
	δ_H	6.9 MPa$^{1/2}$	
Boiling point	Decomposes at 227 °C	Density	1.25 g mL^{-1}
Vapour pressure	0.28 hPa (25 °C)	Viscosity	8.8 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/16252.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.234.612.

6.1.10 *N*,*N*-Dimethyl dec-9-enamide

Table 6.11 *N*,*N*-Dimethyl dec-9-enamide data sheet.

Identification			
Product name	*N*,*N*-Dimethyl dec-9-enamide (STEPOSOL® MET-10U)		
Structure			
CAS number	1356964-77-6		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Stepan (USA)	Purity grade	>97%
Uses	Cleaning products, paint stripper, cosmetics and personal care products		
Biomass information			
Type	Vegetable oil (*e.g.* castor oil)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Olefin metathesis (of castor oil ricinoleic acids) and amidation		
Reaction		Atom econ.	51%
Impact	Unknown		

Bio-based content			
Bio-based carbon content	83%	Class	B
Total bio-based content	78%		
Environmental health and safety			
Flash point	146 °C	Flammability	n/a
Auto-ignition temperature	240 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	H302	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H315, H319, H335	Environmental hazards	H412
End-of-life			
Recovery	Also used as a non-ionic surfactant. Discharged with waste water		
Waste management	Hazardous substance: Toxic, irritant. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.8 MPa$^{1/2}$	
	δ_P	7.3 MPa$^{1/2}$	
	δ_H	5.3 MPa$^{1/2}$	
Boiling point	293 °C	Density	0.893 g mL^{-1}
Vapour pressure	0.0024 hPa (25 °C)	Viscosity	4 cSt (25 °C)

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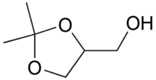
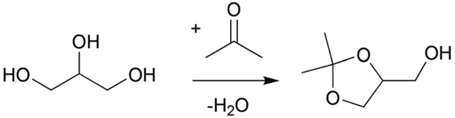
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/12160.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.234.260.

6.1.11 2,2-Dimethyl-1,3-dioxolan-4-yl methanol

Table 6.12 2,2-Dimethyl-1,3-dioxolan-4-yl methanol data sheet.

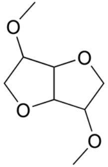
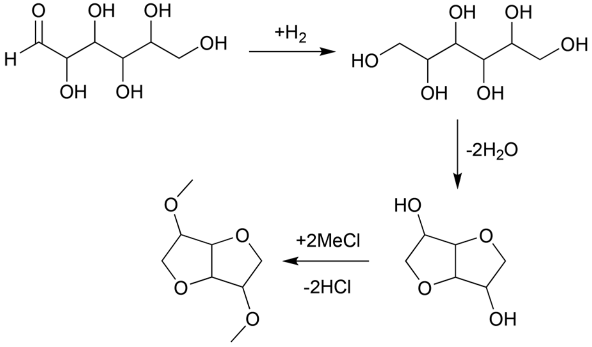
Identification			
Product name	2,2-Dimethyl-1,3-dioxolan-4-yl methanol (Solketal, Augeo™ SL 191)		
Structure			
CAS number	100-79-8		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium)	Purity grade	>97.5% (Aldrich product)
Uses	Cleaning products, coating products, polishes and waxes, cosmetics and personal care products		
Biomass information			
Type	Vegetable oil		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Ketalisation of acetone with glycerol		
Reaction		Atom economy	88%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	50%	Class	B
Total bio-based content	68%		

Environmental health and safety			
Flash point	90 °C	Flammability	n/a
Auto-ignition temperature	390 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H319	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Used in formulations. May be discharged with waste water. Expected to evaporate to the air after application in coatings		
Waste management	Hazardous substance: Eye irritation. Treated as hazardous waste within the EU		
Environmental fate	Inherently biodegradable. High affinity for water		
Technical performance			
Polarity	δ_D	16.0 MPa$^{1/2}$	
	δ_P	7.2 MPa$^{1/2}$	
	δ_H	26.1 MPa$^{1/2}$	
Boiling point	192 °C	Density	1.064
Vapour pressure	0.46 hPa (20 °C)	Viscosity	11 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/12258.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.002.626.

6.1.12 Dimethyl Isosorbide

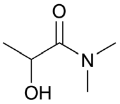
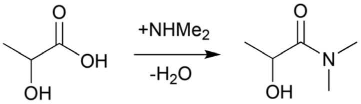
Table 6.13 Dimethyl isosorbide data sheet.

Identification			
Product name	Dimethyl isosorbide (Arlasolve™)		
Structure			
CAS number	5306-85-4		
REACH registration	No	REACH status	n/a
Supplier	Croda (UK)	Purity grade	>90%
Uses	Research and development as well as personal care products		
Biomass information			
Type	Starch		
Origin	Europe		
Sustainability	Roquette's commitment to sustainable raw materials is available online[18]		
Manufacturing			
Process name	Methylation of isosorbide from sorbitol		
Reaction		Atom econ.	61% (from glucose); 70% (from isosorbide)

Impact	Unknown		
Bio-based content			
Bio-based carbon content	75%	Class	B
Total bio-based content	83%		
Environmental health and safety			
Flash point	120 °C	Flammability	n/a
Auto-ignition temperature	Unknown		
Resistivity	Unknown	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	17.6 $MPa^{1/2}$	
	δ_P	7.1 $MPa^{1/2}$	
	δ_H	7.5 $MPa^{1/2}$	
Boiling point	95 °C (0.1 hPa)	Density	1.15–1.17 g mL^{-1}
Vapour pressure	Unknown	Viscosity	6 cSt

6.1.13 *N*,*N*-Dimethyl Lactamide

Table 6.14 *N*,*N*-Dimethyl lactamide data sheet.

Identification			
Product name	*N*,*N*-Dimethyl lactamide		
Structure			
CAS number	35123-06-9		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Agrochemical formulations		
Biomass information			
Type	Corn starch		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Amidation (of lactic acid or its esters)		
Reaction		Atom economy	87%
Impact	Technical information on the synthesis of dialkyl lactamides is available from patents, that also extol the advantages of *N*,*N*-dimethyl lactamide as a solvent for agrochemical formulations[19]		
Bio-based content			
Bio-based carbon content	60%	Class	B
Total bio-based content	62%		
Environmental health and safety			
Flash point	110 °C	Flammability	n/a
Auto-ignition temperature	Unknown		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a

End-of-life			
Recovery	Used in agrochemical formulations and introduced into the environment. Not recoverable		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	18.0 $MPa^{1/2}$	
	δ_P	12.8 $MPa^{1/2}$	
	δ_H	16.9 $MPa^{1/2}$	
Boiling point	Decomposes at 224 °C	Density	1.05 g mL^{-1} (20 °C)
Vapour pressure	≤0.12 hPa (20 °C)	Viscosity	(non-Newtonian fluid)

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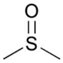
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/11068.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.132.568.

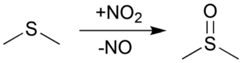
6.1.14 Dimethyl Sulphoxide

Table 6.15 Dimethyl sulphoxide data sheet.

Identification			
Product name	Dimethyl sulphoxide		
Structure			
CAS number	67-68-5		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Chemical synthesis, adhesives, anti-freeze products, coating products, plant protection products		
Biomass information			
Type	Lignocellulose		
Origin	All regions		
Sustainability	Forestry product certification will usually apply		
Manufacturing			
Process name	Oxidation of dimethyl sulphide obtained from sulphide waste liquors in pulp and paper industry		

(*continued*)

Table 6.15 (*continued*)

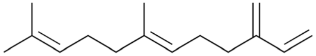
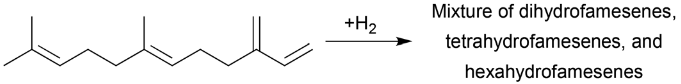
Reaction		Atom economy	72% (NO can be used catalytically, re-oxidised in air to increase atom economy to 100%)
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	87 °C	Flammability	n/a
Auto-ignition temperature	300 °C		
Resistivity	5.0×10^7 Ωm	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	High temperatures result in decomposition, hampering recovery by distillation. Energy recovery requires an incinerator with an afterburner and a scrubber to remove sulphur containing by-products		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Conflicting biodegradability studies, probably inherently biodegradable. High affinity for water		
Technical performance			
Polarity	δ_D	18.4 MPa$^{1/2}$	
	δ_P	16.4 MPa$^{1/2}$	
	δ_H	10.2 MPa$^{1/2}$	
Boiling point	189 °C	Density	1.1 g mL^{-1} (20 °C)
Vapour pressure	0.556 hPa (20 °C)	Viscosity	1.9 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15007.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.604.

6.1.15 1,6,10-Dodecatriene, 7,11-Dimethyl-3-methylene-, (6E)-, Hydrogenated

Table 6.16 1,6,10-Dodecatriene, 7,11-dimethyl-3-methylene-, (6E)-, hydrogenated data sheet.

Identification			
Product name	1,6,10-Dodecatriene, 7,11-dimethyl-3-methylene-, (6E)-, hydrogenated (Myralene™ 10)		
Structure	 Partial hydrogenated *trans*-ß-farnesene (shown)		
CAS number	1581740-29-5		
REACH registration	No	REACH status	n/a
Supplier	Amyris (USA)	Purity grade	Unknown
Uses	Industrial hand cleaner (Muck Daddy brand)[20]		
Biomass information			
Type	Sugarcane		
Origin	Brazil		
Sustainability	Unknown		
Manufacturing			
Process name	Hydrogenation of *trans*-β-farnesene		
Reaction		Atom econ.	100%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

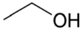
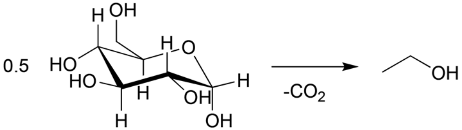
(*continued*)

Table 6.16 (*continued*)

Environmental health and safety			
Flash point	Unknown	Flammability	n/a (data may be lacking)
Auto-ignition temperature	Unknown		
Resistivity	Unknown	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Used in hand cleaning formulations. Likely to be discharged with waste water after rinsing		
Waste management	Unknown		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	~16.4 MPa$^{1/2}$ (*trans*-β-farnesene)	
	δ_P	~0.9 MPa$^{1/2}$ (*trans*-β-farnesene)	
	δ_H	~1.8 MPa$^{1/2}$ (*trans*-β-farnesene)	
Boiling point	Unknown	Density	Unknown
Vapour pressure	Unknown	Viscosity	Unknown

6.1.16 Ethanol

Table 6.17 Ethanol data sheet.

Identification			
Product name	Ethanol		
Structure			
CAS number	64-17-5		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Typically >99%
Uses	Coatings, inks, anti-freeze and cleaning formulations		
Biomass information			
Type	Sugarcane sucrose, corn starch, wheat starch		
Origin	All regions		
Sustainability	Bioethanol made for fuel purposes is typically made of sustainable biomass, and is a legal requirement in some regions, *e.g.* Europe[21]		
Manufacturing			
Process name	Fermentation		
Reaction		Atom economy	51%
Impact	Major production route relies on aerobic fermentation of food-grade biomass (from an aqueous broth containing nutrients and microorganisms). Cumulative energy demand (EU production from carbohydrate) is 71 MJ kg^{-1} with GHG emissions of 1.47 kg CO_2 kg^{-1}. Lower production energy and negative GHG emissions have been reported for lignocellulosic ethanol production.[22] Large scale adoption of so-called second generation bio-ethanol is yet to be widely implemented		

(*continued*)

Table 6.17 (*continued*)

Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	12 °C	Flammability	H225 (highly)
Auto-ignition temperature	363 °C		
Resistivity	7.1×10^7 Ωm	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Distillation and incineration have similar net energy balances[12]		
Waste management	Hazardous substance: Flammable, eye irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.8 MPa$^{1/2}$	
	δ_P	8.8 MPa$^{1/2}$	
	δ_H	19.4 MPa$^{1/2}$	
Boiling point	78 °C	Density	0.789 g mL^{-1}
Vapour pressure	59.5 hPa (20 °C)	Viscosity	1.082 cSt

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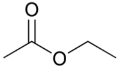
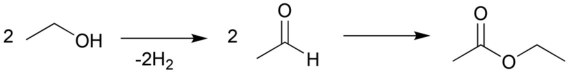
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/16105.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.526.

6.1.17 Ethyl Acetate

Table 6.18 Ethyl acetate data sheet.

Identification			
Product name	Ethyl acetate		
Structure			
CAS number	141-78-6		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Davy-Sasol (UK-South Africa) and Sekab (Sweden)	Purity grade	>99.5% (Davy-Sasol), fuel grade (Sekab)
Uses	Inks, coatings, cosmetics and adhesives		
Biomass information			
Type	Cellulose (rayon grade), sugarcane sucrose, and corn starch		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Ethanol oxidation (to aldehyde) and Tishchenko dimerisation		
Reaction		Atom economy	96%
Impact	Davy technologies patented a procedure to convert ethanol to ethyl acetate. The process was implemented by Sasol in their South African plant. Whether petrochemical ethanol or bio-ethanol is used as a feedstock is entirely economically driven. Information on the industrial process is not available. Sekab have withdrawn their ethyl acetate because of its low purity coming from fuel grade second generation ethanol. Note some ethyl acetate production does not require ethanol (*e.g.* Avada™ process), and so contains no bio-based content. The carbon dioxide emissions balance can be improved by using bio-ethanol as a reactant instead of petrochemical ethanol[23]		

(*continued*)

Table 6.18 (*continued*)

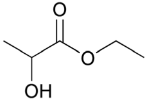
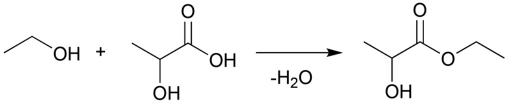
Bio-based content			
Bio-based carbon content	0–100%	Class	Depends on source
Total bio-based content	0–100%		
Environmental health and safety			
Flash point	−4 °C	Flammability	H225 (highly)
Auto-ignition temperature	427 °C		
Resistivity	1.0×10^8 Ωm	Other safety hazards	n/a
Acute toxicity	H336	Chronic toxicity	n/a
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Distillation energetically preferable to energy recovery.[12] Expected to evaporate to the air after coating and cleaning applications		
Waste management	Hazardous substance: Flammable, eye irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.8 $\text{MPa}^{1/2}$	
	δ_P	5.3 $\text{MPa}^{1/2}$	
	δ_H	7.2 $\text{MPa}^{1/2}$	
Boiling point	77 °C	Density	0.895 g mL^{-1} (20 °C)
Vapour pressure	97.3 hPa (20 °C)	Viscosity	0.50 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15437.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.005.001.

6.1.18 Ethyl Lactate

Table 6.19 Ethyl lactate data sheet.

Identification			
Product name	Ethyl lactate		
Structure			
CAS number	97-64-3: Ethyl lactate. 687-47-8: Ethyl L-lactate		
REACH registration	Full (687-47-8)[a]	REACH status	No action needed[b]
Supplier	Galatic (Belgium), Corbion (Netherlands)	Purity grade	98% (Galatic)
Uses	Cleaning formulations, research and development		
Biomass information			
Type	Corn starch, sugar cane		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation and esterification		
Reaction		Atom economy	87%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

(*continued*)

Table 6.19 (*continued*)

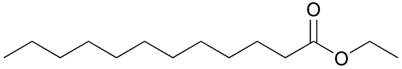
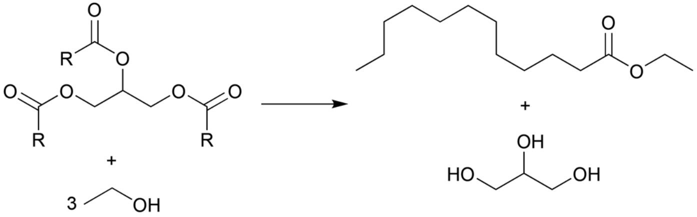
Environmental health and safety			
Flash point	53 °C	Flammability	H226
Auto-ignition temperature	430 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H318, H335	Environmental hazards	n/a
End-of-life			
Recovery	Distillation possible, but an homogeneous azeotrope with water (21%) must be considered[24]		
Waste management	Hazardous substance: Flammable, causes serious eye damage and respiratory irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental ethyl lactate into water bodies (not bioaccumulating, hydrolysed into lactic acid and ethanol)		
Technical performance			
Polarity	δ_D	$16.0\ \mathrm{MPa}^{1/2}$	
	δ_P	$7.6\ \mathrm{MPa}^{1/2}$	
	δ_H	$12.5\ \mathrm{MPa}^{1/2}$	
Boiling point	153 °C	Density	$1.033\ \mathrm{g\ mL}^{-1}$ (20 °C)
Vapour pressure	2.2 hPa (20 °C)	Viscosity	1.4 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/13866.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.010.632.

6.1.19 Ethyl Laurate

Table 6.20 Ethyl laurate data sheet.

Identification			
Product name	Ethyl laurate (Diamosolv™ 323)		
Structure			
CAS number	106-33-2		
REACH registration	No	REACH status	n/a
Supplier	Dow (USA)	Purity grade	100.0% claimed in safety data sheet
Uses	Cleaning and degreasing applications		
Biomass information			
Type	Vegetable oil, rich in short chain saturated triglycerides (*e.g.* coconut)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Transesterification (biodiesel production)		
Reaction		Atom econ.	88%
Impact	Unknown		

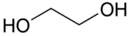
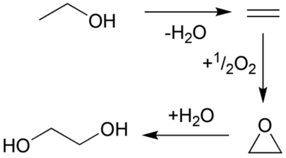
(*continued*)

Table 6.20 (*continued*)

Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	136 °C	Flammability	n/a
Auto-ignition temperature	Unknown		
Resistivity	Unknown	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Used in formulations. Disposal after use expected		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.0 MPa$^{1/2}$	
	δ_P	3.1 MPa$^{1/2}$	
	δ_H	3.6 MPa$^{1/2}$	
Boiling point	275 °C	Density	0.86 g mL^{-1} (25 °C)
Vapour pressure	0.00092 hPa (20 °C)	Viscosity	3.7 cSt (25 °C)

6.1.20 Ethylene Glycol

Table 6.21 Ethylene glycol data sheet.

Identification			
Product name	Ethylene glycol		
Structure			
CAS number	107-21-1		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Greencol Taiwan Corporation (China), JBF Industries Ltd (India)	Purity grade	Unknown (produced as an intermediate for polymer synthesis, not as a solvent)[25]
Uses	Anti-freeze products, textile treatment products and dyes, cleaning products, coatings, non-metal surface treatment products, leather treatment products, inks, heat transfer fluids and hydraulic fluids. A significant amount of global ethylene glycol production is for the purpose of making polyesters		
Biomass information			
Type	Sugarcane sucrose		
Origin	Brazil		
Sustainability	Unknown		
Manufacturing			
Process name	Bio-ethanol oxidation		
Reaction		Atom economy	78%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

(*continued*)

Table 6.21 (*continued*)

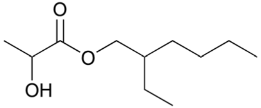
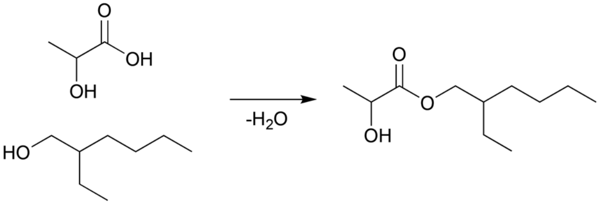
Environmental health and safety			
Flash point	111 °C	Flammability	n/a
Auto-ignition temperature	410 °C		
Resistivity	8.3×10^4 Ωm	Other safety hazards	n/a
Acute toxicity	H302	Chronic toxicity	H373
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Discharged with waste water		
Waste management	Hazardous substance: Toxic. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental ethylene glycol into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	17.0 $\text{MPa}^{1/2}$	
	δ_P	11.0 $\text{MPa}^{1/2}$	
	δ_H	26.0 $\text{MPa}^{1/2}$	
Boiling point	197 °C	Density	1.11 g mL^{-1} (20 °C)
Vapour pressure	0.067 hPa (20 °C)	Viscosity	15 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15973.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.159.

6.1.21 2-Ethylhexyl Lactate

Table 6.22 2-Ethylhexyl lactate data sheet.

Identification			
Product name	2-Ethylhexyl lactate		
Structure			
CAS number	6283-86-9		
REACH registration	Full[a]	REACH status	Sensitiser[b]
Supplier	Galatic (Belgium)	Purity grade	95% (Galatic)
Uses	Plasticiser. Also applicable to lubricants, metal working fluids, coating products, surface treatment products, heat transfer fluids		
Biomass information			
Type	Corn starch, sugar cane		
Origin	All regions		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation and esterification		
Reaction		Atom economy	92%
Impact	Unknown		

(*continued*)

Table 6.22 (*continued*)

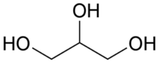
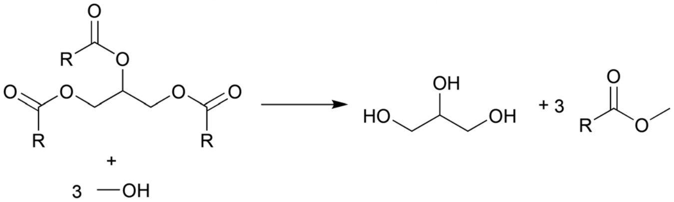
Bio-based content			
Bio-based carbon content	27%	Class	C
Total bio-based content	36%		
Environmental health and safety			
Flash point	113 °C	Flammability	n/a
Auto-ignition temperature	270 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H315, H317, H319	Environmental hazards	n/a
End-of-life			
Recovery	Typically incorporated into formulations and not recovered		
Waste management	Hazardous substance: Sensitising and an irritant. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.3 $\text{MPa}^{1/2}$	
	δ_P	4.7 $\text{MPa}^{1/2}$	
	δ_H	8.6 $\text{MPa}^{1/2}$	
Boiling point	246 °C	Density	0.94 g mL^{-1} (20 °C)
Vapour pressure	0.0012 hPa (25 °C)	Viscosity	3.5 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/11649.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.025.913.

6.1.22 Glycerol

Table 6.23 Glycerol data sheet.

Identification			
Product name	Glycerol		
Structure			
CAS number	56-81-5		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple[26]	Purity grade	80% (crude), 95.5% (technical grade), >99.5% (purified)
Uses	Cosmetics and personal care products, perfumes and fragrances, and textile treatment products		
Biomass information			
Type	Vegetable oil (*e.g.* rapeseed)		
Origin	All regions		
Sustainability	An initiative between Unilever (formulator) and Cargill (rapeseed supplier) has led to sustainable rapeseed production in Germany,[27] according to Unilever's Sustainable Agricultural Code[28]		
Manufacturing			
Process name	Transesterification (biodiesel production)		
Reaction		Atom econ.	~9%
Impact	Glycerol is the by-product of bio-diesel production. The low atom economy is therefore not relevant, only indicating the relative mass of glycerol co-produced alongside bio-diesel		

(*continued*)

Table 6.23 (*continued*)

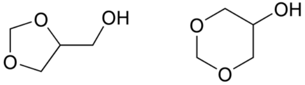
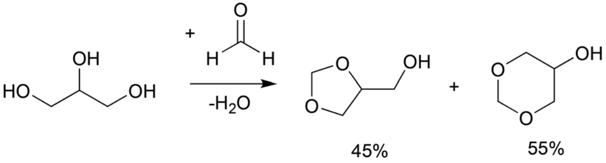
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	160 °C	Flammability	n/a
Auto-ignition temperature	405–440 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used as a solvent in consumer formulations so glycerol is not recovered		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental glycerol into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	17.4 $MPa^{1/2}$	
	δ_P	11.3 $MPa^{1/2}$	
	δ_H	27.2 $MPa^{1/2}$	
Boiling point	290 °C	Density	1.26 g mL^{-1}
Vapour pressure	0.0033 hPa (50 °C)	Viscosity	225 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14481.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.263.

6.1.23 Glycerol Formal

Table 6.24 Glycerol formal data sheet.

Identification			
Product name	Glycerol formal (mixture of 1,3-dioxan-5-ol (55%) and 1,3-dioxolan-4-yl methanol (45%))		
Structure			
CAS number	5464-28-8 and 4740-78-7		
REACH registration	Full[a]	REACH status	Suspected reprotoxin[b]
Supplier	Glaconchemie (Germany), Lambiotte & Cie (Belgium)	Purity grade	>99.5%
Uses	Cleaning products, plant protection, anti-freeze, coating products, and welding/soldering products		
Biomass information			
Type	Vegetable oil		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Acetalisation of formaldehyde with glycerol		
Reaction		Atom economy	85%
Impact	Unknown		

(*continued*)

Table 6.24 (*continued*)

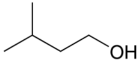
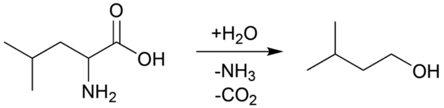
Bio-based content			
Bio-based carbon content	75%	Class	B
Total bio-based content	87%		
Environmental health and safety			
Flash point	98 °C	Flammability	n/a
Auto-ignition temperature	>400 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	H361
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Hazardous substance: Toxic, eye irritation. Treated as hazardous waste within the EU		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	18.4 MPa$^{1/2}$	
	δ_P	10.6 MPa$^{1/2}$	
	δ_H	16.5 MPa$^{1/2}$	
Boiling point	194 °C	Density	1.20–1.22 g mL^{-1}
Vapour pressure	0.3 hPa (20 °C)	Viscosity	11.7 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/12370.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.143.129.

6.1.24 Isoamyl Alcohol

Table 6.25 Isoamyl alcohol data sheet.

Identification			
Product name	Isoamyl alcohol (fusel oil alcohol)		
Structure			
CAS number	123-51-3		
REACH registration	Full[a]	REACH status	Substance included in the Community Rolling Action Plan (CoRAP)[b]
Supplier	Synthetic: Chemoxy (UK). Natural: Advanced Biotech (USA)	Purity grade	Fusel oil is typically 65% isoamyl alcohol[29]
Uses	Coating products, cleaning products, polishes and waxes		
Biomass information			
Type	Sugarcane sucrose, corn starch, wheat starch		
Origin	All regions		
Sustainability	If isoamyl alcohol (fusel oil) is isolated from ethanol production lines made for fuel purposes, sustainable biomass requirements are likely to be in place. If obtained from the brewing industry, the feedstock will be food grade		
Manufacturing			
Process name	Fermentation (side reaction of amino acid catabolism)[30]		
Reaction		Atom economy	59%
Impact	Side product of primary process of fermentation to ethanol. Allocation of environmental impact on a mass basis would result in a minimal contribution to fusel oil. Future increases in demand could make the impact more significant on the basis of economic allocation		

(*continued*)

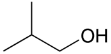
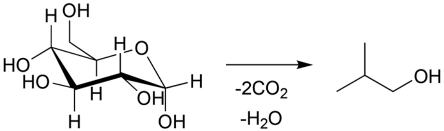
Table 6.25 (*continued*)

Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	45 °C	Flammability	H226
Auto-ignition temperature	335 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	H332	Chronic toxicity	n/a
Other health hazards	H315, H318, H335	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation. Fusel oil contains several near-boiling and azeotropic components, typically water, methanol, ethanol, propanol, butanol, isobutanol and isoamyl alcohol[31]		
Waste management	Hazardous substance: Flammable, causes skin, eye, and respiratory irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.8 $\text{MPa}^{1/2}$	
	δ_P	5.2 $\text{MPa}^{1/2}$	
	δ_H	13.3 $\text{MPa}^{1/2}$	
Boiling point	128 °C	Density	0.81 g mL^{-1} (20 °C)
Vapour pressure	3.3 hPa (20 °C)	Viscosity	5.3 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/13936.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.004.213.

6.1.25 Isobutanol

Table 6.26 Isobutanol data sheet.

Identification			
Product name	Isobutanol		
Structure			
CAS number	78-83-1		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Gevo (USA)	Purity grade	Typically fuel grade. Butamax™ Advanced Biofuels (USA) propose a >99.5% chemicals grade product (pre-commercial stage)
Uses	Mostly used as a chemical or fuel intermediate rather than a solvent		
Biomass information			
Type	Corn starch, sugarcane, sugar beet		
Origin	North America		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation		
Reaction		Atom economy	41%. Fermentation yields up to 86% of theoretical maximum are achievable[32]
Impact	Negative GHG emissions balance expected with cellulosic feedstocks. In the context of a first generation fuel (reflecting the current situation and market) a 32% reduction in GHG emissions compared to gasoline is reported.[33] A technoeconomic assessment and LCA has also been published[34]		

(*continued*)

Table 6.26 (*continued*)

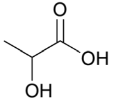
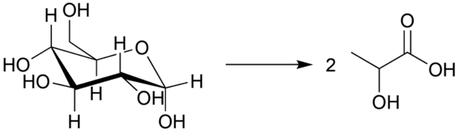
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	28 °C	Flammability	H226
Auto-ignition temperature	430 °C		
Resistivity	$6.3 \times 10^6\ \Omega\text{m}$	Other safety hazards	n/a
Acute toxicity	H336	Chronic toxicity	n/a
Other health hazards	H315, H318, H335	Environmental hazards	n/a
End-of-life			
Recovery	Possible to recover by distillation. Limited solubility in water		
Waste management	Hazardous substance: Flammable, causes eye damage and respiratory irritation. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	$15.1\ \text{MPa}^{1/2}$	
	δ_P	$5.7\ \text{MPa}^{1/2}$	
	δ_H	$15.9\ \text{MPa}^{1/2}$	
Boiling point	108 °C	Density	$0.80\ \text{g mL}^{-1}$ (20 °C)
Vapour pressure	16 hPa (20 °C)	Viscosity	5 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15092.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.001.044.

6.1.26 Lactic Acid

Table 6.27 Lactic acid data sheet.

Identification			
Product name	L-(+)-Lactic acid (Galacid™)		
Structure			
CAS number	50-21-5		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Galactic (Belgium)	Purity grade	80–98%
Uses	Coatings, pH regulators and water treatment products, non-metal-surface treatment products		
Biomass information			
Type	Corn starch		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation		
Reaction		Atom economy	100%
Impact	The polymer of lactic acid, polylactic acid, provides resource depletion and emissions savings compared to petrochemical polymers[35]		

(*continued*)

Table 6.27 (*continued*)

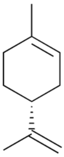
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	110 °C	Flammability	n/a
Auto-ignition temperature	400 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H315, H318	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations including food and pharmaceutical sectors. Discharged with waste water		
Waste management	Hazardous substance: Skin irritation and eye damage. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental lactic acid (anion) into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	17.3 MPa$^{1/2}$	
	δ_P	10.1 MPa$^{1/2}$	
	δ_H	23.3 MPa$^{1/2}$	
Boiling point	217 °C	Density	1.19 g mL^{-1} (80% aq. solution)
Vapour pressure	0.038 hPa (25 °C)	Viscosity	31 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/5165.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.017.

6.1.27 *d*-Limonene

Table 6.28 *d*-Limonene data sheet.

Identification			
Product name	*d*-Limonene		
Structure			
CAS number	5989-27-5		
REACH registration	Full[a]	REACH status	Sensitiser[b]
Supplier	Multiple	Purity grade	Depends on supplier. Orange oil is >90% *d*-limonene
Uses	Cleaning products, degreasers, adhesives and sealants, inks and toners, air care products, biocides, polishes and waxes		
Biomass information			
Type	Essential oil (citrus fruits)		
Origin	Brazil, India, USA, China and others		
Sustainability	Unknown		
Manufacturing			
Process name	Extraction		
Reaction	n/a	Atom economy	n/a
Impact	Low environmental impact compared to petrochemical solvents[36]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	48 °C	Flammability	H226
Auto-ignition temperature	245 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H315, H317	Environmental hazards	H410
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Hazardous substance: Flammable, sensitising, ecotoxic, causes skin irritation. Treated as hazardous waste within the EU		
Environmental fate	Low mobility in soil, expected to absorb into suspended solids and sediment in water bodies. Readily biodegradable in water		
Technical performance			
Polarity	δ_D	17.2 MPa$^{1/2}$	
	δ_P	1.8 MPa$^{1/2}$	
	δ_H	4.3 MPa$^{1/2}$	
Boiling point	178 °C	Density	0.844 g mL^{-1}
Vapour pressure	2.0 hPa (24 °C)	Viscosity	1.0 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15256.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.025.284.

6.1.28 Methanol

Table 6.29 Methanol data sheet.

Identification			
Product name	Methanol (bio-methanol, wood alcohol, Vulcanol™)		
Structure	Me—OH		
CAS number	67-56-1		
REACH registration	Full[a]	REACH status	Substance included in the Community Rolling Action Plan (CoRAP)[b]
Supplier	Multiple: BioMCN (Netherlands), Enerkem (Canada), Carbon Recycling International (Iceland)	Purity grade	Depends on supplier
Uses	Anti-freeze, chemical synthesis		
Biomass information			
Type	Bio-gas or carbon dioxide		
Origin	Europe, North America		
Sustainability	ISCC (carbon dioxide process, Carbon Recycling International)		
Manufacturing			
Process name	Reduction of carbon monoxide/carbon dioxide		
Reaction	$\mathrm{CO} \xrightarrow{+2\mathrm{H}_2} \mathrm{Me{-}OH}$	Atom economy	100%
Impact	Greenhouse gas (GHG) emissions of conventional methanol production from natural gas are 0.84 kg (CO_2 equivalents) per kg of methanol. Alternatively, bio-methanol GHG emissions are estimated to be 0.56 kg (CO_2 equivalents) per kg of methanol (forestry waste feedstock) to 0.64 kg (CO_2 equivalents) per kg of methanol (dedicated crop feedstock).[37] Thirdly, a carbon dioxide feedstock reduces net emissions by 90% compared to the petrochemical process[38]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

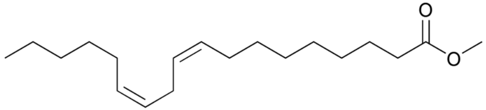
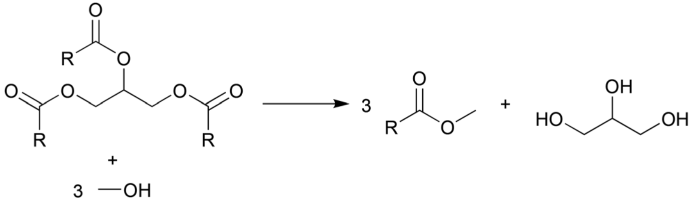
Environmental health and safety			
Flash point	10 °C	Flammability	H225 (highly)
Auto-ignition temperature	420 °C		
Resistivity	6.7×10^7 Ωm	Other safety hazards	n/a
Acute toxicity	H301, H311, H331	Chronic toxicity	H370
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Distillation and incineration have similar net energy balances[12]		
Waste management	Hazardous substance: Flammable, toxic. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	14.7 MPa$^{1/2}$	
	δ_P	12.3 MPa$^{1/2}$	
	δ_H	22.3 MPa$^{1/2}$	
Boiling point	65 °C	Density	0.79 g mL^{-1} (20 °C)
Vapour pressure	169 hPa (25 °C)	Viscosity	0.7 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15569.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.599.

6.1.29 Methyl Soyate

Table 6.30 Methyl soyate data sheet.

Identification			
Product name	Methyl soyate (and other FAMEs)		
Structure			
CAS number	67784-80-9 (also 67762-38-3: fatty acids, C16-18 and C18-unsaturated methyl esters)		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Cargill (USA), Stepan (USA)	Purity grade	>90%
Uses	Degreasers, metal working fluids and hydraulic fluids		
Biomass information			
Type	Vegetable oil (*e.g.* soybean oil)		
Origin	North America		
Sustainability	Unknown		
Manufacturing			
Process name	Transesterification (biodiesel production)		
Reaction		Atom econ.	~90%
Impact	Unknown		

Bio-based content			
Bio-based carbon content	~94%	Class	B
Total bio-based content	~89%		
Environmental health and safety			
Flash point	173 °C	Flammability	n/a
Auto-ignition temperature	261 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	High calorie content makes energy recovery suitable (FAMEs are primarily fuels)		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. High affinity for soils, or if discharged into water suspended solids and sediment (hydrolysed to methanol and fatty acids)		
Technical performance			
Polarity	δ_D	16.6 MPa$^{1/2}$	
	δ_P	2.4 MPa$^{1/2}$	
	δ_H	3.6 MPa$^{1/2}$	
Boiling point	>340 °C	Density	0.89 g mL^{-1} (20 °C)
Vapour pressure	4.20 hPa (25 °C)	Viscosity	4 cSt

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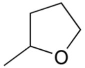
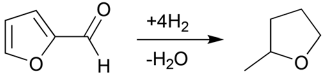
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15554.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.060.905.

6.1.30 2-Methyltetrahydrofuran

Table 6.31 2-Methyltetrahydrofuran data sheet.

Identification			
Product name	2-Methyltetrahydrofuran		
Structure			
CAS number	96-47-9		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Penn A Kem (USA)	Purity grade	>99%
Uses	Research and development		
Biomass information			
Type	Hemicellulose (corncobs, sawdust, bagasse)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Hydrogenation of furfural		
Reaction		Atom economy	83%
Impact	An LCA (cradle-to-gate) considering potential lignocellulosic feedstock options for 2-methyltetrahydrofuran indicates a preference for sugarcane-bagasse over rice straw and corn stover overall. Biomass production has a greater impact than solvent production[39]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	−11 °C	Flammability	H225 (highly)
Auto-ignition temperature	270 °C		
Resistivity	Unknown	Other safety hazards	EUH019
Acute toxicity	H301	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H315, H318	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides). Forms an azeotrope with water (heterogeneous) and some simple alcohols[40]		
Waste management	Hazardous substance: Flammable, peroxide hazard, toxic, skin irritation, eye damage. Treated as hazardous waste within the EU		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	16.9 MPa$^{1/2}$	
	δ_P	5.0 MPa$^{1/2}$	
	δ_H	4.3 MPa$^{1/2}$	
Boiling point	80 °C	Density	0.85 g mL^{-1}
Vapour pressure	135 hPa (20 °C)	Viscosity	5 cSt

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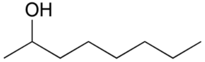
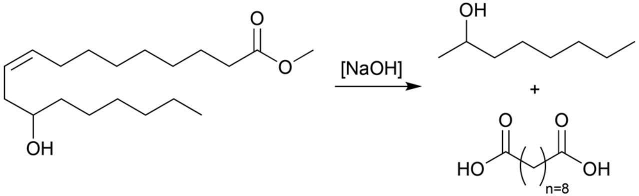
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/13699.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.002.281.

6.1.31 2-Octanol

Table 6.32 2-Octanol data sheet.

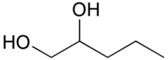
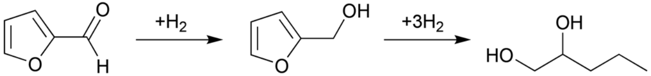
Identification			
Product name	2-Octanol (Oleris®)		
Structure			
CAS number	123-96-6		
REACH registration	Intermediate[a]	REACH status	No action needed[b]
Supplier	Arkema (France)	Purity grade	>99% and >90% available
Uses	As a solvent: coatings and adhesives. However, 2-octanol is only registered in the EU as an intermediate (for plasticiser and surfactant synthesis)		
Biomass information			
Type	Castor oil		
Origin	Unknown. India is the major producer (70% of global exports)[41]		
Sustainability	Unknown		
Manufacturing			
Process name	High temperature alkali fusion of castor oil		
Reaction		Atom econ.	~42%
Impact	Unknown. Production of 2-octanol is highly interdependent with other castor oil product streams		

Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	74 °C	Flammability	n/a
Auto-ignition temperature	282 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H318	Environmental hazards	n/a
End-of-life			
Recovery	Potentially used in formulations. Typically disposed of after use		
Waste management	Hazardous substance: Eye damage. Treated as hazardous waste within the EU		
Environmental fate	Evaporation from water and wet soil is expected		
Technical performance			
Polarity	δ_D	16.1 MPa$^{1/2}$	
	δ_P	4.9 MPa$^{1/2}$	
	δ_H	11.0 MPa$^{1/2}$	
Boiling point	174–181 °C	Density	0.819 g mL^{-1} (20 °C)
Vapour pressure	0.65 hPa (25 °C)	Viscosity	8 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14450.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.004.244.

6.1.32 1,2-Pentanediol

Table 6.33 1,2-Pentanediol data sheet.

Identification			
Product name	1,2-Pentanediol		
Structure			
CAS number	5343-92-0		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Penn A Kem (USA)	Purity grade	Unknown
Uses	Research and development		
Biomass information			
Type	Hemicellulose (corncobs, sawdust, bagasse)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Hydrogenolysis of tetrahydrofurfuryl alcohol		
Reaction		Atom econ.	100%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	105 °C	Flammability	n/a
Auto-ignition temperature	380 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H318	Environmental hazards	n/a
End-of-life			
Recovery	Unknown		
Waste management	Hazardous substance: Eye damage. Treated as hazardous waste within the EU		
Environmental fate	Slowly biodegradable		
Technical performance			
Polarity	δ_D	16.7 MPa$^{1/2}$	
	δ_P	7.2 MPa$^{1/2}$	
	δ_H	16.8 MPa$^{1/2}$	
Boiling point	209 °C	Density	0.98 g mL^{-1} (20 °C)
Vapour pressure	1 hPa (20 °C)	Viscosity	21 cSt

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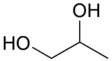
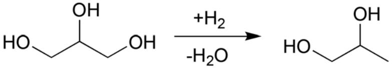
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/2101.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.023.896.

6.1.33 1,2-Propanediol

Table 6.34 1,2-Propanediol data sheet.

Identification			
Product name	1,2-Propanediol (Radianol)		
Structure			
CAS number	57-55-6		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Oleon (Belgium)	Purity grade	99.5%
Uses	Anti-freeze products, coating products, cosmetics and food products		
Biomass information			
Type	Vegetable oil (*e.g.* rapeseed and palm)		
Origin	European and Asian (Malaysia) plants		
Sustainability	RSPO		
Manufacturing			
Process name	Hydrogenolysis of glycerol		
Reaction		Atom economy	81%
Impact	A 70% reduction of "carbon footprint" has been reported compared to petrochemical 1,2-propanediol.[42] Metrics for the production of 1,2-propanediol from glycerol have been calculated by Marinas *et al*.[43]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	104 °C	Flammability	n/a
Auto-ignition temperature	410 °C		

Resistivity	1.7×10^5 Ωm	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Discharged with waste water		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental propylene glycol into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	16.8 $\text{MPa}^{1/2}$	
	δ_P	10.4 $\text{MPa}^{1/2}$	
	δ_H	21.3 $\text{MPa}^{1/2}$	
Boiling point	187 °C	Density	1.03 g mL^{-1} (20 °C)
Vapour pressure	0.2 hPa (25 °C)	Viscosity	42 cSt (25 °C)

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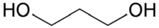
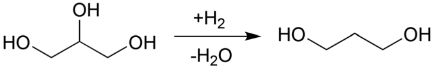
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/16001.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.000.307.

6.1.34 1,3-Propanediol

Table 6.35 1,3-Propanediol data sheet.

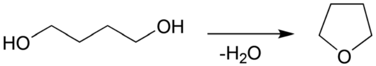
Identification			
Product name	1,3-Propanediol (Susterra®)		
Structure			
CAS number	504-63-2		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	DuPont Tate & Lyle BioProducts (USA)	Purity grade	Unknown
Uses	Formulations (cosmetics), heat transfer fluids		
Biomass information			
Type	Corn starch		
Origin	North America		
Sustainability	Unknown		
Manufacturing			
Process name	Fermentation (from glucose or glycerol)		
Reaction		Atom economy	81%. Fermentation yields up to 76% are achievable[44]
Impact	Life cycle data is available from the supplier.[45] Greenhouse gas emissions and the cumulative energy demand of production are improved compared to petrochemical diols		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	131 °C	Flammability	n/a
Auto-ignition temperature	342 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a

End-of-life			
Recovery	Used in formulations. Discharged with waste water		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Low volatility and high water solubility directs environmental 1,3-propanediol into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	16.8 MPa$^{1/2}$	
	δ_P	13.5 MPa$^{1/2}$	
	δ_H	23.2 MPa$^{1/2}$	
Boiling point	209 °C	Density	1.05 g mL^{-1}
Vapour pressure	0.04 hPa (25 °C)	Viscosity	44.9 cSt (24 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/2099.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.007.271.

6.1.35 Tetrahydrofuran

Table 6.36 Tetrahydrofuran data sheet.

Identification			
Product name	Tetrahydrofuran		
Structure			
CAS number	109-99-9		
REACH registration	Full[a]	REACH status	Substance included in the Community Rolling Action Plan (CoRAP)[b]
Supplier	Penn A Kem (USA)	Purity grade	Unknown
Uses	Chemical synthesis, coatings, research and development		
Biomass information			
Type	Hemicellulose (corncobs, sawdust, bagasse)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	1,4-Butanediol dehydration or succinic acid reduction-cyclisation		
Reaction		Atom economy	80%
Impact	Unknown. Petrochemical production of THF is extremely energy intensive due to distillations used to separate the product from water. The same applies to bio-based THF		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

Environmental health and safety			
Flash point	−21 °C	Flammability	H225 (highly)
Auto-ignition temperature	215 °C		
Resistivity	2.2×10^3 Ωm	Other safety hazards	EUH019
Acute toxicity	H302	Chronic toxicity	H351
Other health hazards	H319, H335	Environmental hazards	n/a
End-of-life			
Recovery	Distillation energetically preferable to energy recovery (danger - peroxides)[12]		
Waste management	Hazardous substance: Flammable, toxic, eye and respiratory irritation. Treated as hazardous waste within the EU		
Environmental fate	Inherently biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	16.8 MPa$^{1/2}$	
	δ_P	5.7 MPa$^{1/2}$	
	δ_H	8.0 MPa$^{1/2}$	
Boiling point	65 °C	Density	0.889 g mL^{-1} (20 °C)
Vapour pressure	170 hPa (20 °C)	Viscosity	0.51 cSt (25 °C)

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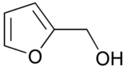
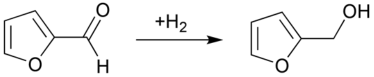
[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15474.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.389.

6.1.36 Tetrahydrofurfuryl Alcohol

Table 6.37 Tetrahydrofurfuryl alcohol data sheet.

Identification			
Product name	Tetrahydrofurfuryl alcohol		
Structure			
CAS number	97-99-4		
REACH registration	Full[a]	REACH status	Reprotoxic[b]
Supplier	Penn A Kem (USA)	Purity grade	>98%
Uses	Research and development		
Biomass information			
Type	Hemicellulose (corncobs, sawdust, bagasse)		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Hydrogenation of furfural		
Reaction		Atom economy	100%
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	84 °C	Flammability	n/a
Auto-ignition temperature	282 °C		

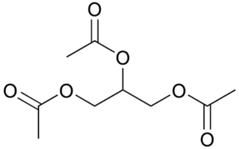
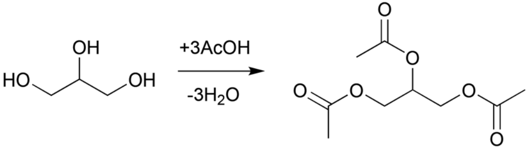
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	H361
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Unknown		
Waste management	Hazardous substance: Toxic. Treated as hazardous waste within the EU		
Environmental fate	Release to the air expected to result in photodegradation. High mobility in soil. Readily biodegradable in water		
Technical performance			
Polarity	δ_D	17.8 MPa$^{1/2}$	
	δ_P	8.2 MPa$^{1/2}$	
	δ_H	12.9 MPa$^{1/2}$	
Boiling point	178 °C	Density	1.05 g mL^{-1} (20 °C)
Vapour pressure	1.07 hPa (25 °C)	Viscosity	6 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/13371.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.002.387.

6.1.37 Triacetin

Table 6.38 Triacetin data sheet.

Identification			
Product name	Triacetin		
Structure			
CAS number	102-76-1		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Eastman (USA)	Purity grade	>99.5%
Uses	Cosmetics and personal care products, coating products, perfumes and fragrances, inks and toners		
Biomass information			
Type	Vegetable oil		
Origin	Unknown		
Sustainability	Unknown		
Manufacturing			
Process name	Esterification of glycerol		
Reaction		Atom economy	80%
Impact	Unknown		

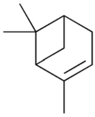
Bio-based content			
Bio-based carbon content	33%	Class	C
Total bio-based content	41%		
Environmental health and safety			
Flash point	>137 °C	Flammability	n/a
Auto-ignition temperature	433 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental triacetin into water bodies (not bioaccumulating, hydrolysed into acetic acid and glycerol)		
Technical performance			
Polarity	δ_D	16.5 MPa$^{1/2}$	
	δ_P	4.5 MPa$^{1/2}$	
	δ_H	9.1 MPa$^{1/2}$	
Boiling point	258 °C	Density	1.161 g mL^{-1} (20 °C)
Vapour pressure	0.003 hPa (25 °C)	Viscosity	18–21 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15139.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.002.775.

6.1.38 Turpentine Oil

Table 6.39 Turpentine oil data sheet.

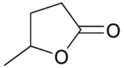
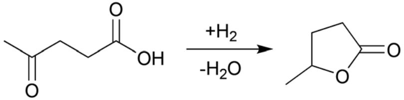
Identification			
Product name	Turpentine oil (high α-pinene content)		
Structure			
CAS number	8006-64-2		
REACH registration	Full[a]	REACH status	Sensitiser[b]
Supplier	Multiple	Purity grade	Natural product consisting of various terpenes (mostly pinenes)
Uses	Degreaser, coatings		
Biomass information			
Type	Sap of pine trees		
Origin	All regions		
Sustainability	Trees can be tapped for sap for more than 20 years, and eventual use for timber is not compromised[46]		
Manufacturing			
Process name	Distillation		
Reaction	n/a	Atom economy	n/a
Impact	Unknown		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	24 °C	Flammability	H225 (highly)
Auto-ignition temperature	270 °C		
Resistivity	Unknown	Other safety hazards	n/a
Acute toxicity	H302, H312, H332	Chronic toxicity	H304
Other health hazards	H315, H317, H319	Environmental hazards	H411
End-of-life			
Recovery	Recoverable by distillation, high calorie content for energy recovery		
Waste management	Hazardous substance: Flammable, toxic, irritant, sensitising, ecotoxic. Treated as hazardous waste within the EU		
Environmental fate	Slowly biodegradable. High affinity for soils, or if discharged into water suspended solids and sediment. Evaporation is important		
Technical performance			
Polarity	δ_D	16.4 MPa$^{1/2}$	
	δ_P	1.1 MPa$^{1/2}$	
	δ_H	2.2 MPa$^{1/2}$	
Boiling point	154–170 °C	Density	0.860 g mL^{-1}
Vapour pressure	26 hPa (25 °C)	Viscosity	2 cSt (10 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15489.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.029.407.

6.1.39 γ-Valerolactone

Table 6.40 γ-Valerolactone data sheet.

Identification			
Product name	γ-Valerolactone		
Structure			
CAS number	108-29-2		
REACH registration	No	REACH status	n/a
Supplier	Multiple (synthetic and natural products available)	Purity grade	>98.5% (Aldrich product)
Uses	Research and development		
Biomass information			
Type	Cellulose		
Origin	Europe. Levulinic acid producers: Avantium (Netherlands), GFBiochemicals (Italy)		
Sustainability	Unknown		
Manufacturing			
Process name	Hydrogenative cyclisation of levulinic acid		
Reaction		Atom economy	85%
Impact	Unknown. Cellulosic levulinic acid is available as a potential feedstock.		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		

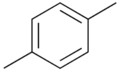
(*continued*)

Table 6.40 (*continued*)

Environmental health and safety			
Flash point	96 °C	Flammability	n/a
Auto-ignition temperature	Unknown		
Resistivity	Unknown	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Unknown		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	16.9 $MPa^{1/2}$	
	δ_P	11.5 $MPa^{1/2}$	
	δ_H	6.3 $MPa^{1/2}$	
Boiling point	207 °C	Density	1.05 g mL^{-1}
Vapour pressure	0.7 hPa (29 °C)	Viscosity	2.1 cSt (25 °C)

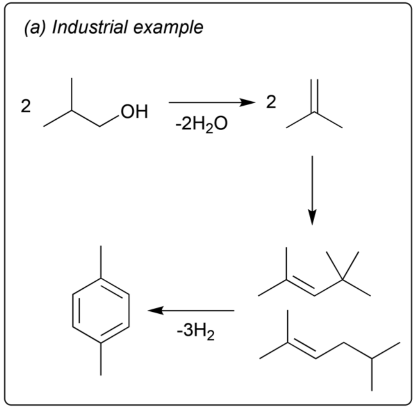
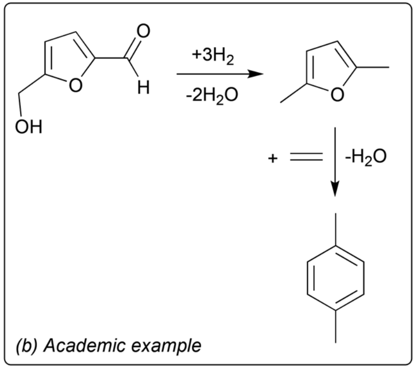
6.1.40 *p*-Xylene

Table 6.41 *p*-Xylene data sheet.

Identification			
Product name	*p*-Xylene		
Structure			
CAS number	106-42-3		
REACH registration	Full[a]	REACH status	Substance included in the Community Rolling Action Plan (CoRAP)[b]
Supplier	Gevo (USA), Virent (USA)	Purity grade	Unknown (produced as an intermediate for polymer synthesis, not as a solvent)[25]
Uses	Adhesives and sealants, fuels, non-metal-surface treatment products, leather treatment products. Purpose of bio-based *p*-xylene is for the production of renewable plastics		
Biomass information			
Type	Corn starch		
Origin	North America		
Sustainability	Unknown		
Manufacturing			
Process name	Dimerisation and dehydrocyclisation of isobutene from isobutanol (GEVO).[25] Aqueous phase reforming of carbohydrate (Virent).[47] An alternative proposal converts 5-hydroxymethylfurfural (HMF) into *p*-xylene[48]		

(*continued*)

Table 6.41 (*continued*)

Reaction	 	Atom economy	(a) 72% (b) 66%

Impact	A technoeconomic analysis is available for the HMF route.[48] An LCA comparing a starch based and wood based process of *p*-xylene production *via* HMF has shown the lignocellulosic feedstock to minimise the environmental impact. Biomass production and the use of petrochemicals (including the reactant ethylene and additional auxiliaries) accounts for the majority of the impact[49]		
Bio-based content			
Bio-based carbon content	100%	Class	A
Total bio-based content	100%		
Environmental health and safety			
Flash point	27 °C	Flammability	H226
Auto-ignition temperature	463 °C		
Resistivity	1.3×10^{14} Ωm	Other safety hazards	n/a
Acute toxicity	H312, H332	Chronic toxicity	n/a
Other health hazards	H315	Environmental hazards	n/a
End-of-life			
Recovery	Distillation and incineration have similar net energy balances[12]		
Waste management	Hazardous substance: Flammable and toxic, skin irritant. Treated as hazardous waste within the EU		
Environmental fate	Slowly biodegradable. Evaporation is important. Low potential for bioaccumulation		
Technical performance			
Polarity	δ_D	17.8 MPa$^{1/2}$	
	δ_P	1.0 MPa$^{1/2}$	
	δ_H	3.1 MPa$^{1/2}$	
Boiling point	138 °C	Density	0.86 g mL^{-1}
Vapour pressure	12 hPa (20 °C)	Viscosity	0.7 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15791.

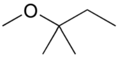
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.088.

6.2 Speciality Petrochemical Solvent Data Sheets

Data for 25 speciality petrochemical solvents is given here. Refer to Chapter 4 for a detailed discussion on neoteric solvents. The data sheets are abbreviated compared to those describing bio-based solvents, but otherwise the key to the data sheets (provided as Table 6.1) still applies. Specifically, information on the feedstock and manufacturing has been excluded because the feedstock is not sustainable, and synthetic routes are not available in the literature for many of the solvents included. Also, due to a lack of data, the resistivity entry was removed. In the case of polymeric solvents (polydimethylsiloxane and polyethylene glycol) the boiling point, vapour pressure, density, and viscosity are not reported due to their dependence on the exact polymer size, which is not reported here.

6.2.1 *t*-Amyl Methyl Ether

Table 6.42 *t*-Amyl methyl ether data sheet.

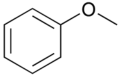
Identification			
Product name	*t*-Amyl methyl ether		
Structure			
CAS number	994-05-8		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Fuel additive		
Environmental health and safety			
Flash point	−18 °C	Flammability	H225 (highly)
Auto-ignition temperature	430 °C	Other safety hazards	n/a
Acute toxicity	H302, H336	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides)		
Waste management	Hazardous substance: Flammable and acutely toxic. Treated as hazardous waste within the EU		
Environmental fate	According to its REACH registration dossier, biodegradation test (OECD 301D) showed that *t*-amyl methyl ether is not readily biodegradable and potentially persistent in the environment, but evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	14.7 MPa$^{1/2}$	
	δ_P	3.2 MPa$^{1/2}$	
	δ_H	2.7 MPa$^{1/2}$	
Boiling point	87 °C	Density	0.77 g mL^{-1} (15 °C)
Vapour pressure	90 hPa (20 °C)	Viscosity	0.494 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14961.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.012.374.

6.2.2 Anisole

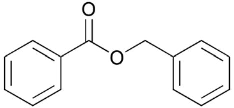
Table 6.43 Anisole data sheet.

Identification			
Product name	Anisole		
Structure			
CAS number	100-66-3		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Research and development		
Environmental health and safety			
Flash point	46 °C	Flammability	H226
Auto-ignition temperature	475 °C	Other safety hazards	n/a
Acute toxicity	H336	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides)		
Waste management	Hazardous substance: Flammable. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	17.8 $MPa^{1/2}$	
	δ_P	4.4 $MPa^{1/2}$	
	δ_H	6.9 $MPa^{1/2}$	
Boiling point	155 °C	Density	0.99 g mL^{-1} (20 °C)
Vapour pressure	4.7 hPa (25 °C)	Viscosity	1 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14423.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.002.615.

6.2.3 Benzyl Benzoate

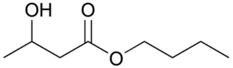
Table 6.44 Benzyl benzoate data sheet.

Identification			
Product name	Benzyl benzoate		
Structure			
CAS number	120-51-4		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Cleaning products, air care products, textile treatments		
Environmental health and safety			
Flash point	158 °C	Flammability	n/a
Auto-ignition temperature	480 °C	Other safety hazards	n/a
Acute toxicity	H302	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a	Environmental hazards	H411
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Hazardous substance: Acutely toxic. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	20.0 MPa$^{1/2}$	
	δ_P	5.1 MPa$^{1/2}$	
	δ_H	5.2 MPa$^{1/2}$	
Boiling point	324 °C	Density	1.11 g mL^{-1} (25 °C)
Vapour pressure	0.0003 hPa (25 °C)	Viscosity	4.5 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/13634.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.004.003.

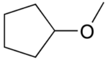
6.2.4 Butyl 3-Hydroxybutyrate

Table 6.45 Butyl 3-hydroxybutyrate data sheet.

Identification			
Product name	Butyl 3-hydroxybutyrate (Omnia™)		
Structure			
CAS number	53605-94-0		
REACH registration	No	REACH status	n/a
Supplier	Eastman (USA)	Purity grade	>98%
Uses	Cleaning formulations		
Environmental health and safety			
Flash point	96 °C	Flammability	n/a
Auto-ignition temperature	303 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Hazardous substance: Eye irritant. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	11.6 $MPa^{1/2}$	
	δ_P	4.0 $MPa^{1/2}$	
	δ_H	7.8 $MPa^{1/2}$	
Boiling point	218 °C	Density	0.971 (20 °C)
Vapour pressure	Unknown	Viscosity	5.97 cSt (25 °C)

6.2.5 Cyclopentyl Methyl Ether

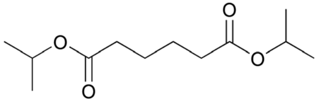
Table 6.46 Cyclopentyl methyl ether data sheet.

Identification			
Product name	Cyclopentyl methyl ether		
Structure			
CAS number	5614-37-9		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Zeon (Japan)	Purity grade	>99.9%
Uses	Research and development		
Environmental health and safety			
Flash point	<3 °C	Flammability	H225 (highly)
Auto-ignition temperature	186 °C	Other safety hazards	n/a
Acute toxicity	H302	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H315, H319	Environmental hazards	H412
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides)		
Waste management	Hazardous substance: Flammable, acutely toxic, irritant. Treated as hazardous waste within the EU		
Environmental fate	Not readily biodegradable. Assumed persistent but not bioaccumulating		
Technical performance			
Polarity	δ_D	16.7 MPa$^{1/2}$	
	δ_P	4.3 MPa$^{1/2}$	
	δ_H	4.3 MPa$^{1/2}$	
Boiling point	107 °C	Density	0.86 g mL^{-1} (20 °C)
Vapour pressure	42.7 (25 °C)	Viscosity	Unknown

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/5130/2/1.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.104.006.

6.2.6 Dibasic Isopropyl Esters (Adipate)

Table 6.47 Diisopropyl adipate data sheet.

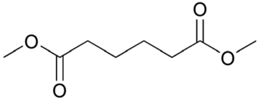
Identification			
Product name	Diisopropyl adipate (also present in commercial blends of dibasic esters: Coasol®)		
Structure			
CAS number	6938-94-9		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Chemoxy (UK)	Purity grade	>99.0%
Uses	Paints and coatings		
Environmental health and safety			
Flash point	105 °C	Flammability	n/a
Auto-ignition temperature	365 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Ambiguous. According to REACH registration dossier information, diisopropyl adipate is not considered as a hazardous substance in the EU. A safety datasheet (Sigma-Aldrich) states diisopropyl adipate is a hazardous substance: Irritant. Therefore treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.0 MPa$^{1/2}$	
	δ_P	3.8 MPa$^{1/2}$	
	δ_H	4.7 MPa$^{1/2}$	
Boiling point	>240 °C	Density	0.97 g mL^{-1} (20 °C)
Vapour pressure	Unknown	Viscosity	2–6 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/5933.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.027.338.

6.2.7 Dibasic Methyl Esters (Adipate)

Table 6.48 Dimethyl adipate data sheet.

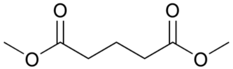
Identification			
Product name	Dimethyl adipate (present in commercial blends of dibasic esters Rhodiasolv® RPDE, Estasol®, and Flexisolve®)		
Structure			
CAS number	627-93-0		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium), Chemoxy (UK), and Invista (USA)	Purity grade	>99.5% (Chemoxy)
Uses	Adhesives, paints and coatings		
Environmental health and safety			
Flash point	118 °C	Flammability	n/a
Auto-ignition temperature	400 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental dimethyl adipate into water bodies (not bioaccumulating, hydrolysed into adipic acid and methanol). May evaporate from dry soil		
Technical performance			
Polarity	δ_D	$16.3\ \mathrm{MPa}^{1/2}$	
	δ_P	$6.8\ \mathrm{MPa}^{1/2}$	
	δ_H	$8.5\ \mathrm{MPa}^{1/2}$	
Boiling point	235 °C	Density	1.06 (20 °C)
Vapour pressure	0.025 (20 °C)	Viscosity	3 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14132.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.010.019.

6.2.8 Dibasic Methyl Esters (Glutarate)

Table 6.49 Dimethyl glutarate data sheet.

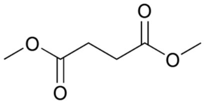
Identification			
Product name	Dimethyl glutarate (present in commercial blends of dibasic esters Rhodiasolv® RPDE, Estasol®, and Flexisolve®)		
Structure			
CAS number	1119-40-0		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium), Chemoxy (UK), and Invista (USA)	Purity grade	Depends on supplier
Uses	Adhesives, paints and coatings		
Environmental health and safety			
Flash point	109 °C	Flammability	n/a
Auto-ignition temperature	440 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.5 MPa$^{1/2}$	
	δ_P	6.4 MPa$^{1/2}$	
	δ_H	8.2 MPa$^{1/2}$	
Boiling point	216 °C	Density	1.09 g mL^{-1} (20 °C)
Vapour pressure	0.14 hPa (25 °C)	Viscosity	1.7 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/5377.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.012.980.

6.2.9 Dibasic Methyl Esters (Succinate)

Table 6.50 Dimethyl succinate data sheet.

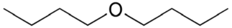
Identification			
Product name	Dimethyl succinate (present in commercial blends of dibasic esters Rhodiasolv® RPDE, Estasol®, and Flexisolve®)		
Structure			
CAS number	106-65-0		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium), Chemoxy (UK), and Invista (USA)	Purity grade	>99.0%
Uses	Paints and coatings, cosmetics and personal care products		
Environmental health and safety			
Flash point	96 °C	Flammability	n/a
Auto-ignition temperature	470 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental dimethyl succinate into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	16.1 MPa$^{1/2}$	
	δ_P	7.7 MPa$^{1/2}$	
	δ_H	8.8 MPa$^{1/2}$	
Boiling point	196 °C	Density	1.12 g mL^{-1} (20 °C)
Vapour pressure	Unknown	Viscosity	2.6 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15043.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.110.

6.2.10 Dibutyl Ether

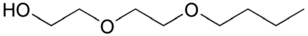
Table 6.51 Dibutyl ether data sheet.

Identification			
Product name	Dibutyl ether		
Structure			
CAS number	142-96-1		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Surface treatment products, cleaning products and coatings		
Environmental health and safety			
Flash point	28 °C	Flammability	H226
Auto-ignition temperature	194 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H315, H319, H335	Environmental hazards	H412
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides)		
Waste management	Hazardous substance: Flammable, irritant, ecotoxic. Treated as hazardous waste within the EU		
Environmental fate	Not biodegradable (persistent in the environment). Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.2 MPa$^{1/2}$	
	δ_P	3.4 MPa$^{1/2}$	
	δ_H	3.2 MPa$^{1/2}$	
Boiling point	140 °C	Density	0.764 g mL^{-1}
Vapour pressure	6.4 hPa (25 °C)	Viscosity	Unknown

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/11808.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.005.069.

6.2.11 Diethylene Glycol Monobutyl Ether

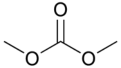
Table 6.52 Diethylene glycol monobutyl ether data sheet.

Identification			
Product name	Diethylene glycol monobutyl ether (butyl carbitol™)		
Structure			
CAS number	112-34-5		
REACH registration	Full[a]	REACH status	Restricted (in relation to spray paints)[b]
Supplier	Dow (USA), Eastman (USA)	Purity grade	>99.0% (Eastman)
Uses	Coatings, cleaning products, metal working fluids, water treatment chemicals, cosmetics and personal care products		
Environmental health and safety			
Flash point	78 °C	Flammability	n/a
Auto-ignition temperature	204 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Hazardous substance: Eye irritant. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental diethylene glycol monobutyl ether into water bodies (not bioaccumulating)		
Technical performance			
Polarity	δ_D	16.0 $MPa^{1/2}$	
	δ_P	7.0 $MPa^{1/2}$	
	δ_H	10.6 $MPa^{1/2}$	
Boiling point	225–234 °C	Density	0.95 (20 °C)
Vapour pressure	0.029 hPa (25 °C)	Viscosity	6.8 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15952.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.601.

6.2.12 Dimethyl Carbonate

Table 6.53 Dimethyl carbonate data sheet.

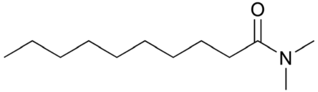
Identification			
Product name	Dimethyl carbonate		
Structure			
CAS number	616-38-6		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Primarily research and development (used as a reactant also)		
Environmental health and safety			
Flash point	17 °C	Flammability	H225 (highly)
Auto-ignition temperature	458 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation		
Waste management	Hazardous substance: Flammable. Treated as hazardous waste within the EU. Dimethyl carbonate is exempt from VOC status in the USA[13]		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.5 $\text{MPa}^{1/2}$	
	δ_P	8.6 $\text{MPa}^{1/2}$	
	δ_H	9.7 $\text{MPa}^{1/2}$	
Boiling point	90 °C	Density	1.07 g mL^{-1} (20 °C)
Vapour pressure	75.7 hPa (25 °C)	Viscosity	0.62 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14944

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.009.527

6.2.13 *N*,*N*-Dimethyl Decanamide

Table 6.54 *N*,*N*-Dimethyl decanamide data sheet.

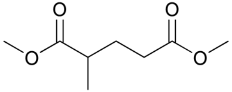
Identification			
Product name	*N*,*N*-Dimethyl decanamide (present in a commercial blend: Rhodiasolv® ADMA 810)		
Structure			
CAS number	14433-76-2		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium)	Purity grade	>97%
Uses	Agrochemical formulations		
Environmental health and safety			
Flash point	147 °C	Flammability	n/a
Auto-ignition temperature	330 °C	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H315, H319, H335	Environmental hazards	H412
End-of-life			
Recovery	Used in agrochemical formulations and introduced into the environment. Not recoverable		
Waste management	Hazardous substance: Irritant. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.8 MPa$^{1/2}$	
	δ_P	6.8 MPa$^{1/2}$	
	δ_H	5.2 MPa$^{1/2}$	
Boiling point	291 °C	Density	0.88 g mL^{-1} (20 °C)
Vapour pressure	0.0011 hPa (25 °C)	Viscosity	5.7 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15021.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.034.898.

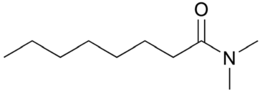
6.2.14 Dimethyl 2-Methylglutarate

Table 6.55 Dimethyl 2-methylglutarate data sheet.

Identification			
Product name	Dimethyl 2-methylglutarate (Rhodiasolv® IRIS)		
Structure			
CAS number	14035-94-0		
REACH registration	No	REACH status	n/a
Supplier	Solvay (Belgium)	Purity grade	>99%
Uses	Industrial cleaning, paint stripping, coatings		
Environmental health and safety			
Flash point	98 °C	Flammability	n/a
Auto-ignition temperature	Unknown	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a (data may be lacking)	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a (data may be lacking)	Environmental hazards	n/a (data may be lacking)
End-of-life			
Recovery	Used in formulations. Typically disposed of after use		
Waste management	Unknown (major data gaps). Assume as hazardous		
Environmental fate	Unknown		
Technical performance			
Polarity	δ_D	16.6 MPa$^{1/2}$	
	δ_P	8.7 MPa$^{1/2}$	
	δ_H	5.0 MPa$^{1/2}$	
Boiling point	216 °C	Density	1.05 (20 °C)
Vapour pressure	<0.1 hPa (20 °C)	Viscosity	Unknown

6.2.15 *N*,*N*-Dimethyl Octanamide

Table 6.56 *N*,*N*-Dimethyl octanamide data sheet.

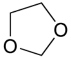
Identification			
Product name	*N*,*N*-Dimethyl octanamide (present in commercial blend: Rhodiasolv® ADMA 810)		
Structure			
CAS number	1118-92-9		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium)	Purity grade	>97%
Uses	Agrochemical formulations		
Environmental health and safety			
Flash point	127 °C	Flammability	n/a
Auto-ignition temperature	305 °C	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H315, H319	Environmental hazards	n/a
End-of-life			
Recovery	Used in agrochemical formulations and introduced into the environment. Not recoverable		
Waste management	Hazardous substance: Irritant. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable		
Technical performance			
Polarity	δ_D	16.8 MPa$^{1/2}$	
	δ_P	7.7 MPa$^{1/2}$	
	δ_H	5.7 MPa$^{1/2}$	
Boiling point	261 °C	Density	0.881 g mL^{-1}
Vapour pressure	≤0.03 hPa (20 °C)	Viscosity	3.8 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/12187.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.012.975.

6.2.16 1,3-Dioxolane

Table 6.57 1,3-Dioxolane data sheet.

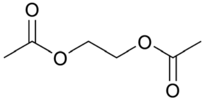
Identification			
Product name	1,3-Dioxolane		
Structure			
CAS number	646-06-0		
REACH registration	Full[a]	REACH status	Substance included in the Community Rolling Action Plan (CoRAP)[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Extractions, coating products, lubricants, cleaning products, adhesives and sealants, heat transfer fluids and hydraulic fluids		
Environmental health and safety			
Flash point	≤2.5 °C	Flammability	H225 (highly)
Auto-ignition temperature	250 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation (danger – peroxides)		
Waste management	Hazardous substance: Flammable, irritant. Treated as hazardous waste within the EU		
Environmental fate	Not readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	18.1 $\text{MPa}^{1/2}$	
	δ_P	6.6 $\text{MPa}^{1/2}$	
	δ_H	9.3 $\text{MPa}^{1/2}$	
Boiling point	78 °C	Density	1.06 g mL^{-1} (20 °C)
Vapour pressure	0.93 hPa (20 °C)	Viscosity	5.53 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15807.

[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.010.422.

6.2.17 Glycol Diacetate

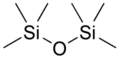
Table 6.58 Glycol diacetate data sheet.

Identification			
Product name	Glycol diacetate		
Structure			
CAS number	111-55-7		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Chemoxy (UK)	Purity grade	>99%
Uses	Textile treatment products and dyes, water treatment products, leather treatment products, lubricants and adhesives		
Environmental health and safety			
Flash point	88 °C	Flammability	n/a
Auto-ignition temperature	482 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental glycol diacetate into water bodies (not bioaccumulating, hydrolysed into acetic acid and ethylene glycol)		
Technical performance			
Polarity	δ_D	16.2 MPa$^{1/2}$	
	δ_P	4.7 MPa$^{1/2}$	
	δ_H	9.8 MPa$^{1/2}$	
Boiling point	190 °C	Density	1.10 g mL^{-1} (20 °C)
Vapour pressure	0.23 hPa (20 °C)	Viscosity	1.71 cSt

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14437.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.529.

6.2.18 Hexamethyldisiloxane

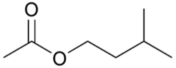
Table 6.59 Hexamethyldisiloxane data sheet.

Identification			
Product name	Hexamethyldisiloxane		
Structure			
CAS number	107-46-0		
REACH registration	Full[a]	REACH status	Substance included in the Community Rolling Action Plan (CoRAP)[b]
Supplier	Dow Corning (USA)	Purity grade	>90%
Uses	Cleaning products for electronics, cosmetics and personal care products, and heat transfer fluids		
Environmental health and safety			
Flash point	−3 °C	Flammability	H225 (highly)
Auto-ignition temperature	420 °C	Other safety hazards	n/a (data may be lacking)
Acute toxicity	n/a	Chronic toxicity	H351
Other health hazards	n/a	Environmental hazards	H400
End-of-life			
Recovery	Used in formulations. May be required to evaporate as part of its function. Methyl siloxanes are exempt from VOC status in the USA[13]		
Waste management	Hazardous substance: Flammable, potentially carcinogenic, ecotoxic. Treated as hazardous waste within the EU		
Environmental fate	Persistent in the environment (not readily biodegradable). High affinity for soils, or if discharged into water suspended solids and sediment. Evaporation is important		
Technical performance			
Polarity	δ_D	12.6 MPa$^{1/2}$	
	δ_P	2.0 MPa$^{1/2}$	
	δ_H	0.0 MPa$^{1/2}$	
Boiling point	100 °C	Density	0.76 g mL^{-1}
Vapour pressure	42 hPa (20 °C)	Viscosity	0.65 cSt (15 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/15156.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.176.

6.2.19 Isoamyl Acetate

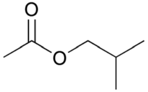
Table 6.60 Isoamyl acetate data sheet.

Identification			
Product name	Isoamyl acetate		
Structure			
CAS number	123-92-2		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Chemoxy (UK)	Purity grade	>99.0%
Uses	Adhesives and sealants, coating products, lubricants and greases, cleaning products, air care products and polishes and waxes		
Environmental health and safety			
Flash point	18–25 °C	Flammability	H226
Auto-ignition temperature	379 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in varnishes and lacquer formulations. Expected to evaporate to the air after application		
Waste management	Hazardous substance: Flammable. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.3 MPa$^{1/2}$	
	δ_P	3.1 MPa$^{1/2}$	
	δ_H	7.0 MPa$^{1/2}$	
Boiling point	140 °C	Density	0.874 g mL^{-1} (20 °C)
Vapour pressure	4.5 hPa (20 °C)	Viscosity	1.0 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/13689.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.004.240.

6.2.20 Isobutyl Acetate

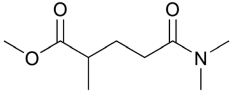
Table 6.61 Isobutyl acetate data sheet.

Identification			
Product name	Isobutyl acetate		
Structure			
CAS number	110-19-0		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Coatings, cleaning products, biocides, anti-freeze products, lubricants and greases		
Environmental health and safety			
Flash point	22 °C	Flammability	H225 (highly)
Auto-ignition temperature	430 °C	Other safety hazards	n/a
Acute toxicity	H336	Chronic toxicity	n/a
Other health hazards	EUH066	Environmental hazards	n/a
End-of-life			
Recovery	Used in coating formulations. Expected to evaporate to the air after application		
Waste management	Hazardous substance: Flammable. Treated as hazardous waste within the EU		
Environmental fate	Readily biodegradable. Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	15.1 MPa$^{1/2}$	
	δ_P	3.7 MPa$^{1/2}$	
	δ_H	6.3 MPa$^{1/2}$	
Boiling point	117 °C	Density	0.871 g mL^{-1} (20 °C)
Vapour pressure	21 hPa (20 °C)	Viscosity	0.8 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/14421.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.406.

6.2.21 Methyl 5-(dimethylamino)-2-methyl-5-oxopentanoate

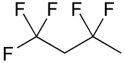
Table 6.62 Methyl 5-(dimethylamino)-2-methyl-5-oxopentanoate data sheet.

Identification			
Product name	Methyl 5-(dimethylamino)-2-methyl-5-oxopentanoate (Rhodiasolv® Polarclean)		
Structure			
CAS number	1174627-68-9		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium)	Purity grade	Unknown
Uses	Agrochemical formulations		
Environmental health and safety			
Flash point	146 °C	Flammability	n/a
Auto-ignition temperature	390 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a (data may be lacking)
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Used in agrochemical formulations and introduced into the environment. Not recoverable		
Waste management	Hazardous substance: Eye irritant. Treated as hazardous waste within the EU		
Environmental fate	Not readily biodegradable according to REACH registration dossier		
Technical performance			
Polarity	δ_D	17.2 MPa$^{1/2}$	
	δ_P	9.5 MPa$^{1/2}$	
	δ_H	10.6 MPa$^{1/2}$	
Boiling point	280 °C	Density	1.039 g mL^{-1}
Vapour pressure	<0.0001 hPa (20 °C)	Viscosity	9.40 cSt (23 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/2181.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.148.956.

6.2.22 1,1,1,3,3-Pentafluorobutane

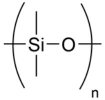
Table 6.63 1,1,1,3,3-Pentafluorobutane data sheet.

Identification			
Product name	1,1,1,3,3-Pentafluorobutane (Solkane® 365, HARP® 365 mfc)		
Structure			
CAS number	406-58-6		
REACH registration	Transferred from old NONS system[a]	REACH status	No action needed[b]
Supplier	Solvay (Belgium), Harp (UK)	Purity grade	>99.7% (Harp)
Uses	Blowing agent		
Environmental health and safety			
Flash point	<-26 °C	Flammability	H225 (highly)
Auto-ignition temperature	580 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Recoverable by distillation		
Waste management	Hazardous substance: Flammable. Treated as hazardous waste within the EU		
Environmental fate	Not readily biodegradable (not bio-accumulating or ecotoxic). Evaporation from water and soil is expected		
Technical performance			
Polarity	δ_D	16.4 MPa$^{1/2}$	
	δ_P	0.0 MPa$^{1/2}$	
	δ_H	0.0 MPa$^{1/2}$	
Boiling point	40 °C	Density	1.27 g mL^{-1} (20 °C)
Vapour pressure	422 hPa (20 °C)	Viscosity	0.3 cSt (20 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/3527.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.102.859.

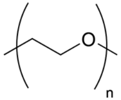
6.2.23 Polydimethylsiloxane

Table 6.64 Polydimethylsiloxane data sheet.

Identification			
Product name	Polydimethylsiloxane		
Structure			
CAS number	63148-62-9		
REACH registration	No	REACH status	Exempt
Supplier	Dow Corning (USA)	Purity grade	Unknown
Uses	Cosmetics, topical medical dispersions, coatings		
Environmental health and safety			
Flash point	>100 °C	Flammability	n/a
Auto-ignition temperature	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in formulations. Not recoverable. Methyl siloxanes are exempt from VOC status in the USA[13]		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Slowly biodegradable. High affinity for soils, or if discharged into water suspended solids and sediment.[50] Non-volatile		
Technical performance			
Polarity	δ_D	17.2 MPa$^{1/2}$	
	δ_P	2.1 MPa$^{1/2}$	
	δ_H	2.9 MPa$^{1/2}$	

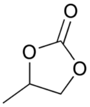
6.2.24 Polyethylene Glycol

Table 6.65 Polyethylene glycol data sheet.

Identification			
Product name	Polyethylene glycol		
Structure			
CAS number	25322-68-3		
REACH registration	No	REACH status	Exempt
Supplier	Multiple	Purity grade	Depends on supplier
Uses	Cosmetics, pharmaceutical formulations, plasticiser		
Environmental health and safety			
Flash point	Unknown	Flammability	n/a
Auto-ignition temperature	Unknown	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	n/a	Environmental hazards	n/a
End-of-life			
Recovery	Used in medical formulations. Not recoverable		
Waste management	Not considered as a hazardous substance in the EU		
Environmental fate	Biodegradable		
Technical performance			
Polarity	δ_D	17.0 $MPa^{1/2}$	
	δ_P	11.0 $MPa^{1/2}$	
	δ_H	5.2 $MPa^{1/2}$	

6.2.25 Propylene Carbonate

Table 6.66 Propylene carbonate data sheet.

Identification			
Product name	Propylene carbonate (JEFFSOL®)		
Structure			
CAS number	108-32-7		
REACH registration	Full[a]	REACH status	No action needed[b]
Supplier	Huntsman (USA)	Purity grade	99.7%
Uses	Coatings, electrolytes, plant protection products and personal care products		
Environmental health and safety			
Flash point	116 °C	Flammability	n/a
Auto-ignition temperature	430 °C	Other safety hazards	n/a
Acute toxicity	n/a	Chronic toxicity	n/a
Other health hazards	H319	Environmental hazards	n/a
End-of-life			
Recovery	Other carbonate solvents (ethylene carbonate, dimethyl carbonate, diethyl carbonate) can be recovered from lithium ion batteries by solvent extraction[51]		
Waste management	Hazardous substance: Eye irritant. Treated as hazardous waste within the EU. Propylene carbonate is exempt from VOC status in the USA[13]		
Environmental fate	Readily biodegradable. Low volatility and high water solubility directs environmental propylene carbonate into water bodies (not bioaccumulating, hydrolysed into 1,2-propanediol and carbon dioxide)		
Technical performance			
Polarity	δ_D	20.0 MPa$^{1/2}$	
	δ_P	18.0 MPa$^{1/2}$	
	δ_H	4.1 MPa$^{1/2}$	
Boiling point	243 °C	Density	1.21 g mL^{-1} (20 °C)
Vapour pressure	0.04 hPa (20 °C)	Viscosity	2.1 cSt (25 °C)

[a] https://echa.europa.eu/registration-dossier/-/registered-dossier/16088.
[b] https://echa.europa.eu/substance-information/-/substanceinfo/100.003.248.

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