Green Solvents for Chemistry: Perspectives and Practice

William M. Nelson

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For Millie, whose love and support has kept me on track
and for Maria, Milee, Liam, and Madeleine,
who are my priceless jewels

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GREEN SOLVENTS FOR CHEMISTRY

Knowledge is of two kinds. We know a subject ourselves or we know where we can find information upon it.

—Samuel Johnson

1

Philosophy of the Environment

1.1 The Emerging Paradigm

Let us put chemical usage in context. There is justifiably a concern over the adverse effects of chemicals on human health and the environment. The source of chemicals may be industrial, commercial, or adventitious. Environmental quality is a concern in the United States and throughout the world. This concern is important today. Our world has heightened environmental awareness, fueled by public interest groups and the media. Public awareness is growing of the processes involved in the use, manufacturing, and effect of many chemicals on the environment, including the generation of waste, the disruption of ecosystems, and the depletion of natural resources. Current patterns of chemical development threaten to exceed the limits of sustainability in terms of resource utilization and waste management, and also pose potential threats to global climate, vegetation, and agriculture. According to the U.S. Environmental Protection Agency (EPA), about 123 billion tons of industrial wastes are generated annually in the United States, and more than a third of this is hazardous waste. This presents a challenge to the chemical industry.

Although the EPA has striven to reduce the impact of toxic chemicals, the efforts have focused primarily on exposure-based approaches. Within the United States, the Pollution Prevention Act of 1990 introduced a new era in regulatory philosophy and policy. The emphasis became the prevention of toxic substances at their source. Green chemistry aims at accomplishing pollution prevention through the design of safer chemicals and the use of more environmentally friendly chemical processes. Green chemistry provides the unifying backbone of this book. Realizing the potential of

green chemistry will require major changes in the current practices of both academia and industry. Fundamentally, all those associated with the development, manufacture, and use of industrial chemicals must understand green chemistry. New ideas, concepts, and technologies, like green solvents, must replace outdated ones.

Designing safer chemicals is essential in today's chemical environment. "Science is necessary but not sufficient" (Maltoni and Selikoff, 1988), and we must balance the contributions of chemistry with the issues of the broader scientific community, public institutions, industry, and those concerned with ethical and social concerns. Experience reveals that safer chemicals and chemical processes provide competitive advantages by reducing the costs of production and waste management, encouraging innovation in novel chemical syntheses, and developing new markets. The chemical industry faces a major challenge in fully embracing this new paradigm (Wicks and Yeske, 1996).

1.1.1 Background

The environment is a complex nexus of interdependent dynamic activities closely related to the internal or external chemistries that support them. Chemists pollute the environment by inducing a change in the supporting chemistry. This occurs when the practice of a human technology jeopardizes any living activities that are recognized to be important (Collins, 1995). The emerging environmental philosophy is a rational reaction to the alarm that pollution has engendered among visionaries such as Rachel Carson who published her alert *Silent Spring* in 1962 (Carson, 1962). The imperative to attend to global environmental issues includes numerous individuals: government officials and scientists who evaluate and regulate against pollution, commentators who raise public consciousness about pollution, corporate executives who shoulder much of the responsibility for minimizing pollution, and concerned citizens.

Chemistry is the tool in the hands of the artisan. However, human activities lead to "randomness." In other words, our activities tend to leave waste. With the power of science and technology comes a great responsibility not to pollute. While excuses continue to be invented, the proportion of our population who realizes how much we have to change is growing substantially. As a result, our collective energy is being redirected wisely, and this is especially true in the area of chemistry (Anastas, 1996). Chemistry comprises so large a component of modern technology that the development of green technologies is significantly a chemical enterprise.

1.1.2 Pollution Prevention

Pollution prevention (P2) is a bold vision that confronts the global problem of environmental pollution. P2 presents an operative paradigm requiring a fundamentally different approach to the way industry and technologies accomplish their tasks. Waste and pollutants are prevented where they originate. This necessitates changes in manufacturing technologies and practices, chemicals and other raw materials, and even products and packaging. In terms of scientific revolutions, this constitutes a paradigm shift (Kuhn, 1996).

The period between 1984 and 1986 marks the beginning of the current P2 movement in the United States. Since that time, the pollution prevention idea has grown into a significant international movement.

The pollution prevention movement represents the first significant step along the road to sustainability (Fiksel, 1996). *Sustainable development* is industrial progress that meets the needs of the present without compromising the ability of future generations to meet their own needs. The 1990 legislation directed the EPA to develop a national pollution prevention strategy, which is administered by the Office of Pollution Prevention and Toxics (OPPT). The act set forth the well-known "pollution prevention hierarchy," which recommends first trying source reduction, then recycling, and finally waste treatment as alternatives to disposal. It also encourages a multimedia, life-cycle approach.

There are four major categories of pollution prevention (Fiksel, 1996):

- Good housekeeping practices to ensure that resources are utilized efficiently;
- Material substitution to reduce or eliminate the presence of undesirable substances;
- Manufacturing process changes to simplify production technologies, reduce water and energy use, or introduce closed-loop recycling; and
- Resource recovery to capture waste materials and reuse them.

As Geiser stated (Geiser, 1998), the P2 movement differed dramatically and fundamentally from the conventional command and control, end-of-pipe, media-specific, compliance and enforcement system that was dominant in environmental protection policy during the 1980s. The P2 movement has been slow to develop the internal capacities that would promote the environmental successes that the pollution prevention concept offers. Geiser laid out five uncompleted tasks in the promotion of pollution prevention (Geiser, 1995). The current text seeks to address only one of these: the chemical substitutes for existing chemicals.

1.1.3 Pollution Prevention Revolution

Hirschhorn wrote in an extremely insightful article (Hirschhorn, 1997) that the pollution prevention revolution has failed, but that it ultimately will succeed. The problem with all the P2 information and technology transfer over the past decade is the absence of a cohesive context, a catalytic enhancement, and a powerful platform to launch P2 advances as part of a total P2 paradigm shift. It cannot be emphasized enough that a key failure of the P2 revolution was its ineffectiveness at translating the fundamental concepts of P2 into nonenvironmental terms and benefits. This would provide a different type of industrial society. It provides a fundamentally new method to judge the quality of virtually everything by moving beyond conventional understandings of performance and economics to include the well-being of the global environment.

Nationally, the P2 revolution cannot be advanced primarily through industry leadership. Leadership must come from scientists and engineers in government, in the environmental community, and in nongovernmental organizations. The P2 revolution is not merely about environmental protection. It is about the search for benign technology (Hirschhorn, 1997). Environmental protection will play a central role in the twenty-first century and will be a major challenge for politicians and scientists alike.

The key aim for the twenty-first century is "sustainable development." Sustainable development seeks to reconcile environmental protection and development; it means nothing more than using resources no faster than they can regenerate themselves, and

releasing pollutants to no greater extent than natural resources can assimilate them (Merkel, 1998). Yet, one must keep in mind that sustainable production and consumption involve not merely technical progress, but also cultural patterns of individual behavior and values.

1.1.4 Regulatory Driver

Regulations still drive much of the chemical usage sectors. For example, recently, the EPA announced a strategy to further reduce toxic air emissions (Grisham, 1999). The agency says the plan, part of the national air toxics program, will increase public health protection. The Integrated Urban Air Toxics Strategy identifies 33 toxic air pollutants (all known or suspected to cause cancer or other health problems) that pose the greatest threat to public health in large urban areas. Included on the list are benzene, mercury, and polychlorinated biphenyls. The strategy also identifies 29 source categories that are responsible for most of these urban area emissions. EPA has regulations in place or under development for 16 of these area sources and is targeting the 13 categories for reductions over the next five years, including industrial inorganic and organic chemical manufacturing, plastic materials and resins manufacturing, and mercury cell chlor-alkali plants. The strategy, which is based on multiple sections of the Clean Air Act, has four components:

- regulations that address sources of air toxics at the national and local level
- national and local initiatives to address specific pollutants and to identify specific community risks
- expanded air toxics monitoring to identify and prioritize areas of concern and to track progress
- education and outreach programs

1.2 Pollution Prevention and Green Chemistry

1.2.1 Chemistry in the New Environmental Philosophy

Chemists play an important role in the new environmental philosophy. Designing intrinsically safe (and functional) compounds or developing safe chemical processes for end-use products is not viewed as practical. Making chemistry (design, synthesis, and manufacturing) more environmentally benign by design must become an integral part of the chemical enterprise. The use of building blocks, reagents, and solvents that pose fewer hazards to mankind and the environment is one aspect.

We have learned how to better evaluate our processes, and this must continue in our scientific practice within the new environmental philosophy. The new issues cannot simply be addressed by minor tinkering with current processes to improve their performance although, undoubtedly, that is one of many of the strategies that will be helpful. Looking beyond the immediate problems, chemists will form new solutions addressing questions of new problems resulting from those solutions. In short, solving one problem frequently creates another, although it must be said that the existence of a new problem was often not recognized at the time because of lack of knowledge.

The bold vision is the realization that a fundamentally different approach is possible and necessary. The green chemistry vision is broad, encompassing changes in fundamental considerations of chemical practice, chemicals and other raw materials, education, manufacturing technologies and practices, and even products and packaging. This vision entails a profound change in thinking—not merely changes in policy, regulations, and technology. As Thomas Kuhn wrote, "A decision between alternative paradigms . . . must be based less on past achievement than on future promise." (Kuhn, 1996). Green chemistry presents those societies that have nurtured an ability to produce original chemistry with a new incentive for technological advancement. This incentive is the optimistic mission of developing technologies that do not detract from the richness or the possibilities of life by incrementally eliminating the sources rather than the symptoms of pollution (Anastas and Farris, 1994; Anastas, 1996; Hancock and Cavanaugh, 1994).

1.2.2 Definition

The term "green chemistry," describes an area of research and chemical practice that arises from scientific discoveries about pollution and ecological interdependence. Green chemistry is not necessarily environmental chemistry, although it may involve some of this. It is chemistry for the environment. The term, which was coined at the Environmental Protection Agency by Paul Anastas, advances the belief that environmentally benign chemical processes are possible and desirable. This supposition has been demonstrated to be true in a number of significant cases.

Green chemistry, environmentally benign chemical synthesis, and alternative synthetic pathways for pollution prevention, benign by design: these phrases all essentially describe the same concept (Anastas and Warner, 1998). Green chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture, and application of chemical products. Green chemistry involves the design of chemical syntheses, and the use of material reagents and processes that prevent pollution.

One can already recognize a number of principles that are fundamental to green chemistry:

- First, genuine green chemistry eliminates pollution at its source.
- Second, chemists must master the scholarship of their particular field, which demands a focused expertise. Collaborations between industrial and academic partners are important to expedite the transfer of significant green products to the marketplace. Governments could undoubtedly facilitate formation of more effective industrial/academic partnerships.
- Third, the complexity of the environment requires us to take the long-term rather than the short-term view in a component of green research.

1.2.3 Vision of Green Chemistry

At the first Green Chemistry and Engineering Conference, held in August of 1997 at the National Academy of Sciences in Washington, D.C., American Chemical Society President Paul S. Anderson said green chemistry "looks beyond controlling waste at

the end of the process. It challenges us to look at the entire life cycle of chemical production to create new ways to more efficiently produce useful products with less waste—or preferably no waste." This becomes the guiding principle affecting all our choices. In all areas of chemical endeavors, this must be true.

Green chemistry is developing into a mainstream strategy for chemical production. In the next 25 years, according to Paul V. Tebo, chemistry will focus on the following:

- reducing emissions and waste, with a goal of zero emissions
- efficiency in use of materials, energy, and water
- inherently safer processes, distribution, and products
- reducing total system impact through tools such as life-cycle assessment
- creating significant customer and societal value per unit of resources extracted
- creating significant shareholder value (Wilkinson, 1997)

This list shows that chemistry in general and, by inference, green chemistry will be influenced by technological drivers, regulatory drivers, and economic drivers.

These drivers are described by Wilkinson. "You can come up with an alternate product made via green processes to substitute for a product made by environmentally unfriendly routes, or you can take an existing product made in an environmentally problematic way and make it differently. Both are fine, but can you make them practically and make them in an industrial setting that makes economic sense? You can scream green all you want, but in the end it's the price in the marketplace that makes the difference" (Wilkinson, 1997).

The traditional view in management circles about the relationship between the environment and business can best be summed up as "pollution pays, pollution prevention doesn't." Many environmentally sound strategies are seen as detrimental to the principal goals of profitability, maintaining markets, controlling costs and efficient production. Together two incentives (government regulation and profit from environmentally sound strategies) serve to turn the traditional vision about the incompatibility between good business and the environment on its head (Gallarotti, 1995).

The United States provides an example of the impact of the regulatory driver in the Clean Air Act Amendments of 1990 (CAAA). The CAAA are affecting firms all around the country. These firms, particularly the small- and medium-sized ones, are not equipped to deal with the effects of the Amendments (onerous control requirements and burdensome record-keeping and reporting obligations). With regard to solvents, there are three provisions of special importance: Title VI (which bans production of certain ozone-depleting solvents); Title V (which requires firms to obtain an operating permit and undergo public scrutiny); and Title III (which requires firms in specific industries using certain processes to apply controls and work-practice improvements.)

One good method of dealing with the CAAA provisions is to adopt appropriate pollution prevention methods. For many firms, this involves analyzing their processes and adopting alternatives that allow them to avoid triggering the provisions. Example of the ways these changes occur are found in an article by Wolf and Morris (Wolf and Morris, 1996) (see table 1.1).

A significant business value is created when the focus is on having all ingredients end up in useful products and less and less in landfills, incinerators, and other places

Table 1.1. Case studies of industrial changes in response to CAAA of 1990.

Number	Problem	Change
1	Small "job shop" used trichloroethane (TCA) in a vapor degreaser	Converted degreaser into a water immersion cleaning unit
2	Small firm used about 4,000 gallons of TCA to clean metal stock	Firm converted to a water-based cleaning system
3	Small firm used up to 5,000 pounds of TCA annually to clean stainless steel pots used in their operations	Firm switched to pots of high-density polyethylene (HDPE), which did not need to be cleaned by TCA
4	Small firm was using about 1,200 pounds of TCA to clean parts	Firm converted to water-based cleaning system
5	Small job shop used TCA in a vapor degreaser to clean aluminum metal parts	Firm converted to water-based cleaning system
6	Small firm uses methylene chloride to strip coatings off small aircraft	Firm identified and tested low methylene chloride–content strippers to replace use of only methylene chloride.

where disposal is a cost to the business and a negative to the environment. Green design in new production facilities is one thing, and green chemistry will gain stronger acceptance as new ways of conducting traditional processes will be sought.

Few topics have commanded as much intellectual and practical concern of investigators and administrators in the chemical sciences in the 1990s as environmentally benign chemistry and chemical technology. While chemistry and chemical engineering technologies have given us a myriad of tangible and intangible assets we automatically associate with civilized living, the implementation of these technologies has come at a cost (Hill, 1996). Investigators in the chemical sciences at most institutions are now cognizant of the environmental impact of their efforts and are seeking better ways to do things.

1.2.4 Methodology of Green Chemistry

Green chemistry is an approach dealing with a fundamental environmental problem of the world, the problem of pollution. Pollution is usually defined as chemical pollution. Most often the approach utilized in the laws has been one of controlling the amount of release of a chemical or controlling the final concentration of that chemical in the medium to which it was released. Green chemistry deals with the above situation somewhat differently: preventing the releases.

The goals of preventing pollution through use of less hazardous and environmentally benign chemistry are achievable. The issues cannot simply be addressed by minor tinkering with current processes to improve their performance, although that is one of many of the strategies that creates new paradigms in chemistry (Trost, 1998). Rather than controlling the concentrations or releases of a particular chemical substance through engineering controls or waste treatment procedures, green chemistry, instead, changes the intrinsic nature of the substances themselves so as to reduce or eliminate the hazard posed by the substances. This is particularly appealing from a science-philosophy perspective because of the nexus between classical chemistry and mecha-

nistic toxicology. To accomplish this, the green chemist must balance the molecular features that are needed for the tasks to be performed with those molecular features that are responsible for the intrinsic hazard of the substance.

1.2.5 Toward the Ideal Chemistry

In 1997 Paul Wender and co-workers at Stanford University wrote that this is an exciting time for science and one of unprecedented opportunity for chemistry (Wender et al., 1997). The writers discussed recent developments in synthetic techniques and considered the possibility of achieving ideal synthesis in the future. They discussed progress in the fields of oligomerization strategies, biosynthetic strategies, cascade strategies, and other complexity-increasing approaches. Although the article focused only on synthesis, and never explicitly mentioned green chemistry, the topics and emphases reflected the environmental concerns and quality of science demanded of those involved in green chemistry.

In this age of great science, chemistry provides a unifying language and methodology for its advancement. Other scientists now increasingly utilize chemistry. For example, many biologists speak and practice the language of chemistry. Some have even adopted "molecular" as a descriptive of their field. Medicine and pharmacology have also become molecular. The use of the word molecular denotes a scientific understanding of the chemical basis for a physical phenomenon.

Increasing sophistication of chemical instrumentation, our expanding knowledge of structure and function (mechanism), and communication among chemists drives these developments. Improved synthesis in particular has become a major indicator of the advancement of science. From medicinal agents and high-technology polymers to diagnostic agents and nanotechnology devices, synthesis has made its mark on our health, standard of living, and economy. The three drivers mentioned earlier (technological, economical, and environmental) are clearly evident.

The full potential of chemistry is far from being realized, however. There is no doubt that we can, for instance, make some molecules well; there are more considerations (see fig 1.1). For many classes of molecules, synthesis has so far been ineffec-

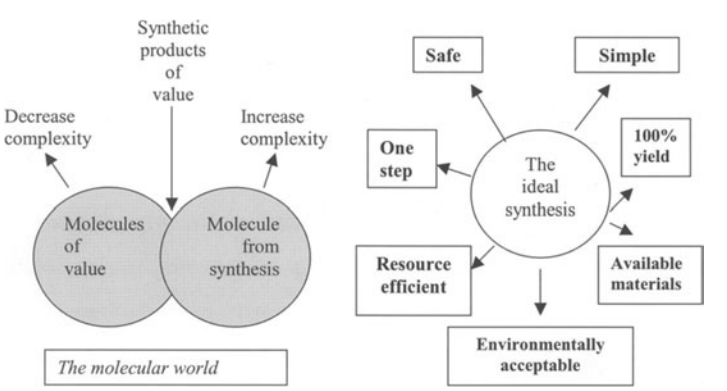


Figure 1.1 In search of the ideal synthesis (Wender et al., 1997).

tive. As a result, two major research strategies have arisen to generate products of value:

- Simplify those molecules of value which cannot be synthesized to less complex mimics, making better use of what they can make.
- Extend the reach of chemistry to the practical construction of more complex molecules, adding new capacity to the system.

Extending the reach of chemistry to green chemistry might seem trivial. The challenge now becomes to accomplish chemistry in the most environmentally benign manner. The belief that the new environmental constraints are equally important and are not "passing fads" is important. When done well, however, it creates new vistas in science and new opportunities for technology.

How do we measure success in the area of green chemistry? The limited availability of raw materials, combined with environmental concerns, require the inclusion of a new parameter to measure the quality of a chemical process. Trost has referred to this as atom economy (Trost, 1991). Often, however, these parameters are used to compare a new synthesis against what had been done previously, a comparison that, not surprisingly, usually favors the more recent work.

If a chemical process were to be measured instead by what is minimally required for success or more generally by what is ideal, progress in the field would be greatly accelerated. In synthesis, for instance, one would seek to design a chemistry in which the target molecule is made from readily available starting materials in one simple, safe, environmentally acceptable and resource-effective operation that proceeds quickly and in quantitative yield. The product should separate from the reaction in 100% purity (Wender and Miller, 1993).

1.3 Philosophy in Practice

There are several possible ways to achieve compatibility between chemical practices and environmental concerns. Technical and scientific innovations provide excellent prospects for environmental protection. As we move into the twenty-first century, industrial society is becoming a knowledge-based society. It is vital that we use our growing knowledge and capabilities responsibly, and that we use them in the interest of environmentally appropriate development.

Chemists must become familiar with several fields. For example, the ultimate objective of those working on assessing toxic hazards associated with chemicals, which must be to provide a sound body of knowledge underpinned by validated theory, is still some way off (Richardson, 1986). Assessing the probability that a chemical will be toxic to humans is a complex task. In order to make the correct diagnosis in a particular instance, one would need to be an expert in methods of chemical analysis for tiny concentrations, the physical chemistry of the relevant environment, and the pharmacology and toxicology of the substance.

Chemical production is another area. A good percentage of the pollution generated by chemical manufacturers and users results from the designers' choices of materials. Although today's manufacturing designers are being asked to factor environmental costs into their designs, they lack the tools they need to do it effectively and consis-

tently. Potential categories for ranking chemicals are technical, health and safety, environment, regulatory, and cost.

There are two main sources for the environmental regulatory, health and safety, and cost information (Betts, 1998). One is EPA's Title 3 List of Lists, which describes which chemicals are regulated by what regulations. The other source is the Materials Safety Data Sheets (MSDSs) that all material manufacturers must fill out for the Occupational Safety and Health Administration (OSHA). The MSDS is a critical element in any environmental study.

The most important conclusions arising from the discussion thus far (and expounded in chapter 3) appear to be, first, that good quality data are vital—many problems in assessing toxic risk have sprung from poor quality data. Secondly, our knowledge should be made more certain. This requires the synergism of several scientific disciplines to find ways to monitor effects in humans at the early stage before these effects become irreversible.

1.3.1 Science and Policy Connection

Within the subject of green chemistry, the hazards of the chemical substitutes are infrequently addressed. No methods have been developed to assess whether implemented pollution prevention programs (through green chemistry) have led to adoption of substitutes that are more dangerous than what they replaced, or whether such may have created more risky products or caused increased risks for workers. This view of entire life cycle of a green substitute will be discussed later. There has some recent effort to integrate life-cycle analyses into pollution prevention programs, including green chemistry as a key component (Anastas and Lankey, 2000).

As would be expected from a scientific revolution like green chemistry, a novel change in thinking manifests itself in a systematic, new approach to doing business (Kuhn, 1996). For example, the German government has chosen the socioecological market economy (okologische und soziale Markwirtschaft) as the framework for shaping production and consumption in keeping with sustainable development, while at the same time encouraging innovation in industry and society. The key in this case is to sever the traditional link between economic growth and the consumption of resources (Merkel, 1998).

Environmental trends appear so daunting and progress toward reversing them seems so slow. Remembering that in responding to the threat of ozone depletion, the international community has largely proved itself up to the task (French, 1997). The trend is reversing itself. This challenge pioneers new relationships between scientists and policymakers. In the area of solvent usage, there is a similar call for international cooperation on research into alternatives.

A preliminary caution is in order. The widespread reliance on substitute chemicals may solve one environmental problem, while contributing to another-something that has happened over and over again as the world has addressed diverse environmental challenges (Zurer, 1999). In this book we are attempting to portray the expanse of the "playing field" with regard to solvent options in green chemistry.

What are the new factors in the area of green chemistry and solvent design? We must view the problem from the perspective of environmental toxicology. In table 1.2

Table 1.2. Scientific disciplines contributing to environmental toxicology.

Area	Contribution
Chemistry	The characterization of toxins
Pharmacology	The mode of entry and distribution of toxins in the body
Biochemistry	The metabolism and interaction of toxins with cell components
Physiology	The effect of toxins on body organs
Biology	The effect of toxins on the environment
Epidemiology	The effect on the population as a whole of chronic exposure to small quantities of suspected agents
Law	Regulation of the use or release into the environment of toxic substances
Economics	Evaluation of the environmental cost v. benefit of economic development and the determination of tradeoffs among economy, health, and the environment.

we present a partial list of subject areas that provide insight into this important area (DeVito, 1996).

1.3.2 Closure of Substance Cycles

Modern microsystems and control technologies are also providing new opportunities to design environmentally friendly production processes and chemicals. While filter and waste treatment technologies have considerably enhanced air and water quality in recent years, they are never more than the second-best solution. A better technology optimizes the use of materials and energy. This involves material-efficient, energy-efficient production processes, as well as the manufacture of environmentally compatible products, especially those that generate little waste. This becomes the driving force behind green chemistry developments. The necessary framework for this is in the Closed Substance Cycle and Waste Management Act, which came into force in 1996.

1.3.3 Hazard and Risk

For the purpose of this book, hazard involves the inherent properties of a chemical substance or mixture, which make the substance capable of causing adverse effects on humans or the environment, when a particular degree of exposure occurs. Hazard is thus linked to exposure. Risk is defined as the predicted or actual frequency of occurrence of an adverse effect of a chemical substance or mixture from a given exposure to humans or the environment (Anastas and Warner, 1998).

1.4 Solvents

Solvents incorporate all the concepts presented thus far. The science of chemistry has matured, and green chemistry emphasizes the creative use and design of chemicals. This necessarily involves the utilization of existing knowledge, wielded in a novel manner by the chemist. Solvents are a necessary component. Green chemistry incorporates the design, manufacture, and use of chemicals and chemical processes into its

practices in such a way that they have little or no pollution potential or environmental risk and are both economically and technologically feasible. This teleological view of green chemistry is counter to traditional expectations in chemistry. Chemists should not be ignorant nor can they claim to be unaware of the effects of the science in which we are engaged (Anastas, 1996). Green chemistry reduces the hazards associated with chemical use. It is the use of chemistry techniques and methodologies that will reduce or eliminate the use or generation of feedstocks, product, byproducts, solvents, reagents, and so on, that are hazardous to human health or the environment. Green chemistry, by espousing rigorous scientific principles, will afford new opportunities and possibilities in this science, which will offer to the world environmentally benign alternatives to existing hazards found in chemistry.

As our chemical knowledge has expanded, the art of chemistry has uncovered more fundamental principles of the relationships between structure and industrial function. This new knowledge must force chemists to incorporate this into how we evaluate the success of any chemical endeavor.

As time passes and our awareness of our global environment increases, the world's populace becomes acutely cognizant of the detrimental effects resulting from human endeavors. Incorporated into its assessment of the success of its chemical activities, an "environmental barometer" will demonstrate the commitment of chemistry to the environment. Green chemistry has as its aim to conduct its chemical activities in such a way as to minimize the generation of waste and to continually increase the beneficial environmental effects relative to previous practices.

The text herein will provide the first authoritative description of solvents for those interested green chemistry. The definition of solvents will be quite broad, as to include the full range of commercial solvents (e.g., cleaners) through industrial solvents to those used in "academic" settings. Solvents, explicitly or implicitly, are a critical component of chemistry. Indeed, in the area of chemical reactions, including solventless systems, it is impossible to neglect the role solvents play. This is intended to provide scientists and nonscientists interested in green chemistry a reference to the considerations for solvents in this new and growing area.

1.4.1 Range of Solvent Usage in Green Chemistry

The range of science and technology included in this is quite broad: chemicals, petroleum and agrochemicals, pharmaceuticals, synthetic materials, electronics, and energy. Industry is already marching ahead in its own interest to reduce waste and emissions through good economics and good housekeeping—controlling fugitive emissions by proper attention to tanks, valves, and the like. Fundamental research is not needed to speed improvements of this type.

The National Science Foundation (NSF) Divisions of Chemistry and Chemical and Transport Systems joined with the Council for Chemical Research in a grant program to reduce pollution at the source by underwriting research aimed at environmentally benign chemical synthesis and processing (Hancock and Cavanaugh, 1994). Some of the generic research areas in which eligible projects might fall include, but are not limited to, the following:

- new chemistries and methodologies for on-demand, on-site production and consumption of toxic chemical synthesis intermediates;
- new, more highly selective catalysts to increase product yield and reduce byproduct formation;
- low-energy separation technologies for feedstock purification and recycling;
- alternative chemical syntheses that bypass toxic feedstocks and solvents;
- improved membrane or molecular sieve technologies that integrate transport and reaction to enhance specificity;
- new processing methods that eliminate hard-to-entrap submicron-sized aerosols;
- alternative chemical syntheses that eliminate or combine process steps;
- novel low-temperature or other energy-efficient methods for synthesis and processing.

With knowledge of how to manipulate and transform chemicals, coupled with the basic hazard data that can be accessed readily from a variety of sources, chemists have the power to reduce or eliminate the risk posed to themselves and society in general by the chemical enterprise (Anastas and Warner, 1998). Specifically in the areas of solvent use, this text will provide leading articles and examples of its practice. Researchers at the vanguard of innovation in this new area know that these goals can be accomplished.

Synthetic chemistry, involving both organic and inorganic chemistry, has been a prominent discipline among the physical sciences for over two centuries. Although the idea of designing safer chemicals is not new, the concept of how to develop this idea, introduce it, and integrate it into the real world of commercially viable industrial chemicals is new. The knowledge and skill of the chemist has been developed and focused primarily on the physical and chemical properties of chemical classes and chemical substituents and the molecular manipulation of these factors to attain the desired industrial properties of the end product. As a result, chemists have been the principal architects of industrial and commercial chemicals, and it is their structural designs that dictate the biological ramifications of these substances on humans and the environment. As the book will point out, however, green chemistry is not limited to synthesis and will span all areas of traditional chemistry, industrial chemistry, and even mundane chemistry.

The concept of designing and using safer solvents brings a new dimension to the chemical enterprise; namely, a far greater consideration of the impact of a new or existing solvent on human health and environment throughout the chemical's life cycle of manufacture, use, and disposal. This involves not only important considerations by chemists regarding the design of new solvents, but, equally important, it includes the reconsideration of and redesign of a wide range of existing chemicals, reactions, and processes.

1.4.2 Current Solvent Use

The U.S. EPA reports that industrial releases of toxic chemicals into the environment decreased by 100 million lb to 2.43 billion lb from 1995 to 1996. That's a 4% de-

crease, and it brings the total decline in toxic emissions to 46% since the nation's premier community right-to-know law began in 1987 (Hanson, 1998). Despite this, Lynn R. Goldman, EPA assistant administrator for prevention, pesticides, and toxic substances, indicated that the agency would like to see companies do more in actually reducing the total volume of wastes. According to EPA data, the chemical industry has registered the largest decrease in emissions of any manufacturing industry in the 10 years of Toxics Release Inventory (TRI), a 51% reduction in releases (table 1.3).

At this time, there is no one source of information on the present state of the science of solvents appropriate for use in green chemistry. Simply stated, it is the aim of this volume is to introduce the use of green solvents throughout chemistry and to provide a comprehensive reference for solvents currently applicable in green chemistry. The book will be divided into two major sections: "solvents in world chemical perspective" (chapters 1–5) and "guide to green solvents" (chapters 6–9). The volume defines characteristics of green solvents and their current usage, and explores their importance (ecologically and economically). It discusses solvents in specific commercial and noncommercial practices. The sections on actual solvents will become a reference for specific solvents and new classes of solvents.

The deployment of solvents directly impacts the design of safer chemicals for use in research, industry, and commerce. Modern day chemists are now expected to develop and to use chemical substances that are safe for human health and for the

Table 1.3. Top 20 chemicals reported under TRI whose emissions changed significantly over 10 years (Hanson, 1998).

1987			*1996*		
Millions of lb	Releases & Transfers	% of Total	Millions of lb	Releases & Transfers	% of Total
Sodium sulfate	12,080	53.6	Methanol	241	9.9
Aluminum oxide	2,435	10.8	Zinc compounds	207	8.5
Ammonium sulfate solution	918	4.0	Ammonia	193	7.9
Hydrochloric acid	657	2.9	Nitrate compounds	164	6.7
Sulfuric acid	643	2.8	Toluene	127	5.2
Sodium hydroxide solution	627	2.8	Xylenes (mixed)	83	3.4
Ammonia	444	2.0	Carbon disulfide	73	3.0
Methanol	420	1.9	n-hexane	72	3.0
Toluene	345	1.5	Manganese compounds	71	3.0
Phosphoric acid	344	1.5	Chlorine	67	2.8
Acetone	235	1.0	Hydrochloric acid	65	2.7
Xylenes (mixed)	218	1.0	Phosphoric acid	63	2.6
Methyl ethyl ketone	193	0.9	Methyl ethyl ketone	60	2.5
1,1,1-Trichloroethane	182	0.8	Copper compounds	57	2.3
Copper compounds	179	0.8	Dichloromethane	54	2.2
Zinc compounds	177	0.8	Styrene	46	1.9
Dichloromethane	152	0.7	Glycol ethers	41	1.7
Carbon disulfide	137	0.6	Chromium compounds	38	1.6
Chlorine	131	0.6	Ethylene	36	1.5
Ammonium nitrite solution	115	0.5	Lead compounds	34	1.4
TOTAL	**22,519**		**TOTAL**	**2,434**	

environment, as well. This flows smoothly into the current understanding of pollution prevention with the belief that a more parsimonious use of raw materials eliminates or reduces "downstream" releases or emissions. The appropriate use of solvents and the development of new, green solvents accomplishes this.

The deeper appreciation of the necessity of designing and producing safer chemicals relates to the total integration of designing safer chemicals as it involves our thinking, planning, development, and implementation of all phases of the design, production, and use of chemicals (Garrett, 1996). In order to attain this goal, it will be necessary to change in the current emphasis, beliefs, policies, procedures, and infrastructure in both academia and industry. This book further seeks to demonstrate how the pervasive role of solvents in green chemistry and how the pursuit of a deeper chemical appreciation of solvents will simultaneously benefit both chemistry in general and green chemistry in particular.

The turn-of-the-century architect and planner Daniel Burnham is remembered for his famous quotation, "Make no little plans; they lack the fire to excite men's minds." Gender aside, Burnham was speaking for a revolutionary vision. The pollution prevention movement should more boldly state a vision and goals for the next century. The plans for green chemistry and green solvents are not little, and in the pages that follow we can readily see that the response of scientists has been great.

1.5 Future Direction

Central to any control of hazardous substances is the question of how standards can be formulated and promulgated. In the environmental field, widespread monitoring of chemical hazards is now becoming commonplace but the preparation of norms for the control of such substances has proved extremely elusive (Luxon, 1986). Proposals have been made for control levels, action levels, short-term levels, and other refinements, which unfortunately all invariably beg the question: what level is acceptably safe? "Acceptably" here must surely mean acceptable to those who may be affected, that is, those coming into contact with the substances under consideration. In some cases, particularly in the radiation field, local liaison committees have been set up to involve the public in such considerations. On the scientific front, the investigation of the toxicological hazards of substances has moved slowly. New methods have been developed to determine the long-term effects of many hazardous chemicals. Unfortunately, the results of such investigations are often ambiguous and therefore need careful interpretation if they are to gain general acceptance. At a time when there is public mistrust of both government and industry, professional societies clearly have an important role to play in such evaluations.

In the development of regulatory standards, account must be taken of acceptable risk, which will involve political considerations. Perhaps the way forward has been indicated over the past 30 years by bodies such as the American Conference of Governmental Industrial Hygienists, who have made a great contribution by publishing annually recommended standards for several hundred toxic substances. These standards have been used extensively with minor modifications by regulatory bodies in many countries.

Given that standards can and must be adopted, then the future of control may not lie in an extension of the present detailed regulatory requirements. Rather, there could be a move towards providing a simpler, more flexible framework for the control of the risks at local level, always providing that the local working rules adopted are acceptable to those who may be affected, coupled with an overriding requirement that the mandatory exposure standard must be met.

In the midst of this sea of uncertainty, there is a need for a beacon of light that will illumine a path. This path may not be the only one, but it offers a way toward the promise of a better future. Green chemistry, in addition to being a scientific revolution, serves as such a beacon. The manner in which solvents are designed, developed, and used is an excellent example of how the "beacon" effects its influence.

1.5.1 Information Overload?

The need for a beacon like green chemistry is more important as the amount of information explodes. Web technology gives wide, rapid, and anonymous access to data. This expansion is raising concerns about data quality and interpretation, confidentiality, competition, and security. If scientists want to participate and be empowered in the environmental protection arena, they should be using the most up-to-date data. As scientists, they must critically evaluate the data.

Data stewardship is a more complicated issue, and the needs change with the audience. It's making sure that the information you are providing is understandable, relevant, and a reasonable characterization of environmental conditions or performance. That's a hard job. It requires an understanding of who is using the information and how they understand it. Very little analysis of that is going on right now—the EPA is doing some, and is being pressed to do more. What this whole movement suggests is that everybody needs to get a lot smarter about risk communication—what it is that people want to know and how they perceive information (Thayer, 1998).

1.6 Subject Content of Book

The book provides a multilevel approach to the subject matter. The first level presents the breadth of basic information needed to appreciate the importance of solvents in the practice of green chemistry. This information will be diffused throughout the book within discussions on the principles of green chemistry, the defining characteristics of solvents appropriate for green chemistry, and practical guidelines for selecting solvents applicable in specific situations. A rigorous explanation of solvents will be included in the text and will be clearly marked (numerous references will be included for interested readers).

The second level of intention will accentuate the role of solvents in the present state and future development of green chemistry. This discussion will include practical and teleological discussions *vis à vis* the environmental concerns important to individuals using solvents. Enough information will be provided for the reader to be able to determine how to evaluate a solvent's appropriateness to green chemistry, in particular applications.

The third level of intention within this volume will be to supply specific, detailed information, and references, so that it will be a basic reference book for green chemistry solvents. This information will be on specific solvents and on discussions of their properties ("why" they are appropriate). This information will have indices, so that it may be easily searched.

1.6.1 Limitations

No book on green chemistry can present absolutes, so this work cannot make that claim. Rather, it will describe guidelines on solvent choice and usage, and it will provide important resources for the gradual emergence of green chemistry as a scientific discipline. Through the presentation of important subjects in broadly considered areas of chemistry, the reader will be led to applying principles to solvents as criteria to determine their use in green chemistry. Assuredly, this exposition will reveal holes and gaps in our present knowledge; these must be filled by future work and research.

2

Chemical Practice and Solvent Usage

2.1 Solvent Usage

Solvents are substances that are liquid during application and will dissolve other substances, which can be recovered unchanged on removal of the solvent. Importantly, the solvents and the solutions involving them must be applicable for some purpose. Solvent systems must be understood before any rationale chemical process can be developed.

Solvents are widely used by chemists. Educators in the physical sciences, especially chemistry, employ solvents in discussions of physical phenomena and in laboratory experiments. Industries around the world utilize the benefits of solvents to accomplish their desired goals. Individuals in all societies use solvents. In the face of these facts, it is imperative that the solvents used result in a minimal impact upon the environment. I list five true premises (Anastas and Williamson, 1998):

- Chemistry and chemical products are the basis of the economy of virtually every industrialized nation.
- The manufacture, processing, use, and disposal of certain chemical substances has resulted in significant and measurable damage to human health and the environment.
- Over the past generation, more than a trillion dollars has been spent on environmental protection.
- Currently, chemists now have the knowledge to design chemicals and chemical manufacturing processes that pose little or no risk to human health and the environment.

- Research in green chemistry is making dramatic achievements in the design of chemicals, chemical syntheses, and chemical processes that are environmentally benign and economically feasible.

Chemicals make up all matter, from lethal to innocuous. The use of solvents is ingrained in much of the lifestyle of chemical practice. Despite the proliferation of environmental regulations during the past several decades, hazardous chemicals resulting from solvent use are still being released to the environment in significant quantities. It is essential that the chemical sciences and industries proceed in a manner that does not cause harm to human health and damage to the environment. Socially, it is imperative that the populace becomes aware of the innocuous and even beneficial chemicals that have been manufactured and used, and that chemicals can be designed to be both safe and efficacious. Achieving these goals in the area of solvents can be regarded as a valid component of the primary objectives of green chemistry. As this book asserts and to which enormous amounts of research testify, research in and deployment of solvents in green chemistry can lead to substances and processes that are more benign to human health and environment.

The goal of green chemistry is to reduce the hazards associated with products and processes that are essential not only to maintain the quality of life achieved by society through chemistry, but also to further advance the technical achievements of chemistry, and to do so in a sustainable manner. Reduction of risk is a beneficial result of green chemistry. Risk can be summarized in simple terms as the product of the hazard of a particular substance and the exposure to that substance:

$$\text{Risk} = \text{Hazard} \times \text{Exposure}$$

Risk is the probability of an undesirable biological response resulting from exposure to a toxicant. Estimating risk requires an integration of the toxicity conclusions (toxicant identification and dose-response evaluation) and exposure assessment. However, since dose-response relationships are not linear (as in the characteristic sigmoidal graph lines), exposure is more accurately expressed as a function (f) as seen in the following equation (Hughes, 1996):

$$\text{Risk} = \text{Hazard} \times f(x)$$

A "healthy" approach to determining acceptable risk is to answer the following questions (Hughes, 1996):

- Is the substance really needed?
- Could alternate, less toxic substitutes be used?
- What is the realistic amount of public exposure?
- What are the risks versus benefits for continued use of the agent?
- What is the environmental impact of the substance?
- Does the procurement of the agent deplete an environmental resource?
- Does existing technology permit the "final" disposal of the substance?
- If used, do we have the technology to ensure the "safe" use of the substance?

Green chemistry seeks to reduce or eliminate the risk associated with chemical activity by reducing or eliminating the hazard side of the risk equation, thereby obviating the need for exposure controls and, more importantly, preventing environmental

incidents from ever occurring through accident (Anastas and Warner, 1998). Recent work, like the Risk Screening Environmental Indicators (RSEI) model allows residents or researchers to determine the toxicity and number of people exposed to a factor's emissions that are reported each year by thousands of companies through the TRI. The results can be expressed as a ranking of most large facilities in the United States by their environmental threat to nearby residents, a ranking of areas by TRI pollution, and much more. The RSEI model currently only considers air releases, both fugitive and stack emissions, whereas TRI includes releases to all media. The program will allow relative risk to be considered (Johnson, 1999a). As green chemistry reduces the hazard value, the risk will be lowered.

It should be noted that hazard is not simply defined as toxicity but rather includes the full range of consequences which can be realized from the use or generation of a substance. Hazard therefore includes, in addition to acute and chronic toxicity, carcinogenicity and mutagenicity; properties such as explosivity, flammability, and corrosivity; direct ecological impacts such as plant and animal toxicity, and atmospheric damage; and indirect ecological impacts such as resource depletion, global climate change, and persistence in the environment.

2.1.1 Solvents as a Green Chemistry Tool

Green chemistry utilizes the information that is now available to the scientific community about the toxicity and other hazards posed by certain chemicals. Through a combination of knowledge of the nature of a chemical's hazardous properties with the ability to manipulate the chemical's structure, chemists possess the ability and skill to mitigate the hazard. Selection of a solvent should be based not only on any hazards that the chemical may possess, but also on existing environmental problems that its use may exacerbate. Selection of solvents needs to optimize the utility of the solvating material and minimize its environmental impact.

To start, one must decide whether the substance itself is benign or whether it poses a hazard in the form of toxicity, accident potential, ecosystem destruction, or other form. Hazard can be evaluated in terms for which there is extensive data on properties ranging from dose response to flammability to ozone-depleting potential. In the absence of empirical data, there is a wide range of structure-activity relationship models which can give reasonable approximations for the properties in question.

2.1.2 Selection of Solvents and Reaction Conditions

The use of solvents in the chemical industry and the chemical-related industries is ubiquitous. In 1991, the production of the 25 most commonly used solvents was more than 26 million tons per year (Anastas and Williamson, 1998). Because solvents are required in such high volumes compared to all other materials used in a synthetic transformation, hazards associated with their use have always been a consideration in the development and selection of solvents.

Is the solvent itself hazardous? Could it be responsible for the generation of waste? Utilizing a solvent that encourages more selectivity means that more of the starting material is going to be converted into the desired form of the product. Ideally, it will facilitate both high selectivity and high conversion to generate little or no waste.

Utilizing highly selective conditions can mean that separation, isolation, and purification of the product will be significantly less difficult. Since separation and purification processes often create environmental burdens, solvents promoting high selectivity are very desirable in green chemistry. When the overall yield of a process is increased by 10 or 20%, less material is ending up in waste streams and more is being converted into product. Can a solvent play a role in improving atom economy (Trost, 1991)?

2.2 Pollution: Effects of Solvents

2.2.1 Definition of the Problem

The problem of toxic pollutants is difficult to handle because of the great variety of chemicals involved. They represent a hazard not only to aquatic life, but also to human health, either through direct exposure or indirectly through consumption of contaminated fish or waterfowl. The degree of hazard depends on the pollutant's toxicity, rate of discharge, persistence and distribution in the aquatic system, and bioaccumulation potential. Some highly volatile compounds, when discharged into water, evaporate and become air pollutants.

The health risk cannot be well defined because very little information is available on the toxicity of most commercial chemicals (Postel, 1987). According to the data published in 1984 by the National Research Council (National Research Council, 1984), very little is known about the toxicity of approximately 79% of commercial chemicals. Fewer than 10% were examined for carcinogenicity, mutagenicity, and reproductive toxicity (National Research Council, 1984). Obviously, nothing is known about pollutants that are byproducts of industrial processes and were never intended for commercial use.

Spent solvents constitute a major source of pollution in the chemical and pharmaceutical industries. Much of this pollution can be prevented by solvent substitution: using solvents that are more environmentally compatible or possess higher performance. This can lead to a reduction in the amount used. However, identifying replacement solvents is often a difficult process performed in an ad hoc manner.

2.2.2 Solvents and Water Pollution

In industrialized countries, the sources of water pollution may be divided into point and nonpoint sources. *Point sources* have a well-defined origin, such as the outlet from a plant or from a municipal sewer line. *Nonpoint sources* lack any well-defined point of origin.

Although both types of pollution sources present a serious problem, point sources can be controlled, at least in principle. Nonpoint sources, however, are difficult to control. Sources and types of nonpoint pollution in impacted rivers and lakes in the United States include agriculture, land disposal, construction, hydromodification, urban runoff, and silviculture, resource extraction. The pollutants in these sources include sediment, nutrients, toxins, pesticides, salinity, and acidity (Institute, 1988). Looking at these lists, one can easily deduce that solvents play roles in the pollution of water.

2.2.3 Urban Pollutants

The sources of urban pollutants are municipal sewage, runoff from city streets and landfills, and industrial effluents. Indirectly solvents contribute to municipal sewage, insofar as they comprise part of the landfill and runoffs. Mostly, industrial effluents have solvent components.

2.2.3.1 Synthetic Organic Chemicals

The synthetic chemicals found in municipal wastewater originate from academic use, household use, and industrial use. Ordinary households in an industrialized society use substantial amounts of organic chemicals such as cleaning fluids, pharmaceuticals, cosmetics, and paints. Residual quantities of these substances may end in the sewage. Hospitals, universities, dry cleaning establishments, garages, and other small commercial shops may also contribute to that total load of chemicals in municipal wastewater.

The problem is aggravated when industrial plants contract with the city to dispose of their liquid waste through the municipal sewer system. Although the Clean Water Act (CWA) of 1972 requires that industrial plants prepurify their effluent before discharging it into municipal sewers, there is always potential for contamination with toxic compounds that are not well identified. The removal of such chemicals from wastewater may be difficult and expensive. Furthermore, most municipal sewage-purification plants are not equipped for this challenge. Toxic chemicals in sewage create potential hazards to aquatic life and inhibit the biological process of degradation of contaminants. In addition, they potentiate the toxicity of sewage sludge that must be disposed of in landfills.

2.2.3.2 Storm Water Runoff

Storm water runoff from cities and villages presents another problem. This runoff contains salts from road deicing, street refuse, animal waste, food litter, residue from atmospheric deposition of sulfuric and nitric acid, metals, asbestos from automobile brakes, rubber from tires, hydrocarbons from motor vehicle exhaust condensates, oil and grease, soil and inorganic nutrients from construction sites, and a variety of other chemicals. Research shows a heavy impact of urban nonpoint pollution on freshwater quality (World Resources Institute, 1988).

2.2.4 Industrial Pollutants

Industrial waste consists of a variety of pollutants. These include:

- sludge from the steel industry;
- toxic chemicals from chemical, mining, and paper industries;
- BOD contaminants from food processing plants;
- heat from power plants (conventional and nuclear) and from steel mills; and
- pH changes from the mining industry.

Results from the first TRI compiled by the EPA, as mandated by the Emergency Planning and Right-To-Know Act, are presented in table 2.1 (1989). Recent release

Table 2.1. Toxic release inventory.

Where Released	Quantity (billion lb)	Percent of Total
Water	9.7	43
Underground wells	3.2	14
Air	2.7	12
Landfills	2.4	11
Municipal sewer	1.9	
Off-site treatment and disposal	2.6	12
Total	22.5	100

of information and the Risk Screening Environmental Indicators (Johnson, 1999b) provides a screening tool, whose use is to point to further research.

2.2.5 Pollution of Groundwater

Groundwater is an important natural resource. About half of the U.S. population depends upon groundwater for drinking. Thus, preservation of clean groundwater is of utmost importance.

The Office of Technology Assessment reported that incidences of groundwater contamination have been found in every state and that a number of organic and inorganic chemicals were detected in various groundwater supplies (Thompson, 1986). Many of these contaminants are known toxins and carcinogens.

As we move into the twenty-first century, groundwater pollution is still a concern. The impact of solvent use, in this case gasoline, is illustrated by the recent events surrounding methyl t-butyl ether (MTBE, see below). MTBE (fig 2.1) is widely used in gasoline as an oxygenate and octane enhancer. Numerous studies and debates have involved this chemical in order to evaluate the uptake, distribution, metabolism, and elimination of MTBE in humans (Nihlen et al., 1998). The 1990 CAAA require fuel oxygenates to be added to gasoline used in some metropolitan areas to reduce atmospheric concentrations of carbon monoxide or ozone. Out of 60 volatile organic chemicals analyzed, MTBE was the second most frequently detected chemical in samples of shallow ambient groundwater from urban areas that were collected during 1993–1994 as part of the U.S. Geological Survey's National Water-Quality Assessment program. At that time only 3% of the shallow wells sampled in urban areas had concentrations of MTBE that exceed 20 mg/L, which is the estimated lower limit of the U.S. EPA draft drinking water health advisory.

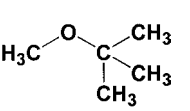


Figure 2.1 MTBE.

Possible sources of MTBE in groundwater include point sources, such as leaking storage tanks, and nonpoint sources, such as recharge of precipitation and storm water runoff (Squillace et al., 1996).

2.3 Applications of Solvents

Table 2.2 surveys typical applications of solvents, without implying exhaustiveness (Marcus, 1998). As is shown below, not all applications are of the solvents as such: in many cases they are added to other materials to improve their properties, to initiate reactions, and accelerate their rates; and they are used as reagents that are consumed by transforming other compounds to more useful ones.

2.4 Broad Areas of Application

We can use Chipperfield's writing to outline four broad areas where their roles are central (Chipperfield, 1999).

2.4.1 Solvent Extraction

Solvent extraction is the process in which one or more solutes partition selectively between two immiscible liquid phases. The process has many applications:

- in hydrometallurgy, for example, recovery of copper and nickel from ores;
- in nuclear fuel reprocessing, to separate uranium and plutonium from fission products;
- in treatment of fermentation liquors, for example, recovery of citric acid;
- in treatment of waste waters, for example, removal of phenolic compounds;
- in organic synthesis, to recover the product or to purify it from impurities, and in analytical chemistry, to separate analytes.

Potential criteria for the choice of a solvent include the chemistry of the extraction involved and the miscibility with the other solvents in the process. One set of criteria concerns the physical properties of the solvent: its density, viscosity, surface tension, volatility, and so on. Further criteria for the choice of a solvent are its availability, cost, toxicity, hazardousness, and other aspects of environmental acceptability.

The three drivers mentioned earlier (regulatory, economic, and technical) will also be important in this section process, as they determine the utilization of the solvents. Analysts may be faced with the problem of finding alternative solvents for established methods, and when developing new methods will want to avoid certain types of compounds (for example, chlorinated solvents that deplete the ozone layer). There are reviews of the literature available, which will help analysts to select alternative solvents, with particular emphasis on solvent extraction and liquid chromatography. Within these works, methods of classifying solvents are discussed and tables of solvent properties are given. Strategies for optimizing mobile phases for high-performance liquid chromatography are also described in detail (Barwick, 1997).

Table 2.2. Solvent applications.

Application	Description
Absorbent	Absorb gases from industrial processes or power plants
Alkylator (also acetylator, aminator, benzolator, etc.)	Reagent in order to transfer an alkyl group acetyl, amine, benzoyl, methyl, etc., groups to other compounds
Antifreeze	Added to radiator fluids of motor vehicles to prevent freezing at low outside temperatures
Binder	Achieve cohesiveness in composite materials
Bleacher	Oxidizing/reducing colored materials or impurities in them, causing colors to fade
Blood substitute	Carry oxygen and hemoglobin through the arteries, veins, and capillaries of living animals
Blowing agent	Used in polymer manufacture to create porosity
Catalyst	Initiates reactions and accelerates their rate, without being consumed. Usually by means of acidic or basic properties.
Chelator	Forms stable chelates with metal ions without causing irreversible damage
Degreaser	A cleaner that specifically removes grease and oily materials
Dehydrator	Removes water from materials
Developer	Used in photoresist materials in order to bring out the imprinted pattern
Diluent	Used in mixtures with other solvents in order to improve their chemical or physical characteristics
Dispersant	Forms suspensions of materials in it without dissolving them
Electrochemistry	Dissolving the electrolyte to permit current to flow between a cathode and an anode, without itself being reduced or oxidized
Eluant	Chromatographic columns, either for analytical or preparative use
Etchant	Reacts with surface of materials, dissolving away layers that are not protected by a nonreactive covering, and may be used in electropolishing and similar processes
Extractant	Either alone, as a solvent, or diluted with a diluent, is used with another liquid phase, in order to separate solutes by their partitioning between the two liquid phases
Fuel	The chemical energy stored in the intramolecular bonds is liberated by combustion in air
Humectant	A hygroscopic material that avidly retains water absorbed from a humid atmosphere, and may be used in cosmetics and pharmaceuticals
Leaching agent	Dissolve desired substances out of solid materials
Lubricant	Used by virtue of its rheological properties, that is, viscosity, to reduce friction between moving parts in machinery
Liquid crystals	By virtue of its long chains
Microemulsions	Implies participation in multicomponent systems, generally involving also water, an alcohol, and a surface active agent, to produce a useful agent
Oxidant or reductant	A reagent to remove, or supply electrons in reactions
Plasticizer	Used to confer on polymers suitable mechanical elastic properties
Propellant	Used as a rocket fuel, being oxidized by a suitable substance, producing a large volume of hot gases, hence a large thrust
Working fluid	Used in order to transmit mechanical forces, a required property being low compressibility
Solvent	Used in order to bring into solution many kinds of material, inorganic, organic, or biochemical, and this usually implies that it is produced as an industrial solvent in large bulk quantities

2.4.2 Electrochemistry

Although many electrochemical processes, such as electroplating, charging and discharging of batteries, and electroanalytical determinations, are carried out in aqueous solutions, green chemistry can be used to improve the aqueous process and to prolong the lifetime of the chemical solutions. The application of nonaqueous solvents in this area grows in importance. For example, the following solvents have been used in electrochemical processes:

methanol	acetonitrile
glycols	nitromethane and nitrobenzene, the amides, whether N-substituted or not
glycerol	
formic acid	dimethyl sulfoxide
ethylene and propylene carbonate	sulfolane
4-butyrolactone	dimethyl sulfate
ethanolamine	hexamethyl phosphoramide

Catalysts and their effects on chemical reactions aid in efficiency, effectiveness and selectivity. A recent example of current research is redox and ligand exchange reactions of the oxygenation catalyst (N,N′-bis(salicylidene)ethylenediaminato)cobalt(II), $Co(SALEN)_2$ (below), and its one-electron oxidation product, $Co(salen)^+_2$. These were investigated in DMF, pyridine, and mixtures of these solvents. Solvent effects on the potentials, the thermodynamics of cross reactions, and the distribution of Co(II) and Co(III) species as a function of the solvent composition are important considerations (Eichhorn, 1997). The results in these solvents should be compared with other work with catalysts using more environmentally benign media (Collins et al., 1998).

2.4.3 Organic Chemistry

The primary reasons for selection of a solvent as the reaction medium is its ability to allow sufficient concentrations of the reactants to be achieved. Simultaneously, the solvent is inert with respect to reactants and the reaction products. Reactants are solvated to give them desired reactivity. Further considerations are the ease of product isolation, possible effects on the relative yields of desired products and undesired byproducts, and effects on the rates at which the reactions proceed.

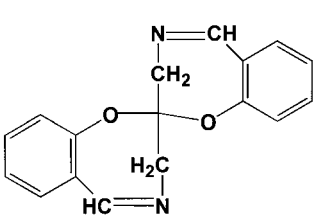


Figure 2.2 $Co(SALEN)_2$.

How can chemists measure the importance of solvents? Solvents "solubilize" solutes. The general rule for organic or nonelectrolyte inorganic solutes, whether gaseous, liquid, or solid, is that they would show adequate solubilities. Expressions for the estimation of solubilities are presented in chapter 3. The effects on the rate of reactions will be discussed there, and comparisons made among classes of solvents.

The stronger the solvating ability of a solvent is, the more it decreases the thermodynamic activity of the reactants and their reactivity, that is, their availability for the reaction. A linear correlation has been found between the activation Gibbs free energy of a series of S_N2 reactions and the acceptor number (AN) of the solvents (Marcus, 1998).

The reactivity (or availability for reaction) can be influenced by solvation. To illustrate, if a salt with a large organic cation, for example, tetraethylammonium, rather than a small cation, for example, sodium (see below), can be used, the importance of the solubility consideration becomes smaller (Miller and Parker, 1961). A balance must be struck between the solubility of the reactant salt and the availability of the anion for the reaction.

The choice of solvents as reaction media thus depends upon their solvating abilities, effects on reaction rates, and positions of equilibrium. When green solvents are to be used, the choice of aliphatic hydrocarbons, mainly *n*-hexane and cyclohexane, due to their convenient physical characteristics, is possible. Nonpolar organic substances are soluble in these hydrocarbons to some extent, polar ones much less so. The latter, for example, long-chain alkylammonium salts, may aggregate in such solvents to inverted micelles or other structures. The alternatives, providing high solubilities but still low or moderate solvation, are aromatic hydrocarbons or halogen-substituted aliphatic hydrocarbons. Among the former, benzene is no longer employed much as a solvent due to the carcinogenic properties ascribed to it.

Solvents and solvating media can be modified or extended by the use of phase-transfer catalysis (PTC). Reagents that are themselves too polar, or of electrolytic nature, to be dissolved in such nonpolar or slightly polar solvents can often be employed by the use of a phase-transfer catalyst. The reagent is dissolved in a second immiscible and polar solvent, generally water, in contact with the reaction medium, and the catalyst is used to convey it to the nonpolar organic phase for the reaction. Such phase-transfer catalysts consist mostly of salts with long-alkyl-chain-substituted ammonium cations with altogether 12–28 carbon atoms in the 1 to 4 chains that are soluble both in water and in the nonpolar organic phase. Phase-transfer catalysis has

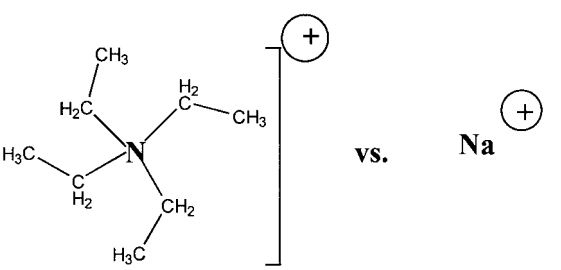


Figure 2.3 Tetraethylammonium vs. sodium.

also been applied to reactions in supercritical solvents, for instance, for bromination of benzyl chloride with potassium bromide in supercritical carbon dioxide with acetone cosolvents using tetraheptylammonium bromide as the catalyst (Eckert et al., 1996).

The use of various solvents as reaction media for diverse reactions is summarized in Reichardt (1988), and Marcus (1998). The following is a partial list of organic reactions requiring solvents. In chapters 5 through 7 we will look at green solvents and provide some examples of more environmentally benign alternatives to some of the more toxic solvents.

- halogenation (Acetic acid, o-dichlorobenzene, CCl_4, nitrobenzene)
- nitration (Acetic acid, CH_2Cl_2, o-dichlorobenzene, CCl_4, nitrobenzene, sulfuric acid)
- sulfonation (Heptane, 1,4-dioxane, acetic acid, chloroform, CCl_4, nitrobenzene, sulfuric acid)
- diazotization (Benzene, water, ethanol, acetic acid DMF, sulfuric acid)
- ozonation (Methanol, acetic acid ethyl acetate, CH_2Cl_2, 1,2-dichloroethane, chloroform, CCl_4)
- epoxidation (Benzene, diethyl ether, 1,4-dioxane, acetone, acetic acid, chloroform, CCl_4)
- oxidation (Benzene, water, *t*-butanol, 1,4-dioxane, acetic acid, ethyl acetate, CH_2Cl_2, $CHCl_3$, pyridine, nitrobenzene, sulfolane, sulfuric acid)
- hydride reduction (Benzene, toluene, diethyl ether, DME, tetrahydrofuran, 1,4-dioxane)
- hydrogenation (Cyclohexane, heptane, water, methanol, ethanol, tetrahydrofuran, 1,4-dioxane, acetic acid, ethyl acetate, DMF)
- aldol reaction (Benzene toluene, water methanol, ethanol, diethyl ether, DME, tetrahydrofuran, acetic acid, pyridine, dimethylsulfoxide)
- Wittig reaction (Benzene, toluene, methanol, ethanol, t-butanol, diethyl ether, DME, tetrahydrofuran, acetic acid, CH_2Cl_2, pyridine, acetonitrile, DMF, dimethylsulfoxide)
- Diels-Alder reaction (Benzene, toluene, water, methanol, ethanol, diethyl ether, tetrahydrofuran, 1,4-dioxane, acetone, CH_2Cl_2, 1,2-dichloroethane, *o*-dichlorobenzene, chloroform, acetonitrile)
- Grignard reaction (Diethyl ether, tetrahydrofuran)
- Friedel-Crafts reaction (Heptane, CH_2Cl_2, 1,2-dichloroethane, *o*-dichlorobenzene, nitrobenzene, carbon disulfide, sulfolane)
- S_N1 reactions (Water, methanol, ethanol, t-butanol, acetic acid)
- S_N2 reactions (Acetone, acetonitrile, DMF, dimethylsulfoxide sulfolane)

Crystallization is often used as a method of product isolation. Crystallization of the reaction product may be induced if, to the reaction medium, in which it is well soluble, a cosolvent is added in which the product is insoluble. Because for the latter purification method the solubility should be high at high temperatures but much lower at low temperatures, the temperature coefficient of the solubility becomes an important criterion for the employment of a solvent. A further guide is the fact that substances tend to dissolve in solvents with similar polarities, so that a solvent and cosolvent for the recrystallization of a given product can be selected according to the polarities.

A further major application of solvents in organic chemistry is in high-pressure liquid chromatography (HPLC), for the chromatographic separation of solutes, be it for preparative or analytical purposes.

2.4.4 Applications in Polymer Science and Technology

Many of the considerations discussed above in connection with organic chemistry are, of course, also valid for polymer technology. Solvents for polymers, used in such materials as paints and lacquers, and as media for the polymerization reaction, provide examples of industrial applications of solvating media.

When polymers are used as constituents of coatings, paints, and lacquers, they require solvents as dispersing agents. Whether true solutions are formed or emulsions, the solvents used have to conform to environmental specifications, but should be sufficiently volatile so as to permit rapid drying of the applied polymer and pigment, if present. One should examine chapter 6 and the appendix for green examples of coatings solvents.

Polymerization of suitable monomers takes place according to one or more of several catalyzed mechanisms: anionic, cationic, free radical, or with Ziegler-Natta catalysts. The steps involved are initiation of the polymerization, propagation by the addition of monomers to shorter, reactive polymers or oligomers, and termination of the polymer chain growth. Appropriate media are employed: the bulk liquid monomer or its melt, a solution of it, or its suspension/emulsion. In the cases where a solution is used, the solvent should dissolve the monomer as well as the growing oligomers to a high degree, but the polymer may become insoluble when it reaches a sufficient molecular weight. This is the case for the polymerization of perfluorinated monomers in a green solvent, supercritical carbon dioxide (Eckert et al., 1996). When a solvent is used, its main roles are to decrease the viscosity of the reaction mixture and to remove the heat evolved in the reaction by virtue of its heat capacity and heat transfer properties. One further example would be ethylene in liquid alkanes or in supercritical fluid ethylene.

2.5 Domain and Range of Solvent Employment

In the material that follows we describe high solvent use areas. It will be these areas where green solvent research and solvent substitution will have the greatest impact.

In the chemical industry and in research alone more than 1700 trade name products and chemicals are used as solvents (Ash and Ash, 1996). The worldwide solvents market is estimated at over 30 billions pounds per year. Solvents are used in a wide range of industries and applications including metal cleaning and degreasing, dry cleaning operations, automotive and aviation fuel additives, paints, varnishes, lacquers, paint removers, plastics and rubber products, adhesives, textiles, printing inks, pharmaceuticals, and food processing.

Current solvents include a variety of commonly used chemical groups such as

- alcohols (amyl, butyl, ethyl, isopropyl, etc.),
- esters (amyl, butyl, and ethyl acetates),
- glycol ethers, ketones (acetone, methyl ethyl ketone),

- chlorinated hydrocarbons (ethyl and methylene chloride, etc.),
- petroleum-derived hydrocarbons (benzene, toluene, xylene).

Halogenated solvents are still used extensively (Callahan and Green, 1995). A recent study by the Source Reduction Research Partnership (SRRP 1992) placed the total amount of the halogenated solvents (TCE (trichloroethylene), PERC (perchloroethane), METH (methylene chloride), TCA (trichloroethane), and CFC-113) used in the United States in 1988 at 802,600 metric tons (MT). Virgin solvent use amounted to 735,000 MT, while the extent of recycled solvent use was 67,600 MT. The total amount of virgin and recycled halogenated solvent used for parts cleaning, electronics, and paint stripping was 484,000 MT. This is equivalent to 97 million gallons (gal). An additional 27,100 MT was used in automotive and industrial aerosol formulations. The development of solvent databases and computational methods that aid in the selection and/or design of feasible or optimal environmentally benign solvent alternatives for specific applications will make the transition to more environmentally friendly solvents easier (Crabtree and El-Halwagi, 1994; Sherman et al., 1998).

The solvents TCA and METH are the two most commonly used halogenated solvents in the automotive and industrial aerosol product sector. These two solvents represent more than 90% of the total. TCA is formulated into electrical cleaners because it allows the equipment to be cleaned while operating (i.e., it is nonflammable and nonconductive). We must bear this in mind as we evaluate alternatives. Other products and the types of halogenated solvents used, in descending order of use, include general-purpose lubricants (TCA, then METH), silicone lubricants (TCA, then METH), mold-release agent (METH, then TCA), engine cleaners (TCA, METH, then PERC), brake cleaners (TCA and PERC), and carburetor cleaner (METH). Solvent selection is based on desired property such as evaporation rate and issues regarding solvent toxicity. Solvent toxicity has been a major driving factor in the favored use of TCE over METH and PERC.

Unlike parts cleaning and electronics, which use a variety of halogenated solvents, paint stripping primarily employs the use of METH in a formulated stripper product. Estimated usage of METH only (not stripper) in 1988 was reported to be 66,000 MT. Of this amount, 60,000 MT was virgin solvent and 6000 MT was recycled solvent. Much of the recycled solvent consumed by this industrial sector would be extracted from waste solvents generated by the parts cleaning and electronics industry. Usage of METH in paint strippers has been declining in recent years because of regulatory pressures.

2.6 Global Effects of Solvent Usage

There are critical needs with regard to protecting the environment (Medina, 1996). The use of solvents introduces stresses on ecosystems, ultimately on the global level. More testing for acute human toxicity is needed, but increasingly, researchers will strive to include effects on entire ecosystems, and long-term, multigenerational effects on fertility, reproductive quality, and hormonal functions. Any solvent that leads to environmental problems, that can be persistent, toxic, and bioaccumulative, or any combination of these three attributes, needs to be evaluated (Division, 1996). This

risk assessment criteria must take into consideration cost-benefit analysis, resource allocation, as well as toxicity and ecological impact.

The increasing burden of government regulations and restrictions is driving industry toward environmentally preferred technologies. Underpinning most, if not all, of these regulations are a subset of environmental and/or worker safety issues. Concerns about chemicals in the environment have focused major attention on the possible consequence for humans, animals, and whole ecosystems. However, basic knowledge and procedures for evaluating the potential impacts of chemicals, compound mixtures, or artificial concentrations of natural substances that have an adverse effect on human health and the environment is lacking. Such knowledge will be essential for developing products with adequate safeguards against unwanted side effects.

2.6.1 Measuring the Effects of Solvent Use

Reasonably good methods are available for testing the potential carcinogenic effects of chemicals on surrogate species for humans, particularly rodents. The correlation between these surrogates and humans is far from proven and is hotly debated. However, on the basis of experience and buttressed by significant testing, use of surrogate species seems to have been most helpful in reducing exposure to many suspect carcinogens.

However, there is a need for better tests to assess ecological damage potentially caused by single-compound chemicals, the byproducts of various waste treatment processes, and the degradation products of intentional processes or unintentional process emissions that find their way into the environment.

The last 50 years have seen the introduction of many new chemicals. Many have stood the test of time and shown their benefits to outweigh their environmental risks. For some, however, important adverse environmental effects emerged. The search to replace those without further environmental effects has become a strong driving force in industry, in the scientific community, and in the general public.

2.6.1.1 Scaling Effects of Solvent Use

Some of the surprise effects of chemicals have been due to a failure to predict the scale on which technologies might be used once they were shown to be beneficial when used on a limited scale. For example, DDT has side effects that have increased nonlinearly with the scale of application; as a result, the incremental benefits of a seemingly benign technology reversed when it was applied on a larger scale (the problem of MTBE was discussed earlier in this chapter). New technologies have to be constantly reevaluated in anticipation of scale effects.

New adverse environmental impacts will continue to be found, even with some of the substitutes. In some cases, biodegradable substitutes might be possible. The search for alternative pesticides or other products that have less adverse environmental impact has been rewarding to society and industry. Such efforts need to be continued and will be driven by the marketplace's responding to public and government interests.

A better understanding of global ecology is needed. Some persistent chemicals with a variety of uses do not bioaccumulate in birds or other higher species but instead

partition readily into water and do not bind well to soils, so they migrate through the ground and cause groundwater contamination. Examples are the triazine group of herbicides, dibromochloropropane (DBCP, a nematocide), and some industrial solvents.

The disposal of chlorinated solvents in landfills and their leakage from storage tanks have caused extremely expensive groundwater-contamination problems that have not yet been solved. Substitutes for chlorinated solvents are now widely used, and care in their disposal is required.

Substitutes for the CFCs that cause depletion of stratospheric ozone are being developed. Those which will be used in the near future (hydrochlorofluorocarbons, HCFCs) are of concern because a decomposition product, trifluoroacetic acid, might be very persistent and, under extreme conditions, have the potential to cause an undesirable environmental impact.

How do we determine what adverse environmental impacts the byproducts of new technologies—whatever they might be—can cause? And how do these environmental problems compare with those of the alternatives? Global transport of persistent chemicals is increasingly recognized as an issue that must be dealt with by all, or at least by a combination of, nations.

The potential of any chemical for environmental damage must be assessed before its commercialization, and our capability for doing so, should be expanded, although we recognize the possibility that the new chemical might replace another substance, natural or manmade, already in use that could be even more damaging. Those cases demonstrate the need for continuous review of costs and benefits, which might not be the same for all countries and communities.

2.6.2 Global Changes Due to Effects of Solvent Use

Much of the global effects of solvent use are felt in atmospheric change. Atmospheric change comprises many phenomena, namely climate change, acidic deposition, stratospheric ozone depletion, smog, increasing trend of suspended particulate matter, and hazardous air pollutants (HAPs). Among HAPs, a particular group of persistent organic pollutants (POPs), such as some organochlorine pesticides, has shown a variety of toxic effects, altering the biodiversity of many ecosystems. Because of their persistence in the environment, and of their long-range transport, the study of the global cycle of POPs is important in understanding how they can affect biodiversity (Finizio et al., 1998).

Numerous studies have been conducted to determine the effect of chemicals, in particular solvents, into the atmosphere. Information is learned from studies, but conclusions are often incomplete, due to the lack of a fully rigorous and universally applicable model. The observed reductions in stratospheric ozone since the late 1970s are likely to have affected the penetration of UV radiation into the troposphere. Ozone is reduced in most areas when the UV radiation increases, but the percentage reductions in ozone are significantly smaller than the percentage UV increases (Fuglestvedt et al., 1994).

This example demonstrates a fact regarding our understanding of chemical effects on the environment: they are incomplete and in some instances contain gaping holes. The same is true of terrestrial effects from solvent use.

2.6.2.1 Problem of VOCs

The complexity of the situation of problems of VOCs is included. Institutional and legal knowledge is needed to understand the continuing regulatory efforts in the United States and the world. Beyond this, mathematical programming models ranging from fairly simple deterministic linear programs to quite sophisticated stochastic models that have appeared in the literature dealing with these topics can be used to gain some insight into the problem.

A study was conducted in Albany, New York, to investigate whether volatile organic compounds (VOCs) were measurable in the blood and in the breathing-zone air of people exposed to gasoline fumes and automotive exhaust. In this study, organic vapor badges provided data on VOC exposure that correlated with blood assay results. Albany was selected as the site for this investigation because MTBE is used in only small (generally less than 5% by weight) concentrations in this area. As part of this study, participants' exposure to VOCs was determined via organic vapor badges and personal breathing-zone charcoal tube samples on the same day that their blood was collected for VOC level measurement. The researchers were able to determine how well the VOC levels from the organic vapor badges and charcoal tube samples correlated with VOC levels measured in the blood (Mannino et al., 1995).

For a better idea of the toxicity of VOCs, we can look more closely at some studies of TCE (Bogen et al., 1998). In vitro uptake of C-14–labeled trichloroethylene (TCE) from dilute (similar to 5-ppb) aqueous solutions into human surgical skirt was measured using accelerator mass spectrometry (AMS). The AMS data obtained positively correlate with (ρ approximate to 0) and vary significantly nonlinearly with (ρ = 0.0094) exposure duration. These data are inconsistent (ρ approximate to 0) with predictions made for TCE by a proposed EPA dermal exposure model, even when uncertainties in its recommended parameter values for TCE are considered but are consistent ($\rho = 0.17$) with a 1-compartment model for exposed skin-surface. This study illustrates the power of AMS to facilitate analyses of contaminant biodistribution and uptake kinetics at very low environmental concentrations. Further studies could correlate this with toxicity.

2.6.3 Risks Surrounding Solvent Use

2.6.3.1 Air Quality Issues

Principal air quality issues of local, national, and international concern are listed below in increasing order of difficulty based on the number of different types of pollutants and problems in quantification of the risks the pollutants pose (Cooper et al., 1997):

- Stratospheric ozone depletion—one relatively easily controllable class of trace gases—ozone depleting chemicals (ODCs), principally chloroflurocarbons (CFCs)—with relatively well quantified risks
- Criteria pollutants: six common pollutants—ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), lead (Pb), and particulate matter less than 10 microns (10 μm) in size—regulated since 1970 in the United States and presenting relatively well quantified risks

- Acid precipitation—two relatively easily controllable classes of trace gases—oxides of nitrogen (NO_x) and oxides of sulfur (SO_x) with relatively well quantified risks
- Global warming/climate change—a few difficult-to-control trace gases—principally carbon dioxide (CO_2), methane (CH_4), nitrous oxide (N_2O), and CFCs—with highly uncertain risks
- Toxics or HAPs (hazardous air pollutants)—hundreds of types of gaseous chemicals and particles with uncertain risks

The CAAA of 1990 identify hazardous air pollutants and require significant reductions in their release from major emissions sources. Relevant to the control of these substances, governmental agencies and organizations rely on several different cancer and noncancer endpoint benchmarks, standards gauging the adequacy of measures taken to protect the public. A comparison of EPA's Reference Dose and Reference Concentration data with the U.S. Agency for Toxic Substances and Disease Registry's Chronic Minimal Risk Level data shows agreement with health risk endpoint estimates for most chemicals. Discrepancies arise because of different uncertainty factors and differences in the selection and interpretation of studies used to assess health risks (Goldhaber and Chessin, 1997).

1.6.3.2 Risk Assessment

The National Research Council (NRC) published a report, "Science and Judgment in Risk Assessment," that critiqued the current approaches to characterizing human cancer risks from exposure to chemicals. One issue raised in the report relates to the use of default options for assessing of cancer risks. These general guidelines can be used for risk assessment when specific information about a chemical is absent. Research on 1,3-butadiene indicates that two default options may no longer be tenable: Humans are as sensitive as the most sensitive animal species; and the rate of metabolism is a function of body surface area rather than inherent species differences in metabolic capacity.

Butadiene, a major commodity chemical used in the production of synthetic rubber, is listed as one of 189 hazardous air pollutants under the 1990 Clean Air Act Amendments. Butadiene is a carcinogen in rats and mice, with mice being substantially more sensitive than rats. The extent to which butadiene poses risk of cancer to humans exposed to this chemical is uncertain. The data include in vitro studies on butadiene metabolism using tissues from humans, rats, and mice as well as experimental data and physiological model predictions for butadiene in blood and butadiene epoxides in blood, lung, and liver after exposure of rats and mice to inhaled butadiene (Bond et al., 1996).

The variability of hazardous air pollutants (HAPs) is an important factor in determining human exposure to such chemicals, and in designing HAP measurement programs. The factors that contribute to HAP variability in an urban area also affect their global impact. Temporal variation was the major contributor to HAP variability for 19 of the 39 frequently detected compounds (Spicer et al., 1996). In the future, more precise measurement tools will be available to determine HAPs. Open-path monitoring of the atmosphere using Fourier transform infrared spectrometry has recently become

a useful real-time in situ analytical technique. The EPA formulated Method TO-16, a protocol for infrared remote sensing of the hazardous air pollutants (HAPs) identified in EPA's Clean Air Act of 1990 (Chu et al., 1998).

2.6.3.3 Model Development

The development of new models for the prediction of chemical effects in the environment has improved. An Eulerian photochemical air quality model for the prediction of the atmospheric transport and chemical reactions of gas-phase toxic organic air pollutants has been published. The organic compounds were drawn from a list of 189 species selected for control as hazardous air pollutants in the Clean Air Act Amendments of 1990. The species considered include benzene, various alkylbenzenes, phenol, cresols, 1,3-butadiene, acrolein, formaldehyde, acetaldehyde, and perchloroethylene, among others. The finding that photochemical production can be a major contributor to the total concentrations of some toxic organic species implies that control programs for those species must consider more than just direct emissions (Harley and Cass, 1994). This further corroborates the present weakness in many atmospheric models.

2.6.4 Global Implications of Regulatory Change

International cooperation is needed to accomplish regulation of solvent usage. The multilateral consensus that led to the signing and ratification of the Montreal Protocol in 1987 and its London (1990) and Copenhagen (1992) Amendments resulted in the near-complete phase-out of chlorofluorocarbon (CFC) use in industrialized countries by the end of 1995. To meet their economic development needs, the treaty permits developing countries to continue producing and consuming CFCs for an additional 15 years, until 2010. This delay in eliminating ozone-depleting substances slows the recovery of the ozone layer, and has generated a global black market in CFCs. The estimated cost of replacing CFCs with hydrofluorocarbon (HFC) and hydrochlorofluorocarbon (HCFC) technological options is substantially greater than available financial resources, and this cost rises as CFC replacement is postponed. Additionally, manufacturing and maintenance problems with the predominant HFC refrigeration alternative make it less suitable for developing-country markets. Available technologies are environmentally and economically sounder alternatives than HFC/HCFC substitutes for both developed and developing countries, but the failure of industrial countries to agree on a common option is slowing the transition by developing countries to a CFC-free economy (Papasavva and Moomaw, 1997).

Depletion of the ozone layer has been observed on a global scale. Ozone depletion increases the biologically harmful solar ultraviolet radiation reaching the surface of the earth, which leads to a variety of adverse effects, including an increase in the incidence of skin cancer. The 1985 Vienna Convention provided the framework for international restrictions on the production of ozone-depleting substances. The consequences of such restrictions have not yet been assessed in terms of effects avoided, although the ozone hole appears to be closing (Zurer, 1999). Slaper presented a method of estimating future excess skin cancer risks to compare effects of no restrictions with two restrictive scenarios specified under the Vienna Convention: the Mon-

treal Protocol, and the much stricter Copenhagen Amendments (Slaper et al., 1996). The no-restrictions and Montreal Protocol scenarios produce a runaway increase in skin cancer incidence, up to a quadrupling and doubling, respectively, by the year 2100. The Copenhagen Amendments scenario leads to an ozone minimum around the year 2000, and a peak increase in incidence of skin cancer of almost 10% occurring 60 years later. These results demonstrate the importance of the international measures agreed upon under the Vienna Convention.

An integrated analysis of future halocarbon emissions and their environmental impact shows that strict global compliance is required if the Montreal Protocol is to accomplish the goal of eliminating the lower stratospheric ozone hole. This analysis showed that demographic, economic, and regulatory processes controlling future production were linked explicitly to the technological factors translating production into emissions and the environmental processes transforming emissions into environmental impacts. This research suggests that if a small percentage of nations continue to expand production at modest rates, the ozone hole will not be eliminated. In addition, high growth rate assumptions for halocarbon production by noncompliance nations will result in significantly increased ozone depletion. This research also shows that the continued use of small amounts of ozone-depleting substances for essential uses and the failure to adequately replace all ozone-depleting substances can eliminate the possibility of returning the atmosphere to pre–ozone hole conditions (Holmes and Ellis, 1996).

2.6.5 Industrial and Domestic Sources of Risk

The global risks of solvent use have sources that are transnational and are not confined to academic institutions, companies, or individuals. Based on the flammability and combustibility classifications, regulators then specify or provide guidance on the appropriate methods to transport, handle, package, store, dispense, and protect these materials. Exceptions to these classifications include products such as alcoholic beverages and medicines stored in relatively small containers, which have historically presented a limited fire hazard. Many companies are now reformulating their consumer liquid products to meet customer and regulatory demands for low volatile organic compounds (VOCs). Low VOC formulations often do not inherently result in the total elimination of flammable or combustible liquid solvents.

2.6.5.1 Construction Industry

The substitution of more benign solvents in many formulations will have global ramifications. For example, water-reducible coatings are products where the solvent system used to disperse and suspend solids is primarily water. The remainder of the solvent system may contain liquids that are classified as flammable or combustible liquids. Inherent limitations in these systems relate to product viscosity, accuracy in predicting overall fire hazard, ability to assess physical changes of state when a product is tested, and test method reliability and ease of use (Scheffey and Tabar, 1996).

Although there have been several studies examining emissions of criteria pollutants from some human activities (for example, in-use alternative fuel vehicles (AFVs)), little is known about overall total emissions of hazardous air pollutants (HAPs) (Wine-

brake and Deaton, 1999), VOCs (Wolkoff, 1999), and ODCs (Cooper et al., 1997) from these activities. Consideration of these sources can immensely affect the evaluation of green solvents, when used here.

Many industrial activities, such as construction, use solvents. For instance, the primary emissions of VOCs from building products influence the perceived indoor air quality during the initial decay period. However, secondary emissions will continue thereafter (chemical or physical degradation, for example, oxidation, hydrolysis, mechanical wear, and maintenance), in addition to sorption processes. Methods to distinguish between the two types of emissions are required. Also, the influence of climate parameters on the emission rates is necessary to know for proper testing. Future product development and selection strategies of new building products should consider the secondary emissions, in addition to the contribution from the use of auxiliary agents for cleaning, maintenance, and other potential impacts, either physical or chemical in nature. More work needs to be done on the possible impact of VOCs on health and comfort in the indoor environment (Wolkoff, 1999).

Another example is unpleasant odor from wall, ceiling, and floor coverings made of composite cork. Emissions of phenol and furfural were found to be high, particularly those from cork parquet. The ranges of emission factors were found to be similar for some solvents such as cyclohexanone or toluene, which are constituents of varnishes used to protect cork surfaces. The emission of furfural may result from chemical reactions in the cork during the production process or may be caused by additives such as binders (Horn et al., 1998).

The 1990 CAAA required Publicly Owned Treatment Works (POTWs) to inventory and control their hazardous air pollutant (HAP) emissions, primarily from the aeration tanks. The spatial characteristics of hazardous air pollutants in the form of VOCs from the aeration units of POTWs have been investigated by systematic monitoring and mathematical modeling (Zhu et al., 1998). Using a simple model, we can accurately estimate air emissions and the simulation results are useful to support an emission control analysis.

The asphalt and road construction activities present some issues. The EPA has developed emission factors for estimating the emissions of filterable particulate, total organic compounds, and carbon monoxide from asphalt blowing operations. Owens Corning has taken extensive data in various manufacturing facilities and an asphalt pilot plant to provide more information on air emissions from these operations. The results of that work clearly show that the current emission factors for asphalt processed by air blowing are deficient in that they omit significant emissions of SO_x and HCl, overestimate particulate and CO emissions, and potentially underestimate both VOC and NO_x emissions. In fact, SO_x is the major air emission contributed by the fumes from the asphalt blowing process when those fumes are incinerated. With the exception of HCl, the hazardous air pollutants encountered in the asphalt blowing process are minimal (Trumbore, 1998).

2.6.5.2 Domestic

Emissions of organic fragmentation products, so-called secondary emission products and reactive species from wood-based furniture coatings have been studied (Salthammer et al., 1999). Aliphatic aldehydes and some photoinitiator fragments have a strong

odor, while acrylates and diisocyanates cause irritation of skin, eyes, and upper airways. Terpenes and reactive solvents like styrene undergo indoor chemistry in the presence of ozone, nitrogen oxides, or hydroxyl radicals. Secondary emission products and reactive species can achieve significant indoor concentrations. On the other hand, it has been reported that even small quantities can cause health effects.

Occupational and toxicological studies have demonstrated adverse health effects from exposure to toxic air contaminants. Data on outdoor levels of toxic air contaminants have not been available for most communities in the United States, making it difficult to assess the potential for adverse human health effects from general population exposures. Models and new experiments provide a great amount of new data (Woodruff et al., 1998).

2.6.6 Ozone Depletion and Possible Solvent Replacements

2.6.6.1 Chemistry

The abundance of ozone in the stratosphere is, in part, determined by photochemical production of ozone and the abundance of reactive trace chemical species (HO_x, NO_x, ClO_x, BrO_x) that catalyze ozone removal processes. Significant stratospheric ozone losses, first detected during spring over Antarctica, now extend to all seasons and all latitudes pole-ward of 30 degrees in both hemispheres. Observations have demonstrated that gas phase and heterogeneous chlorine and bromine chemistries play major roles in the chemical destruction of ozone in both the midlatitude and polar lower stratospheres. Agricultural, industrial, and domestic activities can influence the abundance of these ozone-destroying catalysts and therefore can affect the levels of ozone in the stratosphere. Observations from monitoring networks worldwide have demonstrated either slowdowns or reversals in the growth rates of most of the major halocarbon species (CFCs, long-lived chlorinated solvents, halons), whereas the HCFCs, which are interim replacement chemicals for CFCs under the Montreal Protocol, are still increasing rapidly and the HFCs, the long-term replacements for CFCs, have now been found in the atmosphere for the first time. At present the Montreal Protocol appears to be working in controlling ozone-depleting sub stances (ODSs) in the background atmosphere. However, there may still be some problems ahead for stratospheric ozone, associated with the economic costs of replacement of some ODSs, the growth of the use of ODSs in the developing world and the uncertain effect of long-term climate change on ozone depletion (Fraser, 1997).

2.6.6.2 Effects Due to Ozone Depletion

Measured total column ozone has fallen between about 1970 and 1994. Ultraviolet irradiation increases at the surface of the earth due to ozone depletion should peak at about 15% in midlatitudes. The incidence of harmful health effects of UV radiation can be expected to rise, eventually, at midlatitudes. Public health action is still necessary to reduce sun exposure, increase protection against the sun, and develop clear policies on the action that should be taken on early detection and treatment of skin cancers (Armstrong, 1997).

Reductions in stratospheric ozone (O_3) cause increased penetration of ultraviolet-B (UV-B) radiation to the troposphere. This increases the chemical activity in the lower atmosphere (the troposphere). Tropospheric ozone levels are sensitive to local concentrations of nitrogen oxides (NO_x) and hydrocarbons. Model studies suggest that additional UV-B radiation reduces tropospheric ozone in clean environments (low NO_x), and increases tropospheric ozone in polluted areas (high NO_x). Assuming other factors remain constant, additional UV-B will increase the rate at which primary pollutants are removed from the troposphere. Increased UV-B is expected to increase the concentration of hydroxyl radicals (OH) and result in faster removal of pollutants such as carbon monoxide (CO), methane (CH_4), nonmethane hydrocarbons (NMHCs), sulfur and nitrogen oxides, hydrochlorofluorocarbons (HCFCs), and hydrofluorocarbons (HFCs). Concentrations of peroxy radicals (both inorganic and organic) are expected to increase, leading to higher atmospheric levels of hydrogen peroxide (H_2O_2) and organic peroxides. The effects of UV-B increases on tropospheric O_3, OH, methane, CO, and possibly other tropospheric constituents will be difficult to detect because the concentrations of these species are also influenced by many other variable factors (e.g., emissions). Trifluoroacetic acid (TFA, CF_3COOH) is produced in the atmosphere by the degradation of HCFC-123 (CF_3CHCl_2), HCFC-124 (CF_3CHFCl), and HFC-134a (CF_3CH_2F), which are used as substitutes for ozone-depleting substances. The atmospheric oxidation mechanisms of these replacement compounds are well established. Reported measurements of TFA in rain, rivers, lakes, and oceans show it to be a ubiquitous component of the hydrosphere, present at levels much higher than can be explained by reported sources. The levels of TFA produced by the atmospheric degradation of HFCs and HCFCs emitted up to the year 2020 are estimated to be orders of magnitude below those of concern, and to make only a minor contribution to the current environmental burden of TFA. No significant effects on humans or the environment have been identified from TFA produced by atmospheric degradation of HCFCs and HFCs (Tang et al., 1998). On the basis of the combined results of the laboratory tests and a previously reported semi-field study, a TFA concentration of 0.10 mg/L is safe for the aquatic ecosystem (Berends et al., 1999).

The health risks associated with ozone depletion will principally be those due to increased ultraviolet-B (UV-B) radiation in the environment, that is, increased damage to the eyes, the immune system, and the skin. Some new risks may also be introduced with the increased use of alternatives to the ozone-depleting substances (ODSs). However, the data are insufficient to develop similar estimates for effects such as immunosuppression and the toxicity of alternatives.

Suppression of local (at the site of UV exposure) and systemic (at a distant, unexposed site) immune responses to a variety of antigens has been demonstrated in both humans and animals exposed to UV-B. There is reasonably good evidence that such immunosuppression plays a role in human carcinogenesis; however, the implications of such immunosuppression for human infectious diseases are still unknown.

2.6.6.3 Toxicology of Some Green Solvents

Testing of a number of the chlorofluorocarbon (CFC) alternatives indicates that most of these chemicals have low acute toxicity, and low to moderate chronic toxicity. Some chemicals, originally proposed as alternatives, have been dropped from consid-

eration. This is because these tests raised concerns about toxicity and/or manufacturing difficulties. Recent quantitative risk estimates have been developed for cataracts, melanoma, and all skin cancers combined (Longstreth et al., 1998).

CFC replacements with much lower or absent ozone depleting potential are being developed. The toxicology of these compounds that represent chlorofluorohydrocarbons (HCFCs) or fluorohydrocarbons (HFCs) has been intensively studied. All compounds investigated (1,1-dichloro-1-fluoroethane (HCFC-141b), 1,1,1,2-tetrafluoroethane (HFC-134a), pentafluoroethane (HFC-125), 1 chloroo-1,2,2,2-tetrafluoroethane (HCFC-124), and 1,1-dichlor-2,2,2-trifluoroethane (HCFC-123)) show only a low potential for skin and eye irritation. Chronic adverse effects on the liver (HCFC-123) and the testes (HCFC-141b and HCFC-134a), including tumor formation, were observed in long-term inhalation studies in rodents using very high concentrations of these CFC replacements (Dekant, 1996).

All CFC replacements are, to varying extents, biotransformed in the organism, mainly by cytochrome P450-catalyzed oxidation of C-H bonds. The formed acyl halides are hydrolyzed to give excretable carboxylic acids; halogenated aldehydes that are formed may be further oxidized to halogenated carboxylic acids or reduced to halogenated alcohols, which are excretory metabolites in urine from rodents exposed experimentally to CFC replacements. The chronic toxicity of the CFC replacements studied is unlikely to be of relevance for humans exposed during production and application of CFC replacements (Dekant, 1996).

2.6.7 Risk Assessment and Science Policy

If we continue with an analysis of the effects of air pollutants, as representative of the effects of solvents, several issues arise. Hazardous air pollutants are regulated under Title III of the 1990 Clean Air Act Amendments. The Amendments replace the risk-based approach mandated in the 1977 Amendments with a prescriptive technology-based approach requiring that maximum achievable control technology (MACT) is applied to all major industrial sources of 189 hazardous air pollutants. The change reflects political, rather than scientific consensus, that the public health benefits justify the costs. Particular emphasis is given to examining the interrelationships among facts (science), judgments (science policy), and policy (values) in the context of the risk assessment paradigm. In the article by Sexton (Sexton, 1995), it is argued that a balanced research program is needed to obtain the facts about hazardous air pollutants, including research to meet statutory requirements, to reduce uncertainties in risk assessment, and to address strategic issues. Such an approach is also applicable to other global effects from solvents.

Six atmospheric "issues" are currently being assessed by scientists, modelers, and policy analysts:

- Climate change;
- Stratospheric ozone depletion (including UV-B radiation increases);
- Acidic deposition; smog (for example, ground-level ozone episodes);
- Suspended particulate matter; and
- Hazardous air pollutants.

Munn provides a brief historical review of how these particular issues came to be important (Munn and Maarouf, 1997). Historically, each air issue has been treated as

a separate problem—from root causes, through the atmospheric processes involved, through the impacts on the biosphere and society, and finally to the design of policies to slow down or eliminate unwanted impacts. In recent years, however, recognition has been growing that the six air issues are interrelated through complex feedback, lags, and synergism. The lesson to be learned by both scientists and policy analysts is therefore that strategies for dealing with a particular issue may not be optimal for the whole.

2.6.7.1 Environmental Sustainability

In order to successfully resolve the atmospheric issues (a policy question) requires communication of the relevant science to nonscientists in plain language. Nonscientists need to be part of the development of the structure of the communications vehicle. This question of communication is crucial when decisions are being made to implement green chemistry alternatives. Sustainability is a balance among ecological, economic, and social needs. Although the environment is the basis of all life, humankind has created society and has defined how that society will function (the economy). The means by which the balance is maintained is a direct function of how well the lines of communication are developed. The challenge is to maintain the tensions in such a way that all three benefit and grow. This measure of "sustainability" must respond to individual and collective actions, which improve or degrade the environment. Young presents such a framework for a "sustainability index" and outlines the next steps that need to be taken (Young, 1997). The framework starts from the premise that ecosystem, economy, and society are equal parts of "sustainability." Ecosystem indices are representative measures of the state of the environment while economic indices are representative measures of the state of the economy. Social indices in some way have to measure the state of society. A successful sustainability index, will be to ensure that the important aspects of the ecosystem, the economy and society, are included. The overall index must be relatively stable but must be responsive to changes.

An alternate compliance strategy (ACS) is developed which incorporates pollution prevention and flexibility to replace traditional end-of-pipe control strategy regulation. The ACS takes into consideration the intent of the 1990 CAAA to incorporate pollution prevention into regulations and provides a viable mechanism for implementation. This proposed new compliance strategy is developed after studying the CAAA regulations, related compliance issues, and pollution prevention literature. A change in regulation is considered reasonable only if it forces the same emission reductions, reduces risk a comparable amount, and is acceptable to the public, the regulators, and the regulated industry. One example application is summarized from an ethylene oxide-ethylene glycol plant (Brothers, 1997). The example demonstrates that the ACS reduces hazardous air pollution (HAP) emissions. Three evaluation methods are developed and applied to further demonstrate the acceptability of the ACS:

- Qualitative evaluation matrix;
- Total cost assessment; and
- Risk reduction measurement model.

McClellan provides a brief overview of the report "Science and Judgment in Risk Assessment," prepared by a committee of the National Research Council/National

Academy of Science in response to an EPA request mandated by the CAAA (McClellan, 1994). The report offers specific recommendations that address the role of default options, data needs, methods and models, uncertainty, variability, and the aggregation of data.

In some instances, the specific data on a given chemical or pollutant source will replace conservative default options used in earlier assignments. The report includes two authored appendices that address issues related to the use of default options and their replacement by specific scientific information. One appendix (by Finkel) advocates a principle of "plausible conservatism" for choosing and altering default options and in making cancer risk estimates. The second appendix (by McClellan and North) advocates the full use of scientific information in the risk assessment process.

2.6.7 Lifetime of Solvents in the Environment

Current regulatory policies for HAPs target the sources of direct emissions. Over 40% of the HAPs being regulated under Title Ill of the CAAA have atmospheric lifetimes of less than one day. The transformation products of these HAPs with low atmospheric persistence are important for assessing risks to human health, especially for cases where the transformation products are more toxic than the HAP itself. Formaldehyde and acetaldehyde are produced by almost every hydrocarbon photo-oxidation reaction (Kao, 1994).

Emissions of most, but not all, ozone-depleting chemicals controlled by the Montreal Protocol are continuing to decrease (Zurer, 1999). However, there are exceptions. Emissions of a fire-fighting halon still being produced in developing countries (CBrClF, known as H-1211) are holding steady and may even be growing. Recovery of the damaged stratospheric ozone layer—which continues to undergo massive destruction over Antarctica each spring and less noticeable depletion worldwide year-round—will come only if emissions continue to decline.

Despite the growth of HCFCs, the National Oceanic & Atmospheric Administration (NOAA) researchers' data show that ozone-depleting chemicals in the atmosphere have declined overall about 3% since 1994. But that decrease is due almost entirely to a dramatic drop in the amount of methylchloroform, which was used as a cleaning solvent. Natural oxidation processes in the atmosphere remove methylchloroform so efficiently that its atmospheric concentration has been falling rapidly since production stopped.

As a first step, it is important to predict the lifetime of all chemicals introduced into the environment. As an example, using recent kinetic data, two-dimensional (2-D) chemical-transport modeling of the atmospheric lifetimes of dimethyl ether and fluorinated ethers CH_3OCF_3 (E143a), CHF_2OCHF_2 (E134), and CHF_2OCF_3 (E125) shows that E134 and E125 have substantially longer lifetimes than previously estimated. Dimethyl ether has a short atmospheric lifetime of 5.1 days and a relatively insignificant radiation forcing, leading to a relatively low global warming potential. Increasing fluorination is accompanied by slower rates of reaction with hydroxyl radical and ultimately longer lifetimes. E143a, E134, and E125 were found to have lifetimes of 5.7, 29.7, and 165 years, respectively (Good et al., 1998).

Kanakidou attempted to use a global three-dimensional model of the troposphere to study the degradation chemistry of the alternative chlorofluoro- and fluorohydrocar-

bons HCFC-22, HCFC-123, HCFC-124, HFC-134a, HCFC-141b, and HCFC-142b and the main removal processes from the troposphere of these halogenated hydrocarbons and their oxidation products (Kanakidou et al., 1995). Lifetimes of the parent hydrochlorofluorocarbons (HCFCs) and HFC-134a range from 1.3 to 20 years, with oxidation by the OH radical being the dominant removal process. Using the emission scenarios, they calculated that HCFC-22 volume mixing ratios will reach a maximum of 190 parts per trillion by volume (pptv) around the year 2005, the mixing ratios of all other HCFCs remaining below 100 pptv. Based on recent kinetic information, it is calculated that none of the relatively stable intermediate oxidation products such as COF_2, COFCl, CF_3COF, and CF_3COCl will substantially build up in the atmosphere, the global abundance of these compounds being generally less than 1% those of the parent compounds. Organic nitrates from all HCFCs studied will not reach substantial concentrations and will not contribute to chlorine delivery to the stratosphere.

2.6.8.1 Evaluating Uncertainty by Means of Fuzzy Logic

The application of fuzzy logic to the risk assessment of the use of solvents in order to evaluate the uncertainties affecting both individual and societal risk estimates is an area with relevance to the present considerations (Bonvicini et al., 1998). In evaluating uncertainty by fuzzy logic, fuzzy numbers describe the uncertain input parameters and calculations are performed using fuzzy arithmetic; the outputs will also be fuzzy numbers. The results of these considerations' work are an attempt to justify some of the questions the use of fuzzy in the field of risk analysis stimulates.

In so far as the input parameters in a risk analysis try to describe reality, they are not known with certainty, and in so far they are known with certainty, that is, they can be expressed by a single-point value, they do not refer to reality. This reminds us that risk considerations on uncertainty evaluation becomes a key variable that cannot be neglected. The use of fuzzy logic to evaluate solvents is innovative. This section will only develop these concepts briefly, allowing more rigorous texts to explain it in detail (Rouvray, 1997).

2.6.8.2 Risk Models

In order to calculate the individual and societal risks that are relevant to solvent selection, mathematical models must be used. In a fuzzy logic approach, the characterization of the effects of solvent use is strictly connected with the fuzzy representation of the input variables, that are based on individual risk and societal risk (Bonvicini et al., 1998).

2.6.8.3 Fuzzy Logic

It is also worth noting that the fuzzy logic methodology allows, like the Monte Carlo method, the identification, from all uncertain variables, of those which most greatly influence the output, and the rapid evaluation of the effect that changing the values of these variables has on the final result. The importance of this flexibility makes the proposed technique useful in the overall evaluation of environmentally benign sol-

vents, since decision makers can quickly test the suitability of alternative choices in the adoption of preventive and protective measures (Tanaka, 1991).

2.7 Challenge Offered to the Chemical Community

2.7.1 Environmentally Friendly Chemicals and Processes

Regulatory pressures and their impact on the cost of production are driving forces for the development and deployment of inherently less polluting processes. From the standpoint of the number of options available and cost, it is desirable to deal with environmental issues early in the process life cycle rather than during plant operation. While the near-term approach is regulatory compliance, in the longer term, environmental considerations, like safety, will become an integral part of process design. Continued development and application of reaction engineering tools will accelerate the development of both environmentally friendly processes and end-of-pipe technologies (Pereira, 1999). Making chemical manufacturing more environmentally benign by design must now become an integral part of the product development process (Trost, 1998).

The conventional view is that thinking preceded feeling and that emotion was impossible without cognitive awareness. However, the research has shown that crude reflex-type emotions can, and do, precede recognition. These results do not apply to complex emotions, such as shame, guilt, or embarrassment, but only to the snap decision to like or dislike or to advance or retreat (Concar, 1996). As the chemical industry strives to restore its image and build credibility in the eyes of the public, companies have come to realize that they can no longer afford to surrender responsibility for their products at the close of a sales transaction. As a result, chemical makers are taking on a broader role in the marketplace as responsible stewards of their products. Although considerable advances have been made, there is still a great need to improve the ability to predict the environmental consequences of a new chemical on a variety of scales before the great expenditure of getting it into the marketplace is undertaken. Even then, unforeseen environmental questions may arise after product is introduced. Industry needs to have greater assurance that its often expensive product development and commercialization will be successful and not quickly overturned by unforeseen human health or environmental problems. Thus, both to encourage the development of desirable products and to provide adequate safeguards against potential environmental liabilities after products are introduced into the marketplace, sound procedures for evaluating potential impacts of products on human health and the environment are essential.

2.7.2 Steps in a Response

Reasonably good testing methods exist for acute toxicity. The tests use surrogate animals, and the correlation to humans is the weakest element. The quality of predictive modeling for acute effects based on SAR (Structure Activity Relationships), is only modest. For chronic effects, testing with surrogates for humans is modestly good, particularly for cancer. Tests for chronic toxicity in animals are only fair and for

cumulative effects on ecosystems are very weak. Predictive modeling for chronic effects in general is poor. Modeling to predict persistence is fair and to predict bioaccumulation potential is moderately good, at least for many common classes of chemicals (e.g., cholorinated organics.)

For both the byproducts of various waste-treatment processes and the degradation products of intended products or processes that find their way into the environment, there will be the same need to assess potential ecological damage as there is to assess damage caused by specific intentional chemicals. "Daughter" (byproduct and degradation) chemicals pose additional complications in that their chemical formula and structure might not be known. Small or laboratory-scale "miniecosystems" have been found highly useful for examining a wide range of conditions to sort out such variables so that the major biological processes affected by new chemicals on ecosystems can be better understood.

Ultimately, because of the sheer diversity and complexity of potential chemical commercial products and their "daughter" products, modeling might prove to be important. When sufficient specific industrial chemicals have been assessed for their potential for ecological damage, scientists should be able to estimate this property for postulated chemicals. Similar modeling of treatment facilities and degradation processes should make it possible to estimate the potential effects of undetermined byproduct and degradation chemicals. This would help identify the facilities or chemicals that require more careful sampling and analysis and the need for containment or substitution.

Unexpected synergy between something already in the environment, whether anthropogenic or not and whether global or local, and a new chemical that was tested and shown safe by existing methods will remain a problem. In the long run, a better understanding of the basic biochemical process in the environment will be the strongest means to decide where to look and what to look for.

The United States chemical industry has raised the standard of living in America and has contributed enormously to the country's economic vitality in the twentieth century, but this success has come at a price to the environment. Plentiful and cheap, petroleum has been the dominant feedstock for chemical manufacturing since World War II. The development of biotechnology methods for chemical manufacture is quietly taking place. These emerging technologies including the conversion of cellulose to glucose, the use of microbes as biocatalysts, metabolic pathway engineering, aromatic chemical pathways, bioprocessing, and the use of catalytic antibodies can all contribute to lessening the overall impact that solvents have on our environment (Webster et al., 1996).

At least for the present, it seems impractical to hope that we will be able to identify, empirically, all the environmental impacts that should be evaluated. Increasingly, researchers are working on collections of cells, micro-organisms, and entire mini-ecosystems, in which a broad range of subjects and surrogates are combined with mathematical models in an attempt to develop a more-accurate and holistic prediction or measurement of the effect of a chemical on an ecosystem.

2.7.3 Broad-based Support for Pollution Prevention

For a final time, let us return to the idea of pollution prevention. Industrial ecology can be considered as the aggregation of several environmental trends, including industrial

metabolism, design for the environment, life-cycle analysis, green chemistry, pollution prevention, environmentally conscious manufacturing, and sustainable development. Anastas and Breen reviewed the Design for the Environment and Green Chemistry Programs of the EPA Office of Pollution Prevention and Toxics (Anastas and Breen, 1997).

Since pollution prevention first entered the environmental lexicon in the 1980s, it has become a touchstone of U.S. environmental policy. To succeed, pollution prevention programs need sustained top management support and defined links to the company's core business activities. Equally important, the values represented in the program must fit with the academic institution, company, or individual's existing values. For example, syntheses that minimize wastes are environmentally friendly and may provide quality improvements and cost and energy savings. Environmental consciousness should be incorporated early into chemical research (Lunt and Bowen, 1996).

Benign chemistry seeks to develop and institutionalize alternative chemistries for pollution prevention. Significant challenges are available for chemists to design new products and processes that are less polluting (Anastas and Farris, 1994).

Every successful pollution prevention program has three basic components: strategic direction, infrastructure, and implementation. An iterative and evolutionary approach to pollution prevention can generally be categorized into three stages of development:

- Incremental improvement through relatively straightforward fixes of existing systems (the "low-hanging fruit" that brings many P2 programs impressive early gains);
- Redesign of established systems for greater overall efficiency;
- Rethinking of the total production process, looking for opportunities "outside the box" of accepted processes and materials.

Commitment to pollution prevention involves more than providing vision. It requires active leadership and meaningful involvement in defining, instilling, and sustaining values. When organizations rank and select pollution prevention projects, they almost always base decisions on measurements of cost or savings. Conventional accounting systems do not capture all costs. Largely through a lack of sophistication and attention during the early days of the chemical industry, our chemical technologies have lead to a host of environmental difficulties (Hill, 1996).

2.7.4 Business Sense

The traditional view in management circles about the relationship between the environment and business can best be summed up as pollution pays, pollution prevention doesn't. Notwithstanding the recent proliferation of literature on the benefits of green management, many managers continue to see environmentally sound strategies as detrimental to the principal goals of profitability, maintaining markets, controlling costs and efficient production. Together two incentives (government regulation and profit from environmentally sound strategies) serve to reverse the traditional vision about the incompatibility between good business and the environment (Gallarotti, 1995).

Prosperity without pollution has become the fundamental environmental theme. Support for the new approach—the new ethic—must be broad based and includes

environmentalists, industrialists, law-makers, academicians, government regulators and policy-makers, and general public. The roles and contributions of the chemical engineer, the synthetic organic and inorganic chemist, and the process analytical chemist will be integral to the full realization of the new vision (Breen and Dellarco, 1992).

2.8 Solvent Supply and Demand

December 31, 1995 was the last day of production for all ozone-depleting solvents in the United States (although some production for essential uses still occurred). While supplies of TCA or CFC-113 are low, the nonozone-depleting halogenated solvents such as TCE and PERC are readily available. However these, too, are facing regulatory actions, so they are becoming less available. A growing cadre of scientists is finding ways to reduce pollution, not by changing existing products, but by inventing cleaner ways to make them.

In addition to the availability issue, short-term price pressure on all regulated solvents is being felt in the form of taxes. Market forces have historically created prices inflated in excess of the newly taxed price. As additional solvents come under increased regulatory scrutiny, we may see the hazard excise tax used again, as it has proved successful in speeding the move away from ozone-depleting solvents.

Process chemistry, the practice of scaling up chemical production from grams and kilograms to thousands of gallons, while always of vital importance, has lately become a highly visible enterprise. This essential link between discovery research and commercial production has begun to involve institutions that make it easier for practitioners to meet, to publish, and to exchange ideas and experiences. As the field of process chemistry becomes increasingly visible in coming years, chemists in all fields of research and development will see advances in transforming long, linear discovery routes into short, convergent processes. Others will replace such solvents as CH_2Cl_2 and benzene with toluene or isopropyl alcohol, while toxic and costly tellurium and selenium will be replaced by sulfur. Instrumentation and combinatorial methods will be improved (Stinson, 1999).

2.8.1 Corporate Image and Liability

Environmental concerns are very important. Some groups promote the purchase and use of "green products." Other groups act as watchdogs, calling public attention to manufacturers and corporations they perceive to be lagging in environmental responsibility. It is not easy on anyone using hazardous solvents, especially if they are released into the environment and can be linked to holes in the ozone layer or to ecosystem disturbances.

Major activities or approaches that fall into the category of pollution prevention include source reduction and in-process recycling, energy conservation, and water conservation. Source reduction involves making changes to the product or process so as to avoid the generation waste. Process changes may include such activities as input material changes, technology changes, or improved operating practices. All these activities have proven to be highly successful ways to eliminate solvent waste generation

at the source. Improvements made at the source may also be effective in reducing waste generation elsewhere in the system.

New manufacturing software could give product designers instant information on how to avoid pollution. Called the Expert Process Advisory System (EPAS), the software's aim is to instantaneously present designers with information about the environmental ramifications of their design options (Betts, 1998).

2.8.2 Chemist's Liability

New concepts in "citizens' right-to-know" have significantly changed environmental management. Congress required the EPA to give information concerning chemicals in the community directly to the public, hoping that the availability of the information would cause change. This was particularly relevant to the releases and transfers of toxics. This program, together with additional legislation that builds upon it, will provide significant new opportunities and challenges to the chemist (Newburg-Rinn, 1992).

This chapter provided a basic understanding of the chemical, toxicological, and ecological factors involved when the solvents used in chemistry act on natural systems. It does not deal with the direct effects on humans and human health since this is another topic requiring full and detailed consideration. A chemical and ecotoxicological approach shows that the nature and effects of pollutants are considered from their sources and chemical properties, through dynamics in the environment resulting in toxic and other detrimental effects on organisms and ecosystems (Connell and Miller, 1984).

3

Solvation and Solvent Phenomena

3.1 Introduction

The role of solvents in chemical reactions has been well documented. It may be characterized as a carrier for another substance, as a medium for conducting a chemical reaction, or as a means of extracting or separating other substances. Whatever the precise definition used, solvents are a ubiquitous feature of modern chemical research, industry and everyday life.

A change of solvents or the use of different solvating media entirely can alter the rate of the chemical process, can shift the product mixture, and can significantly change the economics of the chemical process. The critical role that solvents play in chemistry (intentionally and inadvertently) is undisputed. An initial understanding of the basic chemistry involved is necessary.

3.2 Physical Properties of Solvents

The physical properties of solvents greatly influence the choice of solvent for a particular application. The solvent should be liquid under the temperature and pressure conditions at which it is employed. Its thermodynamic properties, such as the density and vapor pressure, temperature and pressure coefficients, as well as the heat capacity and surface tension, and transport properties, such as viscosity, diffusion coefficient, and thermal conductivity, also need to be considered. Electrical, optical, and magnetic properties, such as the dipole moment, dielectric constant, refractive index, magnetic susceptibility, and electrical conductance are relevant, too. Furthermore, molecular

characteristics, such as the size, surface area, and volume, as well as orientational relaxational times, have appreciable bearing on the applicability of a solvent or on the interpretation of solvent effects. These properties will be briefly summarized; a full development can be found in the book by Marcus (Marcus, 1998c).

For the majority of the solvents listed in this book as green solvents, many of the properties have been listed and annotated in numerous reference texts, as for example Riddick et al. (1986) and Ash and Ash (1996). The use of these references to provide necessary data for determination of the appropriateness of these solvents will help tremendously in solvent selection.

3.2.1 Physical Characteristics of Solvents

A fundamental guide to understanding the manner in which solvents influence chemical reactions is sketched out in table 3.1 (Marcus, 1998a).

3.2.2 General Comments

In a solution of a solute in a solvent there can exist noncovalent intermolecular interactions of solvent–solvent, solvent–solute, and solute–solute pairs. The noncovalent attractive forces are of three types, namely, electrostatic, induction, and dispersion forces. We speak of forces, but physical theories make use of intermolecular energies (Connors, 1990).

Table 3.1 can be used to classify the solvents. These properties can lead to understanding of various physical phenomenon (Chiou and Kile, 1994). They can be used in selecting potential solvent alternatives. This is carried out, for example, through a group contribution molecular design of solvents (MOLDES) approach in molecular modeling (Pretel et al., 1994).

Table 3.1. Physical characteristics of solvents.

Liquid range of solvents	Under ambient conditions solvents are liquid between their freezing point and their normal boiling point.
Equation of state	The mutual dependence of the pressure, volume, and temperature of a substance is described by its equation of state.
Vaporization properties of solvents	The vapor pressure, p, of a solvent at 25°C is an important quantity and varies considerably among common solvents, some being very volatile (*n*-pentane and diethyl ether) whereas others are quite nonvolatile (*n*-hexadecane and dibutyl phthalate).
Heat capacity of solvents	The measure of the energy input required for raising the temperature of a mole of solvent by a unit is the molar heat capacity (at constant pressure), C_p.
Molecular sizes of solvents	The intrinsic volume of a mole of the solvent molecules as they are in the liquid solvent should be a temperature- and pressure-independent quantity.
Electrical and optical properties	The response of solvent to an electrical field depends on the intrinsic dipole moment of its molecules, but depends also on cooperative effects of adjacent dipoles, when these are correlated in the liquid.

3.3 Chemical Properties of Solvents

The chemical properties of solvents have obviously a strong bearing on their applicability for various purposes. The solvents function by selectively dissolving desired solutes, by remaining inactive in the chemical reactions undergone by the solutes, and by solvating (selectively), reactants, transition-state intermediates, and products (Marcus, 1998a).

3.3.1 Structuredness of Solvents

The volatility, viscosity, diffusion coefficient and relaxation rates of solvents are described quantitatively by their structuredness. This property can be expressed by "stiffness," "openness," or "ordering" (Marcus, 1998a).

- Stiffness. This is expressed by the cohesive energy density, $\Delta_V U/V$. This quantity is proportional to the work that must be done against this stiffness in order to create cavities to accommodate a solute of given size in a series of solvents.
- Openness. (The openness of the solvent depends on its so-called free volume. It is approximately the difference between its molar and intrinsic volumes ($V_{free} = V - V_{intrinsic}$).
- Ordering. This is the deficit of entropy of the liquid solvent relative to the solvent vapor or the dipole orientation correlation.

3.3.2 Polarity in Molecules

In a simple homonuclear diatomic molecule, like dihydrogen or dinitrogen, the electron distribution is symmetrical; both atoms have the same electron density. The bond and molecule are *nonpolar*. In a heteronuclear diatomic molecule, like hydrogen fluoride, there is charge separation. Electrons are drawn towards the electronegative fluorine atom, and so the hydrogen atom is slightly positive. The H-F bond is polar, and as the molecule has a dipole; it is dipolar (often called polar). In polyatomic molecules the polarity of the molecule is broadly determined by the combined effect of all the bond dipoles present. Polyatomic molecules can be dipolar like water, with a net dipole, or like carbon dioxide with no net dipole. The charge distribution in carbon dioxide is not uniform since the oxygen atoms are negatively charged, leaving the carbon somewhat positive. Although carbon dioxide is a nondipolar molecule, the C-O bonds are still polar (Chipperfield, 1999).

3.3.2.1 Dispersion Forces

Molecules that have no permanent dipole still have their electrons in movement. Although the time-averaged distribution of electrons is symmetrical, at any instant the electrons are not uniformly distributed, so the molecule has a small instantaneous dipole, μ. This instantaneous dipole can polarize electrons in a neighboring molecule, giving a small dipole in the molecules. This is the dispersion attraction responsible for molecules sticking together. These dispersions forces are the weakest of all inter-

molecular forces. If the distance between two molecules is r, the dispersion interaction energy is proportional to $1/r^6$, so dispersion forces only operate over very short ranges. The van der Waals forces comprise the repulsive forces between electrons and nuclei on adjacent molecules, as well as the dispersion attractions.

3.3.2.2 Polarization and Polarizability

In most liquids, molecules are randomly arranged and in constant movement. If the molecules have a dipole but there is no applied electric field, the dipoles are randomly orientated. Dipole–dipole interactions between rotating dipolar molecules are small. Only for molecules with large dipoles, and where hydrogen bonding is absent, such as DMSO (dimethyl sulfoxide) and acetonitrile, do dipole–dipole attractions contribute significantly to molecular association. The *polarization*, the average electric dipole per unit volume, is zero. In an electric field, such as that caused by a solute ion, the random orientations of dipoles disappear as the dipoles align along the direction of the electric field. This results in orientation polarization of the liquid in the electric field around the ion.

Even if the liquid molecules have no net dipole, electrons in the molecule will be affected by an electric field. The ability of electrons to move in the presence of an electric field is called their *polarizability*. The movement of electrons results in an induced dipole, and the alignment of the induced dipoles with the electric field gives induced polarization.

3.3.2.3 Polarity of a Solvent

The idea of solvent polarity refers not to bonds, nor to molecules, but to the solvent as an assembly of molecules. Qualitatively, polar solvents promote the separation of solute moieties with unlike charges and they make it possible for solute moieties with like charges to approach each other more closely. Polarity affects the solvent's overall solvation capability (solvation power) for solutes. The polarity depends on the action of all possible, nonspecific and specific, intermolecular interactions between solute ions or molecules and solvent molecules. It covers electrostatic, directional, inductive, dispersion, and charge-transfer forces, as well as hydrogen-bonding forces, but excludes interactions leading to definite chemical alterations of the ions or molecules of the solute.

3.3.3 Assessment of Solvent Polarity

Physical properties of the solvent are used to describe polarity scales. These include both bulk properties, such as dielectric constant (relative permittivity), refractive index, latent heat of fusion, and vaporization, and molecular properties, such as dipole moment. A second set of polarity assessments has used measures of the chemical interactions between solvents and convenient reference solutes (see table 3.2). Polarity is a subjective phenomenon. (To a synthetic organic chemist, dichloromethane may be a polar solvent, whereas to an inorganic chemist, who is used to water, liquid ammonia, and concentrated sulfuric acid, dichloromethane has low polarity.)

Table 3.2. Properties used for assessment of solvent polarity.

Physical properties	Chemical properties
Bulk properties	Donor numbers
cohesive pressure	Acceptor numbers
dielectric constant	Solvatochromic properties
refractive index	E_T^N scale
	β scale
Molecular properties	α scale
dipole moment	π^* scale

3.3.4 Polarity Assessment from Physical Properties

3.3.4.1 Cohesive Pressure of a Solvent and Solubility Parameter

As a cavity has to be opened in a solvent in order to introduce a solute, the strength of the solvent–solvent bonding will be a factor in determining solubility. The *cohesive pressure*, *c*, is defined by eqn. 3.1.

$$C = (\Delta H_{vap} - RT)/(V_m) \tag{3.1}$$

where ΔH_{vap} is the molar enthalpy of vaporization and V_m is the molar volume. It reflects the fact that all solvent–solvent bonds are absent in the vapor, and so covers the total strength of all solvent–solvent forces in the liquid. As a measure of solvent polarity it ignores all solvent–solute interactions, so works best when these are small, as for nonpolar solutes dissolving in low-polarity solvents. Hildebrand defined the *solubility parameter*, δ, as the square root of the cohesive pressure ($\delta = c^{1/2}$). The concept has been very useful and successful in predicting solubilities of nonelectrolyte solutes in low polarity solvents. The cohesive energy, ΔE, is composed of a nonpolar component, ΔE_{np}, from the dispersion forces between solvent molecules, a polar component, ΔE_p, from the interaction of dipoles, and a hydrogen-bonding component, ΔE_H, if hydrogen bonding takes place (eqn. 3.2).

$$\Delta E = \Delta E_{np} + \Delta E_p + \Delta E_H \tag{3.2}$$

Accordingly, the solubility parameter, δ, is composed of a nonpolar part, δ_{np}, a polar part, δ_p, and a hydrogen-bonding part, δ_H (eqn. 3.3).

$$\delta^2 = \delta_{np}^{\ 2} + \delta_p^{\ 2} + \delta_H^{\ 2} \tag{3.3}$$

Typical values for a few solvents are shown in table 3.3.

In practice, to choose a good solvent for a solute the individual parameters δ_{np}, δ_p, and δ_H are individually matched for solvent and solute. For example, solubility parameters are used in the paint industry for choosing suitable solvents for surface coatings, in choosing solvents for polymers and for pharmaceuticals for calculations on the solubility of gases, and for optimizing chromatography column coatings.

Table 3.3. Solubility parameters.

Solvent	δ/Mpa$^{1/2}$	δ_{np}/Mpa$^{1/2}$	δ_p/Mpa$^{1/2}$	δ_H/Mpa$^{1/2}$
Hexane	14.9	14.9	0	0
Ethanol	26.1	12.6	11.2	20.0
Acetic acid	26.5	13.9	12.2	18.9
Water	48.0	12.2	22.8	40.4
Acetone	19.7	13.0	9.8	11.0

3.3.4.2 Dielectric Constant (Relative Permittivity), ε_r

The dielectric constant (also called relative permittivity), ε_r, of a solvent is measured by placing it between the plates of a capacitor. The dielectric constant is given by eqn. 3.4. Dielectric constants range from 2 (alkanes) to over 100 (N-methylacetamide, 191). Between the charged plates, molecules with permanent or induced dipoles are aligned into an ordered arrangement. The dielectric constant represents the ability of a solvent to separate its charges and orient its dipoles. Some typical values are shown in table 3.4.

$$\varepsilon_r = E_o/E \tag{3.4}$$

3.3.4.3 Ion–Solvent Interactions

According to electrostatics theory, the force between two charges q_1 and q_2 depends on their distance apart, r, and the dielectric constant of the medium in which they are placed, ε_r, (eqn. 3.5).

$$\text{Force} \propto q_1 q_2 / r^2 \varepsilon_r \tag{3.5}$$

Thus the force attracting two ions of opposite unit charge is about 40 times less if they are water, ε_r, = 79, compared with an alkane (hexane), ε_r, = 2. Ion pairs are common in low-polarity solvents. The dielectric constant of the solvent also appears in the Born equation. This calculates the Gibbs free energy of solvation ΔG°_S of a mole of ions of charge ze (where z is the charge number, e the elementary charge) from considering

Table 3.4. Dielectric constants, ε_r, of some solvents at 25 °C.

Solvent	ε_r,	Solvent	ε_r,
Hexane	1.88	HMPTA, HMTA	29.6
Cyclohexane	2.02	Methanol	32.66
Diethyl ether	4.20	Acetonitrile	35.94
Acetic acid	6.17	DMF	36.71
Tetrahydrofuran	7.58	Dimethyl sulfoxide	46.45
Acetone	20.56	Water	78.3
Ethanol	24.55	Sulfuric acid	100

transferring them from free space, $\varepsilon_o = 1$, to a solvent with dielectric constant ε_r (N_A is the Avogadro constant) (eqn. 3.6).

$$\Delta G^o_S = -(N_A z^2 e^2)/(8\pi\varepsilon_o r) \times (L^{-1}) \tag{3.6}$$

Also, the dielectric constant of a solvent near an ion may differ from that of the bulk liquid. Although the Born equation is only an approximation, it does indicate that free energies of solvation of ions will be larger as the solvent dielectric constant increases.

3.3.4.4 Dipolar Solutes and Solvent

In a similar way, Kirkwood calculated the Gibbs free energy change of a molecule (assumed spherical with radius r and dipole moment μ) going from free space to a solvent with dielectric constant ε_r by eqn. 3.7.

$$\Delta G^o_S = -((N_A\mu^2)(\varepsilon_r - 1))/((4\pi\varepsilon_o r^3)(2\varepsilon_r + 1)) \tag{3.7}$$

Accordingly, as the free energies of solvation of both ions and dipolar molecules are affected, dielectric constants are widely used as a measure of polarity. Such a simple approach is bound to limitations. This electrostatic approach treats the solvent as a continuum, not as a collection of interacting molecules. Consequently, interactions between solvent molecules, such as hydrogen bonding, are not specifically treated. Similarly, specific solvent–solute interactions such as hydrogen bonding, or interactions between electron pairs on the solvent and electron-poor regions of the solute, are ignored.

3.3.4.5 Refractive Index

The refractive index, n_D, is a measure of induced polarizability. Dispersion forces are especially high for aromatic hydrocarbons, which have highly polarizable π electrons. This is reflected in the high refractive indices of aromatic compounds, often 0.1 to 0.2 units higher than comparable nonaromatic compounds (table 3.5). Solvents with high polarizabilities are often good solvents for *soft* anions (i.e., those with high polarizabilities) such as SCN^-, I^-, and I_3^-.

3.3.4.6 Dipole Moment

Dipole moments (μ) are calculated for individual molecules. Solvent–solute and solvent–solvent interactions are poorly calculated from μ, as models generally assume

Table 3.5. Comparison of n_D for aromatic and nonaromatic compounds.

Nonaromatic		*Aromatic*	
Compound	n_D	Compound	n_D
Cyclohexane	1.426	Benzene	1.501
Cyclohexylamine	1.456	Aniline	1.584

point dipoles. Dipole moments are determined from dielectric constant and refractive index measurements.

Table 3.6 shows the dipole moments of some common solvent molecules. While dipole moments for HMPA and DMSO are different, the values for water, HF, and THF are similar. Water and HF, which both readily dissolve ionic compounds, are more polar solvents than THF. The use of dipole moments as a polarity indicator, seriously underestimates the polarities of water and HF as solvents.

3.3.5 Polarity Assessment from Chemical Properties

There have been many attempts to assess solvent polarity in a more chemical way. The most important ways are described below. Chemical interactions between solvent and solute can lead to polarity.

3.3.5.1 Donor Number

An important chemical measure of solvent polarity is the donor number, DN. It is a measure of the Lewis base donor power of the solvent. DN is defined as the negative enthalpy for the reaction of the solvent with the standard Lewis acid $SbCl_5$ (eqn. 3.8). The enthalpy measurements are carried out in an inert solvent, 1,2-dichloroethane, which has a donor number of zero. The units are kcal/mol.

$$S: + SbCl_5 \leftrightarrow SbCl_6 \quad DN = -\Delta H^o \tag{3.8}$$

DNs range from zero (solvents like hexane, tetrachloromethane), through modest donors (acetonitrile 14.1, acetone 17), to good donors like water (18), to superb donors like DMSO (29.8) and, best of all, HMPA (38.8) (see table 3.7). The DN enables us to rationalize why a solvent such as nitromethane, ($\varepsilon_r = 35.8$) is considered to be fairly nonpolar, although it has a higher dielectric constant than diethyl ether ($\varepsilon_r = 4.2$) and tetrahydrofuran ($\varepsilon_r = 7.6$) which are often thought to be more polar solvents than their dielectric constants would indicate. The DN of nitromethane is only 2.7, compared with that of 19.2 for diethyl ether and 20 for tetrahydrofuran. These ether solvents are much better electron-pair donors than nitromethane.

Table 3.6. Dipole moments of some solvents.

Solvent	Dipole moment, μ/D
Benzene	0
HMPA	5.54
DMSO	3.9
Acetone	2.69
Hydrogen fluoride	1.83
Water	1.83
THF	1.75

Table 3.7. Donor numbers of some solvents.

Solvent	Donor number DN/kcal mol^{-1}
Water	18–33
Acetone	17
Dimethyl sulfoxide	29.8
HMPA	38.8
Hexane	0
Ethane	32

3.3.5.2 Acceptor Number and the E_T^N Scale

The converse of the donor number is the *acceptor number*, AN, of a solvent. This is a measure of its power to accept electron pairs as a Lewis acid. There are a number of ways of assessing the acceptor ability. One convenient way is to use NMR to measure the interaction between a standard reference Lewis base, $(C_2H_5)_3PO$, and the solvent by looking at the ^{31}P shift (eqn. 3.9).

$$S + (C_2H_5)_3PO \leftrightarrow (C_2H_5)_3PO\text{-}S \tag{3.9}$$

The standards are set as zero for solvent hexane, and 100 for solvent $SbCl_5$. The range of ANs is thus similar to that for DNs (see table 3.8).

Another widely used solvent parameter, especially popular with organic chemists, is the E_T^N parameter proposed by Reichardt (Reichardt, 1988). The UV spectrum of some dyes strongly depends on the nature of the solvent. There is a change in electron distribution in the ground and excited states, and consequently the two states have different dipole moments. The longest wavelength band is λ_S. Thus, for diphenylether $\lambda_S = 810$ nm, while for water $\lambda_S = 453$ nm. The dye has a different color according to the interaction with the solvent—it is solvatochromic. The transition energy of the longest wavelength solvatochromic absorption band (in units of kcal/mol) gives the solvent parameter E_T. This ranges from 30.7 (for tetramethylsilane, TMS, little interaction) to 63.1 (for water). A normalized parameter, E_T^N, lying between 0 (TMS) and 1 (water) is more convenient to use than E_T (table 3.8).

Table 3.8. Acceptor numbers and the E_T^N scale for common solvents.

Solvent	Acceptor number	E_T^N
Cyclohexane	0	0.006
Acetonitrile	18.9	0.47
DMSO	19.3	0.444
Ethanol	37.9	0.654
Acetic Acid	52.9	0.82
Water	54.8	1

3.3.5.3 Hardness and Softness in Solvents

The HSAB (hard and soft acids and base) principle is that "hard" acids prefer to interact with a "hard" base, and "soft" acids with "soft" bases. "Hard" bases are not polarizable, and include those with O-donor atoms. "Soft" bases are more polarizable, and include S-donor bases. Solvent hardness/softness can be assessed by comparing the Gibbs free energy of transfer of a "soft" cation like Ag^+ from "hard" water to the solvent with the Gibbs free energy of transfer of similarly sized "hard" cations like Na^+ and K^+. Table 3.9 shows some solvents listed in increasing "softness."

3.4 Solvation Chemistry

Solvent use in chemistry is pervasive (Nelson, 1998). Probably one of the most critical components of a reaction or chemical process is the identity of the solvent(s) used. In the emerging area of green chemistry, careful reasoning must enter into the choice of solvents. Chemists use solvents for many reasons, but primarily they are used as reaction media, in separation/purification technologies and in cleaning technologies.

The most general effect a solvent may have on a solute dissolved in it is the solvation of the solute. Often the solute may not only be a solute foreign to the solvent, but may also be a molecule of the solvent itself. There is no limitation on the concentration of the solute, so that it may dissolve and be solvated in a solution that already contains this solute as well as other ones (Marcus, 1998b).

The quality and suitability of reactions and chemical processes are usually dependent upon the quality of the solvent utilized. As mentioned previously, the largest volume of solvents is used in the manufacturing and cleaning industries.

3.4.1 Green Solvents in Green Chemistry

According to the end goal of green chemistry, the criteria for what determines a green solvent will vary, depending upon the use and ultimate fate of the solvent during the process. Likewise, the determination of what constitutes appropriate solvent usage in

Table 3.9. Solvents listed by increasing softness.

Water	Hard
Methanol	
Nitromethane	
Acetone	
Ethanol	
DMF	
DMSO	
HMPA	
Acetonitrile	
Pyridine	
Ammonia	Softer

green chemistry might include redesign of the exact chemical nature of the solvent via synthesis, identification of equally useful but less toxic substitutes of another chemical class for use instead of a "traditional" solvent, or even reducing or eliminating the use of solvents for particular chemical processes. Understandably, therefore, the discussion of green solvents will include input from such diverse subject areas as chemistry, ecology, and philosophy. From the outset, the traditional considerations of synthesis yield (if we are dealing with reactions), perfect product recovery (separations), or commercial usefulness are no longer the only ones for a chemist during the choice of solvents in green chemistry.

Initially, solvents must be understood. The development of our knowledge of solutions reflects to some extent the development of chemistry itself (Walden, 1910). What is beginning to be recognized within the scientific community is that all chemists will need to focus attention on ways of preventing environmental problems as effectively as chemists in general have been at solving them (Amato, 1993). Fundamentally, solvents provide the reaction media in which chemical transformations occur, and for that reason they must be evaluated as to whether they are environmentally benign. The use and development of environmentally benign solvents must be dependent upon reasoned chemical thinking.

What, then constitutes an appropriate solvent for green chemistry? Fundamentally, it must be a solvent which allows the chemist to accomplish his or her task, but in an environmentally conscious manner. The modern chemist is expected to consider toxicity as part of the key elements affecting choice of solvents, so that they are minimally toxic to human health and the environment, and disposed of in ways that do not contribute to pollution (DeVito, 1996). The considerations for what constitutes a safe solvent might contain some of the following considerations:

- it must have reduced absorption;
- its toxicity should be understood;
- knowledge of its environmental fate is understood.

In accord with this, chemists today who can recognize toxicophoric substituents (the structural portion of a substance that causes toxicity) have a knowledge of the environmental fate of the chemicals they use, or can obtain information pertaining to both areas, are in a much better position to express the mandates of green chemistry. They must consider the potential dangers particular solvents pose to the global ecology or to the individuals who will contact the chemicals directly (chemists, workers, local populace, etc.). Chemists must seek to reduce the toxicity and to influence the resultant toxicology of those chemicals while attempting to maintain the overall commercial usefulness of the substance.

The toxicology of a solvent is determined by many factors, such as bioavailability, metabolism, and the presence of structural features that may attenuate or enhance the reactivity of the parent molecule. Despite the structure-activity data available for many classes of commercial chemical substances, chemists have not recognized the use of structure-activity relations as a rational approach for choosing or designing new, less toxic commercial chemical substances. With qualitative structure-activity relationships, comparing the structures of the substances in the series with corresponding effects on the toxicity makes the correlation between toxic effect and structure. Through these, it may then be possible to predict a relationship between structure and toxicity

and identify the least toxic members of a class of compounds as possible commercial alternatives to the more toxic substances.

Like the challenges of the Total Quality Management (TQM) and Life-Cycle Assessment (LCA), the current environmental revolution presents the science of chemistry with a new adaptation imperative. While initially incorporating the ideals of pollution prevention into all its operating paradigms may seem counterproductive, it will eventually open up new vistas and unexplored realms in chemical sciences. The chemist is already finding that sensitivity to the changing priorities among the world's populations will demand a movement toward greener strategies.

The implications of the pervasiveness of green chemistry incentives for present-day and future chemists suggest that at the most general level of science, it has become clear that the green chemist will be one who: (a) strives for efficiency (maximizes output per unit of input, minimizes costs, minimizes waste), (b) minimizes risk, and (c) thinks globally and in long-range terms. As a key player in this area, the chemist must determine whether the new chemistry results in a net improvement to human health and the environment, or whether other additional incremental improvements are necessary in order to complement the original change in order to ensure that the entire process is more benign. Obviously, the chemist is in a pivotal position to provide both information in this area and initiate action contributing to the success of the pollution prevention movement.

Novel solvent design and use must become institutionalized and combined to afford various environmentally benign processes for laboratory-scale organic synthesis and for the production of fine chemicals, intermediates, and pharmaceuticals. New technologies should emerge using a vast array of possible solvent deployment scenarios, including continuous and batch microwave reactors and catalytic membranes, to name a few. The methodologies should include solvent-free conditions, catalyzed or uncatalyzed processes, and the use of aqueous media at high temperature and nonextractive techniques for product isolation. In traditional chemistry, potential applications will include Hofmann eliminations, Willgerodt and Jacobs-Gould reactions, indole transformations, aldol condensation, Rupe and Meyer-Schuster rearrangements and C-C coupling reactions (including a tandem Heck coupling-dehydrogenation). New processes for catalytic etherification, uncatalyzed hydrogen transfer, and a one-step arylamidation have also been developed. Typical products include N-(4-hydroxyphenyl)acetamide, carvacrol, alpha-phenylacetamide, cinnamaldehyde, cinnamyl alcohol, acetophenone, indole, 3-hydroxy-1,2-dimethyl-4-pyridone, di(2-phenylethyl) ether, di(cyclopropylmethyl) ether, 3-methylcyclopent-2-enone, and a synthetic precursor of nalidixic acid (Strauss, 1999). These are the beginnings of rich and relatively untapped fields of research.

3.4.2 Solvent Functions

As a reaction medium, solvents are used to bring reactants at suitable concentrations. For endothermic reactions, heat can be supplied readily by heating the solvent; for exothermic reactions, the solvent can act as a heat sink. If necessary, surplus heat can be removed by allowing the solvent to boil. After the reaction, products have to be freed of solvent. As diffusion in solids is slow, solid–solid reactions are slow at room temperature. To get reactants to mix at a molecular level requires use of the gas phase,

or solution. Gas-phase reactions are limited to those that involve volatile reactants. High pressures are sometimes necessary to increase reactant concentrations. When solutions are used, the concentrations of reactants can be readily adjusted over some ten orders of magnitude. Compounds too reactive to study in one solvent can be used in another solvent.

As a reactant, solvents frequently react with solutes. Substances that are insoluble in one solvent can dissolve in another by reacting with it. Thus, bone (hydroxyapatite, $Ca_5(OH)(PO_4)_3$) is insoluble in most solvents but dissolves in 100% sulfuric acid, with protonation of the phosphate. When any solute is dissolved in a solvent, possible solute–solvent reactions must always be considered. Solvents can be used to modify the properties of solutes. Nitric acid dissolved in water behaves quiet differently to nitric acid dissolved in concentrated sulfuric acid.

As a carrier, solutions are a convenient way of delivering chemical compounds to their point of use in the required quantities. Samples are dissolved in solvents for injection to mass spectrometers and chromatographs; NMR and UV/Vis spectra are routinely measured in solvents. The ready removal of the solvent by evaporation leaves the solute where it is required. Coatings (such as, paint, adhesive) can be applied and then the solvent removed. In solvent extraction, compounds dissolved in one solvent (such as water) are shaken with another solvent immiscible with water. Solutes, which are more soluble in the nonaqueous solvent than in water, are concentrated into the nonaqueous phase.

3.4.3 Scope of Solvents

There are three quite different solvent types, each of which acts as a solvent to quite different solutes.

- Molecular. These are the usual "solvents." Solvent molecules may adhere together by van der Waals forces alone, or involve stronger intermolecular bonding;
- Metals. Molten metals dissolve other metals well, forming alloys, but also dissolve nonmetals like carbon, nitrogen, phosphorus, and boron;
- Polar framework compounds. These are compounds where no individual molecules exist, and range from ionic compounds like sodium chloride, through part-ionic, part-covalent compounds like aluminum oxide, to polar covalent framework solids like silicon dioxide.

Solvents can be also be classified according to their chemical bonds:

- Molecular liquids (molecule melts; covalent bonds only);
- Ionic liquids (either molten salts or room temperature; only ionic bonds); and
- Atomic liquids (low-melting metals liquid mercury or liquid sodium; metallic bonds).

Numerous transitions are possible by mixing solvents of these three classes, and research into this area is still far from exhausted. A triangle can be used to illustrate how the three solvent types are not mutually exclusive (see fig. 3.1). Each corner represents a solvent type. The sides show where one type will dissolve another.

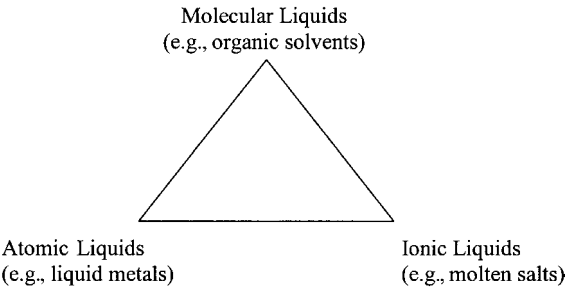


Figure 3.1 Diagrammatic representation of the three solvent types.

3.4.3.1 Solvent Classification

Due to the physical and chemical differences between the numerous organic and inorganic solvents, it is difficult to organize them in a useful scheme. Reichardt presented five attempts at classification of solvents, which should prove useful to the chemist (Reichardt, 1988). In the following discussion we will summarize four of them.

3.4.3.1.1 Classification of Solvents using Physical Constants The following physical constants can be used to characterize the properties of a solvent: melting and boiling point, vapor pressure, heat of vaporization, index of refraction, density, viscosity, surface tension, depose moment, dielectric constant, polarizability, specific conductivity, and so on.

Solvents can be broadly classified as low, middle, or high boiling, viz. $t_{bp} < 100°C$, 100, . . . 150°C, or > 150°C at 1 bar. Similarly, liquids can be classified according to their *evaporation number* using diethyl ether as reference (evaporation number = 1 at 20°C and 65 cl/1 relative air humidity). Thus, low volatility signifies evaporation numbers < 10, medium volatility 10–35, and high volatility > 35 (Duve et al., 1976). Using viscosity as a criterion, solvents are of low viscosity when the dynamic viscosity < 2 mPa · s at 20°C, medium viscosity (2–10 mPa · s), and high viscosity (> 10 mPa · s) (Duve et al., 1976).

The degree of association of molecules in a liquid can be estimated by means of its *Trouton constant* (Nash, 1984). At the normal boiling temperature, T_{bp}, vaporization proceeds with standard molar changes of enthalpy, ΔH^{o}_{bp}, and entropy, ΔS^{o}_{bp}, from which Trouton's rule is derived as given in eqn. 3.10.

$$\Delta S^{o}_{bp} = \Delta H^{o}_{bp}/T_{bp} \sim 21 \text{ cal} \cdot \text{mol}^{-1} \cdot \text{K}^{-1} \text{ or } 88 \text{ J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1} \qquad (3.10)$$

This rule works best for apolar, quasi-spherical molecules. Large deviations occur when chemical association is involved (e.g., carboxylic acids), from molecular dipolarity (e.g., dimethyl sulfoxide), and from molecular asphericity (e.g., neopentane/*n*-pentane). Strongly associating solvents (e.g., HF, H2, NH3, alcohols, carboxylic acids) have Trouton constants which are higher than the average value of 88 $J \cdot mol^{-1} \cdot K^{-1}$ found for nonassociating solvents such as diethyl ether and benzene.

The *cohesive pressure c* is a measure of the total molecular cohesion per unit volume, given by eqn. 3.11

$$C = \Delta U_v / V_{mm} = (\Delta H_v - R \cdot T)/V_m \tag{3.11}$$

where ΔU_v and ΔH_v are, respectively, the energy and enthalpy (heat) of vaporization of the solvent to a gas of zero pressure, and V_m is the molar volume of the solvent. On vaporization of a solvent to a noninteracting vapor, *all* intermolecular solvent–solvent interactions will be broken.

On the other hand, the *internal pressure* π is defined as the change in internal energy of a solvent as it undergoes a very small isothermal expansion, as seen in (eqn. 3.12).

$$\pi = (\partial U / \partial V_m)_T \tag{3.12}$$

(U = molar internal energy; V_m = molar volume; T = absolute temperature.) This small expansion does not necessarily disrupt all the intermolecular solvent–solvent interactions.

The square root of the cohesive pressure c as defined in eqn. 3.11 has been termed the *solubility parameter* δ by Hildebrand and Scott (1962) because of its value in correlating and predicting the solvency of solvents for nonelectrolyte solutes. Solvency is defined as the ability of solvents to dissolve a compound. A selection of δ-values is given in table 3.10.

Godfrey gave an alternate approach for the prediction of mutual miscibility of solvents (Godfrey, 1972). As a measure of lipophilicity (that is, affinity for oil-like substances) the so-called miscibility numbers (M-numbers, with values between 1 and 31) have been developed. These are serial numbers of 31 classes of organic solvents, ordered empirically by means of simple test tube miscibility experiments and critical solution temperature measurements. There is a close correlation between M-numbers and Hildebrand's δ-values.

The solvency of hydrocarbon solvents used in paint and lacquer formulations is empirically described by their *kauri-butanol numbers*, that is, the volume in milliliters

Table 3.10. Hildebrand solubility parameters, δ, of 26 solvents at 25°C, taken from Barton (Barton, 1983).

Solvents	δ/MPa$^{1/2}$*	Solvents	δ/MPa$^{1/2}$*
Water	47.9	*t*-Butanol	21.7
Formamide	39.3	Aniline	21.1
N-Methylformamide	32.9	Acetic acid	20.7
1,2-Ethanediol	29.9	1,4-Dioxane	20.5
Methanol	29.6	Carbon disulfide	20.4
Tetrahydrothiophene-1,1-dioxide	27.4	Cyclohexanone	20.3
Ethanol	26.0	Acetone	20.2
N,N-Dimethylformamide	24.8	Ethyl acetate	18.6
Dimethyl sulfoxide	24.5	Tetrahydrofuran	18.6
Acetonitrile	24.3	Tetrachloromethane	17.6
1-Butanol	23.3	Cyclohexane	16.8
Cyclohexanol	23.3	*n*-Hexane	14.9
Pyridine	21.9	Perfluoro-*n*-heptane	11.9

Note: * 1 Mpa$^{1/2}$ = 1 J$^{1/2}$ · cm$^{-3/2}$ = 0.4889 cal$^{1/2}$ · cm$^{-3/2}$.

at 25°C of the solvent required to produce a defined degree of turbidity when added to 20g of a standard solution of kauri resin in 1-butanol (Reichardt, 1988). Standard values are KB = 105 for toluene and KB = 40 for *n*-heptane/toluene (75:25 cl/l). A high KB number corresponds to high solvent power. An approximately linear relationship does exist between Hildebrand's δ-values and KB-numbers for hydrocarbons with KB > 35 (Barton, 1983).

Solvents whose molecules possess a permanent *dipole moment* are designated *dipolar* as opposed to *apolar* or *nonpolar* for those lacking a dipole moment. The permanent dipole moments of organic solvents vary from 0 to 18.5×10^{-30} Cm (0 to 5.5 D). Values of dipole moments increase steadily on going from hydrocarbon solvents to solvents containing dipolar groups such as

$$C^{\delta+\cdots}O^{\delta-},\ C^{\delta+\cdots}N^{\delta},\ N^{\delta+\cdots}O^{\delta-},\ S^{\delta+\cdots}O^{\delta},\ P^{\delta+\cdots}O^{\delta-}.$$

The *dielectric constants* play a particular role in the characterization of solvents. Their importance over other criteria is due to the simplicity of electrostatic models of solvation and they have become a useful measure of solvent polarity. Since both the dielectric constant ε_r and the dipole moment μ are important complementary solvent properties, it has been recommended that organic solvents should be classified according to their *electrostatic factor EF* (defined as the product of ε_r and μ).

The characterization of a solvent by means of its "polarity" is an unsolved problem since the "polarity" itself has, until now, not been precisely defined. Polarity can be understood to mean (a) the permanent dipole moment of a compound, (b) its dielectric constant, or (c) the sum of all those molecular properties responsible for all the interaction forces between solvent and solute molecules (e.g., Coulombic, directional, inductive, dispersion, hydrogen bonding, and EPD/EPA interaction forces) (Kovats, 1968). The important thing concerning the so-called polarity of a solvent is its *overall solvation ability*. This in turn depends on the sum of all-specific as well as nonspecific interactions between solvent and solute.

3.4.3.1.2 Classification of Solvents Using Statistical Methods Chemical experience suggests that more solvent classes may be necessary to classify solute–solvent interactions for a wide range of organic solvents. Multivariate statistical methods have therefore been used recently in the classification and selection of organic solvents (Reichardt, 1988). Compilations of their physicochemical constants (e.g., boiling points, molar volumes, heats of vaporization, dipole moments, dielectric constants, molar refraction, etc.) and sometimes additionally empirical parameters of solvent polarity are used as basic data sets. This kind of analysis is part of the relatively new research field of *chemometrics*[1] (Sharaf et al., 1986; Vandeginste, 1987).

Multiple linear regression analysis (MRA) has been widely used to establish linear Gibbs energy (LGE) relationships. The Hammett equation is an example of the simplest form of MRA, namely bivariate statistical analysis. The other statistical method used for seeking regularities in physicochemical data, factor analysis (FA), was first developed and used in psychometrics (Malinowsky and Howery, 1980). Although these factors are pure mathematical constructs and do not necessarily embody a direct physical significance, the advantage of FA is that an otherwise hidden physical or chemical interpretation will emerge.

Using PCA, Cramer found that more than 95% of the variances in six physical properties (activity coefficient, partition coefficient, boiling point, molar refractivity, molar volume, and molar vaporization enthalpy) of 114 pure liquids can be explained in terms of only two parameters which are characteristic of the solvent molecule (Cramer III, 1980). These two factors are correlated to the molecular bulk and cohesiveness of the individual solvent molecules, the interaction of which depends mainly upon nonspecific, weak intermolecular forces.

3.4.3.1.2.1 Bronsted-Lowry Theory of Acids and Bases. It is possible to classify solvents in terms of Bronsted-Lowry theory of acids and bases (Luder and Zuffanti, 1961). Self-ionizing solvents possessing both acid and base characteristics (e.g., water) are designated *amphiprotic solvents* in contrast to *aprotic solvents*, which do not self-ionize to a measurable extent (e.g., aliphatic hydrocarbons). Davies extended the Bronsted classification and distinguished between solvents with dielectric constants greater or smaller than 20, thus arriving at eight classes of solvents (Davies, 1970).

Water is the prototype of an amphiprotic solvent and all other solvents with similar acid-base properties are called *neutral solvents*. Solvents which are much stronger acids and much weaker bases than water are called *protogenic solvents*, while those which are much stronger bases and much weaker acids than water are designated *protophilic solvents*.

The ionization of the acid depends not only on the basicity of the solvent, but also on its dielectric constant and its ion-solvating ability. The dependence of the acidity and basicity constants of a compound on the basicity and acidity, respectively, of the solvents, leads to a distinction between *leveling* and *differentiating solvents*. When the solvent is a stronger base than water, its leveling effect will apply also to weaker acids. Similarly, strong bases will also have equal basicities in sufficiently acidic solvents. All bases stronger than the HO^- ion are adjusted to the basicity of this ion in water.

Evidently, in a given solvent the more highly ionized acid or base is also the strongest one. However, if the same acid is examined in different solvents, one finds, surprisingly enough, that the most acidic solution is the one in which the acid is the least ionized.

Bronsted acids stronger than pure (100%) sulfuric acid ($H_o = -11.9$) are classified as *super acids*.

With respect to the well-known acid/base properties of water, ammonia, and phenol in aqueous solution, one has to conclude that enormous solvation energies must contribute to the differences from the behavior of isolated water molecules.

3.4.3.1.2.2 Lewis Theory of Acids and Bases. According to Lewis, acids are electron-pair acceptors (EPA) and bases electron-pair donors (EPD) connected through the equilibrium (fig 3.2).

The Lewis acid/base complex is formed via an overlap between a doubly occupied orbital of the donor D and vacant orbital of the acceptor A . This acid/base approach was extended by Pearson who divided Lewis acids and bases into two groups, hard and soft, according to their electronegativity and polarizability (principle of hard and soft acids and bases (HSAB concept). Hard acids (e.g., H^+, Li^+, Na^+, BF_3, $AlCl_3$, hydrogen-bond donors HX) and hard bases (e.g., F^-, Cl^-, HO^-, RO^-, H_2O, ROH, R_2O,

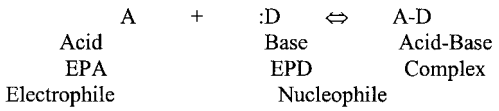


Figure 3.2 Donor acceptor equilibrium.

NH_3) are those derived from small atoms with high electronegativity and generally of low polarizability. Soft acids (e.g., Ag^+, Hg^+, I_2, 1,3,5-trinitrobenzene, tetracyanoethene) and soft bases e.g., H^-, I^-, R^-, RS^-, RSH, R_2S, alkenes, C_6H_6) are usually derived from large atoms with low electronegativity and are usually polarizable.

The application of the HSAB concept to solutions leads to the rule that hard solutes dissolve in hard solvents and soft solutes dissolve in soft solvents (Pearson, 1987). For example, benzene is considered a very soft solvent since it contains only a basic function. Contrary to benzene, water is a very hard solvent, with respect to both its basic and acidic properties. It is the ideal solvent for hard bases and hard acids. The hardness of water is reduced by the introduction of alkyl substituents in proportion to the size of the alkyl group. In alcohols, therefore, softer solutes become soluble.

A quantitative scale describing the softness of solvents has been proposed by Marcus (Marcus, 1998c). His μ-scale of solvent softness (from *malakos* = soft in Greek) is defined as the difference between the mean of the standard molar Gibbs energies of transfer of sodium and potassium ions from water (W) to a given solvent (S), ΔG_t^o (Me^+, W → S)/(kJ· Mol^{-1}), and the corresponding transfer energy for solvent ions, divided by 100.

3.4.3.1.3 Classification of Solvents in Terms of Specific Solute–Solvent Interactions Parker divided solvents into two groups according to their specific interactions with anions and cations, namely *dipolar aprotic solvents* and *protic solvents* (Parker, 1969). The distinction lies principally in the dipolarity of the solvent molecules and their ability to form hydrogen bonds. It appears appropriate to add to these two groups a third one, namely, the *apolar aprotic solvents*.

- An apolar aprotic solvent is characterized by a low dielectric constant ($\varepsilon_r <$ 15), a low dipole moment ($\mu < 8.3 \times 10^{-30}$ Cm = 2.5 D), a low E_T^N-value (ca. 0.0–0.3), and the inability to act as hydrogen-bond donor.
- Dipolar aprotic solvents possess large dielectric constants $\varepsilon_r > 15$), sizeable dipole moments ($\mu > 8.3 \times 10^{-30}$ Cm = 2.5 D), and average E_T^N-values of 0.3 to 0.5. These solvents do not act as hydrogen-bond donors since their C-H bonds are not strongly polarized enough.

Protic solvents contain hydrogen atoms bound to electronegative elements (F-H, -O-H, -N-H, etc.) and are, therefore, hydrogen-bond donors, that is, HBD solvents. With the exception of acetic acid (and its homologues), the dielectric constants are usually larger than 15, and the E_T^N-values lie between 0.5 and 1.0, indicating these solvents are strongly polar.

This classification is not rigid. Protic solvents are particularly good anion solvators due to their hydrogen-bonding ability (Symons and Thomas, 1981). The observation

that protic solvents are far better anion solvators than dipolar aprotic solvents (and the reverse is true for cation solvation) has led to extremely valuable rules for the selection of solvents for specific reactions (Parker, 1969).

3.4.3.1.4 Classification by Chemical Constitution Classification of solvents according to chemical constitution allows certain qualitative predictions. In general, a compound dissolves far more easily in a solvent possessing related functional groups than in one of a completely different nature (see table 3.11). A proper choice of solvent, based on the knowledge of its chemical reactivity, helps to avoid undesired reactions between solute and solvent.

Liquid crystals or mesomorphic compounds occupy a special position. Compounds capable of forming liquid crystals are long, flat, and fairly rigid along the axis of the molecule. Room temperature ionic liquids are a new and growing area of research. This topic will be explored later. Molten network solids (e.g., silica) play a large part in chemistry of the world in the fields of glasses, ceramics, and geochemistry.

Nonpolar molecular compounds dissolve in nonpolar solvents. Polar molecular compounds and ionic compounds may dissolve in polar solvents. Metals dissolve in other molten metals. These can range from copper, silver, gold, alkali metals dissolving in mercury at room temperature, to chromium, molybdenum, and tungsten dissolving in molten iron.

Liquid crystals are classified into lyotropic and thermotropic crystals depending on the way in which the mesomorphic phase is generated. *Lyotropic* liquid-crystalline solvents are formed by addition of controlled amounts of polar solvents to certain amphiphilic compounds. *Thermotropic* liquid-crystalline solvents, simply obtained by temperature variations, can be further classified into nematic, smectic, and cholesteric solvents depending on the type of molecular order present. Liquid crystals are usually excellent solvents for other organic compounds. Nonmesomorphic solute molecules may be incorporated into liquid-crystalline solvents without destruction of the order prevailing in the liquid-crystalline matrix (Michl and Thulstrup, 1986). Ordered solvent phases such as liquid crystals have also been used as reaction media, particularly for photochemical reactions (Nakano and Hirata, 1982).

Ionic liquids occupy the second corner of the above triangle. Of these, molten salts are becoming increasingly important as solvents for inorganic, as well as organic, reactions (Kerridge, 1978) (see table 3.12). In particular, room-temperature ionic liquids possess electrical conductivities which are roughly a factor 10 larger than those of concentrated aqueous solutions of strong electrolytes (ionophores), low viscosity, wide liquid range, low vapor pressure and the resulting possibility of high working tempera-

Table 3.11. Solvent and solutes.

Solvent type	Typical solvents	Typical solutes
Molecular	Hexane	I_2, naphthalene
	Ethanol	Acetamide, $CaCl_2$
Metal	Iron	Carbon
Polar framework	Silicon dioxide	B_2O_3

tures, together with their excellent ability to dissolve salts and metals, make them extremely useful reaction media (Welton, 1999; Wasserscheid and Waffenschmidt, 2000). Therefore, such systems are becoming increasingly important technologically. A further advantage of molten salts is their high heat conductivity, which permits a very rapid dispersal of the heat of reaction.

Although the dielectric constants of molten salts are generally quite small (ε_r = 2–3), they behave as strongly dissociating solvents. This is due to the ability of the solvent ions to exchange places with solute ions of the same charge.

3.4.4 Solvation

The solvent may serve only as the medium for the reaction, or it may in addition be a reactant, as in a solvolysis reaction. It is possible that the reaction mechanism may be changed by a change in solvent (e.g., from S_N1 to S_N2) or that the rate-determining step of a complex reaction may be altered. All of these phenomena can be studied by examining the solvent dependence. One goal of research on medium effects is to achieve a level of understanding that will allow us to make mechanistic interpretations from such data. Handbooks of solubility parameters are valuable (Barton, 1983).

The process of solvation is described as that in which a particle of the solute is transferred at a given temperature and pressure from a fixed position in the ideal gas phase into a fixed position in the liquid phase in which it is solvated (Ben-Naim and Marcus, 1984).

It is important to stress that not only the direct solute–solvent interactions are taken into account in the solvation process, but also the other changes mentioned. Excluded from consideration are effects due to translational degrees of freedom of the solute, which are due to the different volumes at the disposal of the solute particle in these phases.

Table 3.12. Melting points (t_{mp}), boiling points (t_{bp}), and liquid range $\Delta t = t_{bp} - t_{mp}$ of some fused inorganic and organic salt systems in °C (Janz, 1967; Gordon, 1969).

Fused salts[a]	t_{mp}/°C	t_{bp}/°C	Δt/°C
NaCl	8008	1465	657
KCl	772	1407	635
LiCl	610	1382	772
NaOH	318	1390	1072
$NaNO_3$	310	380	70
$ZnCl_2$	283	732	449
$AlBr_3$	97.5	257	159.5
$SbCl_3$	73.2	221	147.8
$(n\text{-}C_4H_9)_3NH^+NO_3^-$	21.5	119[d]	—
$n\text{-}C_4H_9\text{-}NH_3^+SCN^-$	20.5	130[d]	—
$CH_3\text{-}CH_2\text{-}NH_3^+NO_3^-$	12.5[c]	170[d]	—
$(n\text{-}C_6H_{13})^+(n\text{-}C_6H_{13})$ $(C_2H_5)_3B^-$	>–75[c]	87[d]	—

Notes: a. Cf. also the compilation of salt properties in A.J. Gordon and R.A. Ford: *The Chemist's Companion*. Wiley-Interscience, New York: 1972, p. 40ff.

b. By binary and ternary eutectics the figures in parentheses give the portions in cmol/mol.

c. C.F. Poole, B.R. Kersten, S.S.J. Ho, M.E. Coddens, and K.G. Furton, *J. Chromatogr. 352*, 407 (1986).

d. Decomposition temperature.

The use of physical properties and fluid behavior from molecular thermodynamics can lead to better decision-making in the design of substitute solvents and can greatly reduce the expense and time required finding substitutes, compared to designing substitute solvents by experiment. Equilibrium and dynamic properties and the fluid behavior, which are important for designing substitute solvents, are useful properties. For each property, there is a rationale for using the property, the current level of understanding from molecular thermodynamics, the general methodology for estimating the property for single chemicals, and possible methods for liquid mixtures. In addition to bulk physical solvent properties such as viscosity, other solution properties such as activity coefficients are also important for designing substitute solvents (Zhao and Cabezas, 1998).

In the present context, the solvation of a solvent molecule in its own liquid (i.e., condensation from the vapor, the opposite of evaporation) is of interest (Ben-Naim and Marcus, 1984). The solvation properties of solvents (solvent effects) depend mainly on their polarity/polarizability (accounting also for dispersion interactions), hydrogen-bond donation and acceptance abilities, and cohesive energy density (Marcus, 1993).

The vaporization of solvent molecules from a pure liquid solvent should not differ from its vaporization from an infinitely dilute solution of some solutes(s) in it, since the vast majority of solvent molecules have other solvent molecules in their surroundings in both cases. Laboratory, industrial, chemical, or other waste products may have constituents that evolve volatile organic compounds (VOCs) at very high concentrations. These could pose human health risks during handling, storage, and disposal of the waste through inhalation, dermal exposure, or explosion. Additionally, the release of VOCs can adversely impact the tropospheric chemistry, and in the case of halogenated compounds, the stratospheric ozone chemistry as well, as discussed in the previous chapter (Pleil and Stroupe, 1994).

New insights are resulting from the increasing synergism between computer simulation and experimental elucidation of chemical processes in polar solvents. A detailed knowledge of solution-phase chemistry requires understanding the molecular motions that are involved in the reaction dynamics. Advances in laser technology, in particular femtosecond laser spectroscopy, now allow the direct measurement of the dynamical behavior of these chemical systems. Classical and quantum-mechanical dynamical simulations of chemical phenomena on time-scales made accessible by this new technology can be carried out using increasing computational power and new computational algorithms (Rossky and Simon, 1994). This will further aid in understanding solvation and its applicability to green solvents.

3.4.4.1 Solubility

Supercritical CO_2 is emerging as an environmentally friendly alternative solvent in various industrial and analytical processes. This solvent can provide both information and examples in solubility. CO_2 becomes a supercritical fluid at pressures greater than 1,100 psi and at temperatures at or above 88°F. Supercritical CO_2 has already found use in coffee decaffeination, wastewater treatment, and chemical analysis, and it is presently being studied for use in polymer manufacturing, pharmaceutical manufacturing, and soil remediation. According to John Rankin, a chemist working with the New York State Department of Environmental Conservation, the three main advantages of

supercritical CO_2 are speed, the inherent cleanliness of the extracts, and a substantial reduction in the volume of solvents used. The disadvantages are equipment cost and the small sample size obtained in supercritical CO_2 extraction (Kazarian et al., 1996).

New insights can emerge on solubility from studies on supercritical fluids. For example, Fourier transform IR spectroscopy is used to study the effects of solvent density on the H-bonding equilibrium between perfluoro-tert-butyl alcohol (PFTB), $(CF_3)_3COH$, and dimethyl ether (DME), $(CH_3)_2O$, in solution in SF_6 (T_c, 45.5°C; P_c, 540 psi; r_c 5.03 mol/L). The interaction of PFTB and DME is quite strong, and thus it has been possible to use rather more dilute solutions than in previous studies of H-bonding in supercritical fluids. Both PFTB and DME are highly volatile, so the equilibrium could be studied over the full range of densities of SF_6 from the pure gas phase (i.e., in the absence of SF_6) through the supercritical region to liquid-like densities ca. 10 mol/L (1.5 gm/L) and over the temperature range 20–65°C. Both qualitative and quantitative measurements have been made at constant temperature, constant pressure, and constant density. Qualitative studies show explicitly and without any spectroscopic assumptions that increasing density causes an increase in the concentration of free PFTB and a concomitant decrease in the concentration of the H-bonded PFTB/DME complex. More detailed measurements have allowed these changes to be quantified and modeled; particularly interesting are a) the variation of K_c with temperature at constant pressure (4.4 MPa), where the rapid increase in solvent density near the critical temperature cancels almost completely the effects of lowering the temperature, and b) the isothermal dependence of K_c with density, including the unusual behavior at 50°C in the density range ca. 3–6 mol/L of SF_6, behavior which is not observed at 60°C. This unusual behavior provides good evidence of enhanced solute–solute interactions toward the solvent critical temperature (Kazarian et al., 1993).

3.4.4.2 Cosolvent Roles

Current work with supercritical fluids can also illustrate the importance of cosolvents. Cosolvent effects in supercritical fluids can be considerable for systems where the cosolvent interacts strongly with the solute. A correlation suggests that both physical and chemical forces are important in the solvation process in polar cosolvent supercritical CO_2 mixtures. The model coupled with the correlation represents a step toward predicting solubilities in cosolvent-modified supercritical fluids using nonthermodynamic data. This method of modeling cosolvent effects allows a more intuitive interpretation of the data than either a purely physical equation of state or ideal chemical theory can provide (Ting et al., 1993).

3.4.4.3 Solvent Mixtures

The interaction between solvents is important. For example, the development of a successful crystallization process for purification and isolation of an organic compound requires the selection of a suitable solvent or solvent mixture; to date, no logical method has been established for determining the best solvent combination. The process chemist or engineer often employs a trial-and-error procedure to identify an appropriate solvent system, the success of which is dependent on experience and intuition. One approach utilizes a group-contribution method (UNIFAC) to predict a

value for the activity coefficient of the solute in a given solvent system at the saturation point. This value is then used to calculate the solubility of the solute at a "high" temperature and a "low" temperature. Implementation of this strategy will reduce product cycle time, minimize solvent usage, and allow identification of cheaper solvent alternatives (Nass, 1994).

A microbial polysaccharide (lactan gum) produced by bacterium ATCC 55046 was precipitated from fermentation broth by the addition of ethanol, acetone, isopropanol, or tert-butanol. Compositions of the precipitate and supernatant phases were determined as a function of organic solvent concentration and used to construct binodal solubility curves. Lactan did not precipitate at bulk-mixture organic solvent concentrations below 35% (wt) ethanol, 35% acetone, 33% isopropanol, or 25% *t*-butanol. At organic solvent concentrations just exceeding the solubility transition point, the precipitates were soft, moist, and sponge-like in texture, with low lactan concentrations. At higher organic solvent concentrations the precipitates were compact and dense. The maximum lactan concentration in the precipitate was 25–37%, depending on the organic solvent type and concentration. Increasing the organic solvent concentration beyond 50% for ethanol, or 70% for acetone, decreased the lactan concentration in the precipitate. No such decrease occurred for isopropanol and *t*-butanol. Thus, organic solvent usage, from greatest to least, was in the order ethanol, acetone, isopropanol, and *tert*-butanol, but the maximum lactan concentration in the precipitate, from greatest to least, was in the order acetone, isopropanol, ethanol, and tert-butanol (Foufopoulos and Etzel, 1996).

Solvent mixtures, when appropriately chosen, will positively affect chemical reactions. An organic-water interfacial synthesis technique has been developed which is based on the use of a surface-active catalyst complex in conjunction with an aqueous organic solvent mixture and an emulsifier to effect the desired reaction at the organic-water interface. Decoupling the various functions of the reaction medium and meeting them separately with a combination of aqueous and organic phases, instead of a single organic solvent, improves chances for an environmentally benign synthesis. The technique also offers other significant advantages, including the ease of catalyst recovery and processing, a high reactivity, selectivity and reproducibility under mild reaction conditions, and a greater versatility compared to phase-transfer, micellar, and other biphasic techniques (Lim and Zhong, 1996).

The previous extension of solvent mixtures involved solvent interfaces. This organic-water interfacial technique has been successfully extended to the synthesis of phenylacetic and phenylenediacetic acids based on the use of surface-active palladium-(4-dimethylaminophenyl)diphenylphosphine complex in conjunction with dodecyl sodium sulfate to effect the carbonylation of benzyl chloride and dichloro-*p*-xylene in a toluene-aqueous sodium hydroxide mixture. The product yields at 60°C and 1 atm are essentially quantitative based on the substrate conversions, although carbon monoxide also undergoes a slow hydrolysis reaction along with the carbonylation reactions. The side reaction produces formic acid and is catalyzed by aqueous base but not by palladium. The phosphine ligand is stable to the carbonylation reactions and the palladium can be recovered quantitatively as a compact emulsion between the organic and aqueous phases after the reaction, but the catalytic activity of the recovered palladium is about a third of its initial activity due to product inhibition (Zhong et al., 1996).

The excess molar volumes of 10–40 mol % methanol/CO_2 mixtures at 26°C as a function of pressure has been determined. The excess molar volumes varied with composition and pressure; significant interaction between CO_2 and methanol was noted from the observed excess molar volumes. To better characterize the interaction and its effect on analyte solubility, the partial molar volume of naphthalene at infinite dilution in liquid 10 and 40 mol % methanol/CO_2 mixtures was determined. The variation of the partial molar volume at infinite dilution with pressure correlated well with isothermal compressibility of the methanol/CO_2 mixtures (Souvignet and Olesik, 1995).

Effects of solvent mixtures can be seen in biochemical systems. Ligand binding to myoglobin in aqueous solution involves two kinetic components, one extramolecular and one intramolecular, which have been interpreted in terms of two sequential kinetic barriers. In mixed solvents and subzero temperatures, the outer barrier increases and the inner barrier splits into several components, giving rise to fast intramolecular recombination. Measurements of the corresponding solvent structural relaxation rates by frequency resolved calorimetry allows the discrimination between solvent composition and viscosity-related effects. The inner barrier and its coupling to structural relaxation appear to be independent of viscosity but change with solvent composition (Kleinert et al., 1998).

3.4.5 Tuning Solvents

Optimizing solvents and solvent mixtures can be done empirically or through modeling. An example of the latter involves a single Sanchez-Lacombe lattice fluid equation of state, used to model both phases for a polymer-supercritical fluid-cosolvent system. This method works well over a wide pressure range both volumetric and phase equilibrium properties for a cross-linked poly(dimethyl siloxane) phase in contact with CO_2 modified by a number of cosolvents (West et al., 1998).

Examples are the benefits in the area of extraction of vegetable cuticular waxes being separated from the more valuable essential oils, using supercritical CO_2 (Stassi and Schiraldi, 1994). A molecular understanding of how a phenomenon like supercritical behavior affects solvent properties is important (Kazarian and Poliakoff, 1995).

The benefits from tuning the solvent system can be tremendous. Again, remarkable opportunities exist for the fruitful exploitation of the special properties of supercritical and near-critical fluids as solvents for chemical reactions. Solution properties may be tuned, with thermodynamic conditions or cosolvents, to modify rates, yields, and selectivities, and supercritical fluids offer greatly enhanced mass transfer for heterogeneous reactions. Also, both supercritical fluids and near-critical water can often replace environmentally undesirable solvents or catalysts, or avoid undesirable byproducts. Furthermore, rational design of solvent systems can also modify reactions to facilitate process separations (Eckert and Chandler, 1998).

Remarkable tuning of reaction rates has been achieved for the isomerization of several dye molecules in supercritical fluid solvents using both small pressure changes and small additions of cosolvents. Rates of the thermal *cis-trans* relaxation were measured spectroscopically following irradiation for three dyes in supercritical carbon dioxide and ethane, pure and with several polar and protic cosolvents. These results demonstrate the versatility of supercritical fluid solvents, both to examine reaction mechanisms and as a means to tune rates (Dillow et al., 1998).

3.4.6 Evaluation of Solvents

A method, integral equation formalism (IEF), can treat solvent effects. It exploits a single common approach for dielectrics of very different nature: standard isotropic liquids, intrinsically anisotropic media like liquid crystals, and ionic solutions (Mennucci et al., 1997).

Modeling results can be utilized to predict the effects of solvent substitution. For example, the generalized Mulliken-Hush approach for the calculation of the electronic coupling matrix element for electron-transfer processes has been applied to two rigidly linked donor-bridge-acceptor systems having dimethoxyanthracene as the donor and a dicarbomethoxycyclobutene unit as the acceptor. The dependence of the electronic coupling matrix element is a function of bridge type with and without solvent molecules present. Solvents can have a dramatic effect on the electronic coupling matrix element. The behavior with variation of solvent is in good agreement with that observed experimentally for these systems (Cave et al., 1995).

The solvation dynamics following charge-transfer electronic excitation of diatomic solutes immersed in a methanol-water mixture provides a direct window on the molecular changes occurring upon solvent substitution. The solvation response of the mixtures is separated into methanol and water contributions in order to elucidate the role played by each molecular species on the solvation dynamics. Significantly different responses for the two solutes are found and related to the fact that the solute with the smaller site diameters is a much better hydrogen (H)-bond acceptor than the larger diameter solute (Skaf and Ladanyi, 1996).

A linear solvation energy relationship (LSER) has been developed to predict the water-supercritical CO_2 partition coefficients for a published collection of data. The independent variables in the model are empirically determined descriptors of the solute and solvent molecules. The LSER approach provides an average absolute relative deviation of 22% in the prediction of the water-supercritical CO_2 partition coefficients for the six solutes considered. Results suggest that other types of equilibrium processes in supercritical fluids may be modeled using a LSER approach (Lagalante and Bruno, 1998).

Supercritical fluids are versatile solvents in organic separations and extractions. The application of supercritical fluids to metal extractions is a recent extension of this technology. This application requires that three criteria be met: enhanced ligand selectivity/specificity, increased solubility of the ligand in the supercritical fluid, and ease of metal removal from the ligand after extraction. Recent research studied metal complexation and organometallic chemistry in supercritical fluids as a function of pressure and temperature. The application of these spectroscopic techniques to the investigation of inorganic species in supercritical fluids was described (Yonker et al., 1998).

Photochemistry can be used to demonstrate solvent effects in supercritical fluids. The analysis revealed trimodal fluorescence lifetime distributions near the critical temperature, which can be explained by the presence of solvent–solute and solute–solute clustering. This local aggregation causes an increase in nonradiative relaxations and, therefore, a decrease in the observed fluorescence lifetimes. Concentration and density gradients are responsible for these three unique lifetimes (trimodal) in the supercritical fluid, as contrasted with the single lifetime observed in a typical organic solvent. The

pressure has little or no effect on the clustering over the pressure range studied along an isotherm (Rhodes and Fox, 1996).

Modeling can be a predictive tool of solvation. Computer simulations have been performed in order to investigate the role hydroxylic solvents play in catalyzing the excited-state tautomerization of 7-azaindole (7-AI) and 1-azacarbazole (1-AC). Classical Monte Carlo and molecular dynamics methods were used to test the idea that reaction rates in these systems are controlled primarily by the fraction of solutes that are "correctly" solvated. Assuming that correct solvation involves formation of a cyclic 1:1 solute–solvent complex, reactive fractions were computed for a series of eight hydroxylic solvents: methanol, ethanol, 1-propanol, 2,2,2-trifluoroethanol, 2-propanol, tert-butyl alcohol, ethylene glycol, and water. In all cases the reactive fractions so calculated are small (< 2 %) and were of the correct magnitude to account for the relatively slow reaction observed in neat solvents. The underlying cause for these small reactive populations can be rationalized on the basis of the weak hydrogen bonds afforded by a cyclic arrangement (Mente, 1998).

The enthalpies of mixing water and five ethylene glycol oligomers ($C0E_j$; j = 1–5) were measured in an ideal dilute solution at seven temperatures from 283.15 to 313.15 K by using a high-accuracy isothermal titration calorimeter. The differential enthalpies of solution of C0Ej were evaluated by applying the thermodynamic equations to the experimental results. They were negative, and their absolute values increased with decreasing temperature and increasing oxyethylene chain length. It was shown that the dissolution of C0Ej is exothermic and that the interaction between water and C0Ej molecules is stronger than the average of interactions between the same species. It was shown that the partial molar heat capacities of C0Ej in an aqueous solution are increased from the molar heat capacities of the pure liquid state owing to hydration. The enthalpy of mixing of some protic solvents, that is, methanol, ethanol, 1-propanol, and ethylene glycol, with C0E5 was also measured to examine the hydration of the oxyethylene group. It was suggested by comparing the results of C0Ej with those of $C8E_j$ that the hydration of the hydrophobic group is also exothermic at a lower temperature and strongly dependent on temperature (Ohta et al., 1998).

Molecular dynamics computer simulations have been used in conjunction with statistical mechanical perturbation theory to examine the process by which water, ethanol, and ethylene glycol (1,2-ethanediol) molecules are transported from the vapor phase into bulk water. The calculated energetics for solvation in the bulk liquid and surface properties such as the surface tension of water and orientations of ethanol and ethylene glycol adsorbed at the water interface agree well with the corresponding experimental data. Although this dependence agrees with that predicted by the resistance model, the heights of the calculated barriers are again much lower than those predicted by the model (Taylor and Garrett, 1999).

3.5 Solvent Effects on Chemical Phenomena

3.5.1 Solution Composition

For a given solute, different solvents show different departures from ideal behavior, both in terms of the concentration required to observe the onset of such deviations and in terms of their direction and magnitude. For aqueous solutions the molality

scale, moles of solute per kg of water, denoted by *m*, is frequently used. This scale becomes less useful when several solvents are compared, since in one-kg batches of diverse solvents there are a variable number of moles of solvent and they occupy different volumes. Still, the molality scale is in common use for dilute electrolyte solutions in solvents used for electrochemical purposes, as it is for their aqueous solutions.

A commonly used solute concentration scale is the mole fraction one, x, which specifies directly the number of moles of solvent per mol of solute: $(1 - x)/x$. This number is of particular interest in the more concentrated solutions, where a lack of solvent molecules required to surround a solute particle and separate solute particles from one another greatly affects the properties of the solution. However, this scale is useful for the entire composition range, from very dilute solution to such solutions, mixtures, where it is difficult to designate one component as the solute and the other as the solvent. This scale requires knowledge of the chemical nature of the solute and the solvent in view of the necessity to specify a mole of each.

For many practical purposes, as well as for some theoretical purposes involving statistical thermodynamics, it is expedient to deal with the volume concentration, denoted by c or number density, denoted by ρ, that is, the number of moles, or molecules of the solute per unit volume of the solution. In dilute solutions the density is usually linear with the concentration, tending to the limiting value of that of the solvent at infinite dilution. There are different numbers of moles of solvent per unit volume in different solvents and at given molarities c or number densities ρ also per mole of solute. For typical solvents, there are from 55.5 mol for water down to 3.3 mol for hexadecane in 1 dm^3. This constitutes nominally a "solvent effect" that ought not to be neglected.

A further method for the specification of the composition of a solution or mixture, related to the molar scale, is the volume fraction of the solute, ϕ. This takes into account any change in the volume of the system that has taken place on the preparation of the solution-the volume (change) of mixing. Therefore for a solute I:

$$\phi_I = c_i v_I \tag{3.13}$$

where v_I is the partial molar volume of the solute in the solution in $dm^3 mol^{-1}$. The difference between these two volume fraction scales constitutes another nominal "solvent effect," due to the different volumes of mixing exhibited by different solvents.

3.5.2 Solvent Effects on Solubility and Partition

The dissolution of a solute in a solvent always affects the solvent–solvent interactions in the vicinity of the solute particles in addition to the solute–solvent interactions that take place (Marcus, 1998b). This may be viewed in several stages. First, a cavity in the solvent is formed, to accommodate the solute, which breaks down the cohesive forces of the solvent. Next dispersion forces take effect. They apply to nonpolar and hardly polarizable solutes and solvents, as well as to polar and polarizable ones. Other forces that become active provide contributions from interactions of polar molecules with polar or polarizable ones and from donor acceptor interactions, such as electron-pair or hydrogen-bond donation and acceptance, whether from or to the solute, the solvent, or both.

The standard molar Gibbs free energy of solution is:

$$\Delta_{solution} = G^{o} = -RT \ln x_2 \tag{3.14}$$

The Gibbs free energy of solution is the difference between the Gibbs free energy of solvation of the solute in the solvent and any Gibbs free energy of interaction in the pure solute that are lost on dissolution, if it is a solid, a liquid, or a nondilute gas.

To illustrate this a model transesterification reaction catalyzed by subtilisin Carlsberg suspended in carbon dioxide, propane, and mixtures of these solvents under pressure has been studied (Decarvalho et al., 1996). To account for solvent effects due to differences in water partitioning between the enzyme and the bulk solvents. Water sorption isotherms were measured for the enzyme in each solvent. Catalytic activity as a function of enzyme hydration was measured, and bell-shaped curves with maxima at the same enzyme hydration (12%) in all the solvents were obtained. The activity maxima were different in all media, being much higher in propane than in either CO_2 or the mixtures with 50 and 10% CO_2. Considerations based on the solvation ability of the solvents did not offer an explanation for the differences in catalytic activity observed. The results suggest that CO_2 has a direct adverse effect on the catalytic activity of subtilisin.

These studies can be taken further with quantum mechanical calculations. A non-Bornian theory has been proposed for the standard Gibbs free energy of ion transfer at the organic solvent–water interface. In this theory the ionic charge z-dependent term, which has so far been considered as describing electrostatic (i.e., long-range) ion–solvent interactions, is treated as describing the specific (short-range) interactions. A quantum chemical consideration has shown that the short-range interaction energy can be given by a quadratic function of the surface field strength (E) of an ion. It should also be noted that a hydrophilic ion, being preferentially hydrated in the O phase, is assumed to transfer across the interface as the hydrated ion. Regression analyses have shown that in accord with the theory, the z-dependent term can be given by a quadratic function of E for each group of ions. The present theory has been found to be useful for the prediction of similar properties for some hydrophilic ions (Osakai and Kuniyoshi, 1998).

3.5.3 Fundamental Considerations

The following considerations lead to the thermodynamics of dissolution, to the values of the solubility, and to the solvent effects on solubility. When a gaseous solute dissolves in a solvent, provided that its pressure in the gas phase is low or moderate, then its behavior in that phase can be taken to be approximately ideal, that is, interactions in the gas phase are lost on the dissolution. For a solute that is liquid when pure, the interactions among its molecules in the liquid are lost on the dissolution. These lost interactions in the pure liquid are estimated from the enthalpy of vaporization and these are replaced by the solvation enthalpy on dissolution. The corresponding entropy change is estimated from the difference of volume at the disposal of the solute molecules in the solution and the liquid solute and any changes in entropy due to changes in the internal degree of freedom, rotation, and vibration. However, such entropy changes are rather small. A solute that is solid in the pure state can be considered first to form a hypothetical undercooled liquid at the temperature of dissolution, with

appropriate enthalpy and entropy changes. Then it can be treated as a liquid solute (Ben-Naim, 1985).

On the assumption that the solutions are dilute and that there is no direct association of the solute with the solvent, then the only way that the solvent affects the solubility is via its solubility parameter, δ_1. For a given solute and since the term involving δ_1 is negative, the more the solubility parameter of the solvent differs from that of the solute, the lower the solubility (Barton, 1983).

Provided a singly charged, spherically symmetrical ion has a radius greater than ca. 0.2 nm, its distribution to a nonaqueous solvent from water can be accounted for by assigning to it a Hildebrand solubility parameter estimated for an uncharged atom or molecule, regardless of the model assumed for the Gibbs energy of charging the ion in the nonaqueous phase. For smaller ions, however, no choice of solubility parameter or ion size can alone account for their extractability. The extensive data available for the Gibbs energy of transfer of monovalent ions from water to a variety of solvents can be accounted for by assigning to the ion, in addition to a plausible solubility parameter, an effective radius $rs = (r_i^3 + rs^3)^{1/3}$, wherein r_i is the radius of the ion and rs is an adjustable distance characteristic of the solvent. Separate sets of rs values are needed for cations and anions. The distance rs can be predicted for cations from the molar volume of the solvent and its hydrogen-bond acceptance index b. For anions, rs can be predicted from the molar volume and the hydrogen-bond donation index a. On the basis of these correlations, expressions are derived for predicting the extractability of a singly charged, approximately spherical ion and its activity coefficient in the nonaqueous phase (Baes and Moyer, 1997).

A simple expression governs the solubility of a liquid solute in a solvent, provided the solvent is practically insoluble in the liquid solute and that, again, only dispersion forces are operative between them. For a given liquid solute, the solubility parameter of the solvent dictates the solubility and constitutes entirely the solvent effect on it.

The solubility of a solid, provided that it does not form crystal solvates, or solid solutions, with the solvent but remains as a pure solid, and provided again that only dispersion forces are operative, is given approximately by:

$$\ln x_2 \approx \Delta_F S(T_F - T)/RT - V_2\phi^2{}_1(_1 - \delta_2)^2/RT \qquad (3.15)$$

Solutes that, whatever their state of aggregation, undergo solvation interactions with the solvent beyond those due to dispersion forces, exhibit specific contributions to the solubility, that can be attributed to dipole–dipole and dipole-induced dipole interactions and electron-pair or hydrogen-bond donation by the solvent to the solute or vice versa.

3.5.4 Solvent Effects on Chemical Equilibria

The solvent affects the chemical equilibria of reactions. Second-order rate constants and equilibrium constants have been determined for the benzoate ion promoted deprotonation reactions of (*m*-nitrophenyl)nitromethane, (*p*-nitrophenyl)nitromethane, and (3,5-dinitrophenyl)nitromethane in methanol solution. The pKa values for the arylnitromethanes in methanol are the following: pKa = 10.9, 10.5, and 9.86 for (*m*-nitrophenyl)nitromethane, (*p*-nitrophenyl)nitromethane, and (3,5-dinitrophenyl)nitromethane, respectively, relative to benzoic acid (pKa = 9.4). A Bronsted B value of

0.50 and a CH value of 1.31 have been calculated for the 3,4-dimethylbenzoate, benzoate, m-bromobenzoate, and 3,4-dichlorobenzoate ion promoted reactions of (3,5-dinitrophenyl)nitromethane, and for the benzoate ion promoted reactions of (*m*-nitrophenyl)nitromethane, (*p*-nitrophenyl)nitromethane, and (3,5-dinitrophenyl)nitromethane, respectively. The log of the intrinsic rate constants for benzoate ion promoted deprotonations of (m-nitrophenyl)nitromethane, (p-nitrophenyl)nitromethane, and (3,5-dinitrophenyl)nitromethane are 0.0212, 0.270, and 0.877, respectively. These values are 6.3×10^4, 2.0×10^4 and 2.5×10^4 times lower than for the same reactions in acetonitrile solution. The results suggest that the observed solvent effect is a result of an imbalanced transition state (i.e., PNS effects), and a stronger transition-state hydrogen bond between the carbon acid and benzoate ion in acetonitrile than in methanol solution (Gandler et al., 1997).

In moderately dilute solutions the activity coefficients do depart from unity but to a limited extent. If the reactants and products are all uncharged but of similar sizes, and of equal number, that is, the stoichiometric coefficients for the reaction are the same on both sides, then the logarithm of activity coefficient quotient may still be negligible. This is no longer the case when either the reactants or the products are charged, for example, $CH_3COOH \Leftrightarrow CH_3COO^- + H^+$ or both are charged but with different algebraic charge numbers z, for example, for $Cd^{2+} + Br^- \Leftrightarrow CdBr^+$. In such cases solute–solute interactions manifest themselves through the relative permittivity ε of the solvent, and this constitutes a clear-cut solvent effect on the equilibrium quotient.

Another example is the hydroperoxy radical. The structure of HO_2 has been investigated, and a series of alkyl peroxyl radicals ROO· using a variety of quantum-mechanical methods. The geometries, vibrational frequencies, electronic charge distributions, and spin densities for the series of radicals considered in the gas phase were calculated. Significant differences with respect to previous calculations have been pointed out in a few cases. In particular, the fundamental importance of electronic correlation when computing net atomic charges and spin densities, which have generally been estimated in the literature by means of Hartree-Fock SCF electronic densities, were shown. Solvation effects on the geometry and electronic structure were estimated by carrying out self-consistent reaction field computations in a polarizable continuum environment with relative dielectric permittivity equal to that of liquid water. This may be important in order to understand reactive properties of the radicals in different media (Aplincourt et al., 1999).

The differences in solvation of the reactants and the products constitute in general the major difference between the driving force for the equilibrium reaction in solution and that in the gas phase. The molar Gibbs free energy of solvation for any species I that participates in the equilibrium in a given solvent S can be written as

$$\Delta G^*_I = A_{\omega\delta} V_i \delta^2_S + A_{\sigma\pi} s_I \pi^*_S + A_{ba} B_I \alpha_S + A_{\alpha b} \alpha_\iota \beta_S \tag{3.16}$$

The molar volume V_I should strictly be taken as the partial molar volume which is normally unknown or the intrinsic volume of the solute species, rather than its molar volume when pure, or as a hypothetical supercooled liquid when the neat solute is a solid at the working temperature.

Not shown explicitly in the previous equation are the number Δns of solvent molecules released or consumed in the equilibrium, and in the general case, this can only be roughly estimated, if at all. In some cases many of the solvating molecules are

released, as when an uncharged contact ion pair is formed from a cation and an anion of equal formal charge. The dipolar ion pair is assumed to be much less solvated than its separate ionic partners. On the contrary, acid dissociation generally causes solvent molecules to be sequestered, since the resulting hydrogen ion and anion are considerably more solvated than the parent undissociated acid. The solvent effect due to this change of the numbers of solvent molecules involved in the reaction, Δn_s, is in many cases considerable.

Even for a simple reaction, involving just one reactant species and one product species, such as a keto-enol tautomerism or a *cis-trans* isomerization, the above equation for a given solvent is complicated. Still, in specific cases it is possible to unravel the solvent effects of cavity formation, for the solute species have different volumes, polarity/polarizability if the solute species differ in their dipole moments or polarizabilities, and solvent Lewis acidity and basicity if the solutes differ in their electron-pair and hydrogen-bond acceptance abilities.

An investigation of keto-enol tautomerism for perfluorinated keto-enol systems was undertaken. N-methylpyrrolidone (NMP) catalyzes equilibration of the keto and enol forms, but if used in more than trace amounts, it drives the equilibrium strongly toward enol because of hydrogen bonding to the amide. The enol is much more thermodynamically stable than its ketone, and it was found that in mildly Lewis basic solvents, such as ether, THF, acetonitrile, and NMP, the enolization equilibrium lies too far right to allow detection of ketone (Correa et al., 1994).

Not only is the extent of the equilibrium reaction, that is, the ratio of the concentrations of the products to those of the reactants, governed by the initial composition and the equilibrium constant, affected by the solvent, so also is the temperature dependence, that is, the enthalpy and entropy of the reaction. There is again a complicated interplay in the solvation of the two species between polarity and hydrogen-bonding abilities of the solvents. The negative entropies of this reaction, that become more negative along the same sequence, are due more to the solute properties than the solvent ones.

Vapor sorption capacities on a high-organic-content peat, a model for soil organic matter (SOM), were determined at room temperature for the following liquids: n-hexane, 1,4-dioxane, nitroethane, acetone, acetonitrile, 1-propanol, ethanol, and methanol. These data are used to evaluate the effect of polarity on the vapor partition in SOM. The extrapolated liquid solubility from the vapor isotherm increases sharply from 3–6 wt % for low-polarity liquids (hexane, CT, and benzene) to 62 wt % for polar methanol and correlates positively with the liquid's component solubility parameters for polar interaction (p) and hydrogen bonding (h). The large solubility disparity in SOM between polar and nonpolar solutes suggests that the accurate prediction of K_{om} from K_{ow} or Sw (solute water solubility) would be limited to compounds of similar polarity (Chiou and Kile, 1994).

3.5.5 Solvent Effects on Reaction Rates

The rate constant for a chemical reaction in solution, k, is generally expressed in terms of the transition state theory as:

$$k = A_k \exp(-\Delta G^{\neq} / RT) \tag{3.17}$$

Here the pre-exponential factor A_k is the product of a temperature-dependent constant $(k_BT/h) = 2 \times 10^{10} Ts^{-1}$, where k_B and h are the Boltzmann and Planck constants, and a solvent-specific coefficient that relates to both the solvent viscosity and to its orientational relaxation rate. This coefficient may be near unity for very mobile solvent molecules but may be considerably less than unity for viscous or orientationally hindered highly structured solvents. The exponential factor involves the activation Gibbs energy that describes the height of the barrier to the formation of the activated complex from the reactants. It also describes temperature and pressure dependencies of the reaction rate. It is assumed that the activated complex is in equilibrium with the reactants, but that its change to form the products is rapid and independent of its environment in the solution (de Sainte Claire et al., 1997).

The barrier that the reaction must overcome in order to proceed is determined by the difference in the solvation of the activated complex and the reactants. The activated complex itself is generally considered to be a transitory moiety, which cannot be isolated for its solvation properties to be studied, but in rare cases it is a reactive intermediate of a finite lifetime. The solvation properties of the activated complex must generally be inferred from its postulated chemical composition and conformation, whereas those of the reactants can be studied independently of the reaction. For organic nucleophilic substitution reactions, the Hughes-Ingold rules permit qualitative predictions on the behavior of the rate when the polarity increases in a series of solvents, as is shown in Reichardt (Reichardt, 1988).

The effect of pressure on the measured bimolecular rate constant of the Diels-Alder reaction between maleic anhydride and isoprene was investigated in supercritical CO_2 and subcritical propane. The reaction was carried out at 35°C in CO_2 and 80°C in propane. The rate constants in supercritical CO_2 agreed closely with the thermodynamic pressure effect predictions over the entire pressure range. The rate constants in the subcritical propane solvent significantly diverged from the thermodynamic pressure effect predictions and were found to deviate from this linear density dependence at the lower pressures studied. The results show solvent–solute and cosolvent–solute interaction (Reaves and Roberts, 1999).

The general rule is that if net charge is created, or destroyed, in the activated complex relative to the reactants, then there is a large positive, or negative, effect of increasing solvent polarity on the rate. But if the net amount of charge is kept unchanged while it becomes more dispersed, the effects are relatively small. If no change in the charge distribution takes place upon the formation of the activated complex, the change of solvent polarity has but a very small effect.

It is assumed in the Hughes-Ingold rules that the entropy of activation is small relative to the enthalpy of activation, that is, $\Delta G^{\neq} \approx \Delta H^{\neq}$, and that the temperature effect on the rate follows with an assumed temperature independent value of $\Delta H^{\neq}$. If the number of solvent molecules solvating the activated complex is very different from that solvating the reactants, then this assumption is no longer valid. This is the case in the solvolysis of *t*-butyl chloride in water compared to, say, ethanol.

The S_N1 activation free energies and transition-state structure for the series *t*-butyl chloride, -bromide, and -iodide in several solvents over a wide polarity range have been examined theoretically. The analysis is accomplished by using a two-state valence bond representation for the solute electronic structure, in combination with a two-dimensional free energy formalism in terms of the alkyl halide nuclear separation

coordinate and a solvent coordinate. The calculated *t*-butyl halide activation free energies are in good agreement with experiment. In a fixed solvent, a decreasing activation free energy trend is found (Cl : Br : I), as well as a decreasing transition-state ionic character. Both fixed solvent trends, and others, are shown to arise from a decreasing electronic coupling variation between the covalent and ionic solute valence bond states. In addition, it is also demonstrated how a Bronsted plot for each halide in solvents of different polarity, whose slope is shown analytically to be proportional to the square of the transition state ionic character, could be used as an experimental test of these unconventional predictions (Mathis et al., 1993).

A model has been considered for S_N2 reactions, based on two interacting states. Relevant bond energies, standard electrode potentials, solvent contributions (nonequilibrium polarization), and steric effects are included. Applications of the theory are made to the cross-relation between rate constants of cross- and identity reactions, experimental entropies and energies of activation, the relative rates of S_N2 and ET reactions, and the possible expediting of an outer sphere ET reaction by an incipient S_N2-type interaction (Marcus, 1997).

3.5.6 Solvent Effects on Spectroscopy

Spectroscopy provides a window to explain solvent effects. The solvent effects on spectroscopic properties, that is, electronic excitation, leading to absorption spectra in the ultraviolet and/or visible range, of solutes in solution are due to differences in the solvation of the ground and excited states of the solute. Such differences take place when there is an appreciable difference in the charge distribution in the two states, often accompanied by a profound change in the dipole moments. The excited state, in contrast with the transition state discussed above, is not in equilibrium with the surrounding solvent, since the time-scale for electronic excitation is too short for the readjustment of the positions of the atoms of the solute (the Franck-Condon principle) or of the orientation and position of the solvent shell around it.

A template effect by solvent was found in the synthesis of self-assembled capsules. Experimental evidence shows that the solvent molecules control the covalent bond formation through molecular recognition within the monomeric tetrahedral intermediate. It is proposed that solvation effects can be treated as a subset of molecular recognition events (Tokunaga et al., 1998).

The solvent effect is termed solvatochromism and is described in terms of the shifting of the peak position of the lowest energy, longest wavelength, spectral absorption peak. This can be *hypsochromic* (blue shift, negative solvatochromism) when the shift is to lower wavelengths, that is, to higher energies. The solvent effect is *bathochromic* (red shift, positive solvatochromism) when the shift is to longer wavelengths, that is, to lower energies. The former effect takes place when the ground state is more dipolar than the excited state, whereas the opposite occurs when the excited state is the more dipolar one. These shifts pertain to the energy gap between the ground and excited states, and therefore do not tell directly which of these states (or both, to different extents) has its potential energy lowered by the better solvation.

Solvatochromic shifts of the five probe indicators, 2-nitroaniline, 4-nitroaniline, 4-nitroanisole, 4-nitrophenol, and N,N-dimethyl-4-nitroaniline, have been used to specify the solvatochromic solubility parameters π^* and beta of the five pure fluids CO_2,

N_2O, $CClF_3$, SF_6, and NH_3 according to Kamlet, Abboud, and Taft by means of UV/VIS spectroscopy. Plotting π^* versus reduced density of any fluid results in steeply increasing curves with maximum enhanced π^* data at reduced densities of about 0.6 which continuously level out and finally rise again asymptotically as straight lines (Maiwald and Schneider, 1998).

Spectroscopy can also provide insight into the dynamic effects of solvents. Changes in the spectra of metal complexes due to solvent effects are generally related to changes in the geometry and certain distances of the ligands relative to the central metal atom in the complexes, which are accompanied by electronic transitions between orbitals localized on the metal atom. This suggests that the observed solvatochromism of some iron(III)-catecholato chromophores is basically due to the difference in solvation enthalpies of the two electronic transitions in their states of vibrational equilibrium. The effects of the solvent reorganization energies do not appear to be relevant (Dei, 1993).

When a nonpolar solute is in solution in any solvent, either nonpolar or polar, then mainly dispersive forces operate between them, and any solvent effects are very small and bathochromic (Reichardt, 1988), increasing with the polarizability of the solvent. If the solute is dipolar in a nonpolar solvent, then both hypso- and bathochromic shifts, increasing with solvent polarizability, are possible, depending on the dipole moments of the ground and excited states. The situation becomes more complicated for a dipolar solute in a dipolar solvent.

The solvatochromic effects on UV/visible spectra of certain solutes are so large, that they can conveniently be employed as probes for certain solvating properties of the solvents.

In the case of fluorescence spectra, it is the emission of the radiation from the excited state that is measured, rather than its absorption. This also provides valuable information. As an example, tetraethylorthosilicate (TEOS)-based gels were doped with two optically active organic indicators, thionin and nile blue A. Before trapping in a solgel host, thionin and nile blue A were both evaluated for solvent and protonation effects on their spectral properties. Only extreme pH values provided by HCl, NaOH, and NH_4OH produced new absorption and/or fluorescence bands. The absorption and fluorescence spectra revealed a decrease in a pH 11 solution of NH_4OH compared to neutral conditions (Krihak et al., 1997).

There are also profound solvent effects on the vibrational, that is, IR and Raman spectra, of many solutes. A large number of bond vibrations have been studied in this respect, those for stretching of carbonyl (C=O) and hydroxyl, rather, O-D bonds, perhaps, more extensively than others, involving bond stretching and the bending, rocking, and so on, of groups of atoms of solutes in various solvents. Spectra of the mixed-valence complexes $((bpy)_2ClOs(L)Ru(NH_3)_5)^{4+}$ (L = 4,4′-bipyridine, pyrazine; bpy = 2,2′-bipyridine) are highly solvent dependent. They provide oxidation state specific spectral markers which show that oxidation states for L = 4,4′-bpy are OsIII-RuII in solvents of donor number (DN) : 14. Because of the difference in the extent of electronic delocalization between the two isomers, intramolecular electronic transfer is a complex event involving coupled electronic and nuclear motions. There is no simple relationship between optical and thermal electron transfer (Neyhart et al., 1996).

Solvation effects on the conformation of esters of three *p*-substituted 1-phenylethanols with 2-fluoro-2-phenyl acetic acid (FCDA) were studied both experimentally (in five solvents ranging from $CDCl_3$ to DMSO) and quantum mechanically. Semi-empirical (AM1 of MJS Dewar and PM3 of JJP Stewart) and *ab initio* (RHF/3–21 G) calculations were undertaken. Energy maps for the conformers of the esters as a function of the dihedral angles alpha (F-C-alpha acid-C=O) and beta (CO-O-C-alcohol-H) were obtained. Solvent effect calculations, through the self-consistent reaction field on the most stable conformers, were also carried out (Hamman et al., 1996).

Solvent effects on nuclear magnetic resonance (NMR) spectra have been studied extensively, and they are described mainly in terms of the observed chemical shifts, δ, corrected for the solvent bulk magnetic susceptibility. In all cases there is, again, a tradeoff between nonspecific dipole–dipole and dipole-induced dipole effects and those ascribable to specific electron-pair donation of the solvent to the solute or vice versa to form solvates. In basic mixtures of the molten salt composed of aluminum chloride and 1-ethyl-3-methylimidazolium chloride, proton, in the absence of oxides, is partitioned between hydrogen chloride and hydrogen dichloride ion. The equilibrium between these two species has been examined by ^2H and ^1H NMR spectroscopies. An equilibrium isotope effect of 0.712 was calculated from hydrogen chloride and hydrogen dichloride vibrational frequencies. Analysis of the temperature dependence of the hydrogen chloride/dichloride equilibrium constant gave values for the enthalpy of reaction, H_{RXN}, and the entropy of reaction, S_{RXN}, of −9.8 (plus or minus) 0.8 kJ mol-1 and 4.8 (plus or minus) 2.5 J mol-1 K-1, respectively. Comparison of the H_{RXN} for the hydrogen chloride/dichloride equilibrium in the melts with values obtained for other solvents suggests that the melt interacts more strongly with chloride ion than with hydrogen dichloride ion (Trulove et al., 1993).

There are many more solvent effects on spectroscopic quantities, that cannot be even briefly discussed here, and more specialized works on solvent effects should be consulted. These solvent effects include effects on the line shape and particularly line width of the nuclear magnetic resonance signals and their spin–spin coupling constants, solvent effects on electron spin resonance (ESR) spectra, on circular dichroism (CD) and optical rotatory dispersion (ORD), on vibrational line shapes in both the infrared and the UV/visible spectral ranges, among others.

3.5.7 Solvent Effects in Electrochemistry

The importance of solvents and their effects play roles in electrochemistry as well. The properties of a family of novel quaternary ammonium salts based on the bis(trifluoromethylsulfonyl)imide and triflate anions are reported in a paper by Sun (Sun et al., 1998). Binary phase diagrams for some of their mixtures and their electrochemical windows of stability were reported. The highest conductivity observed in the pure salt systems at 25°C was 7×10^{-4} S cm-1. An electrochemical window of stability of up to 5V was measured on graphite electrodes. The effect of salt structure and solvent on conductivity of the salts is also discussed.

Solvent effects in electrochemistry are relevant to those solvents that facilitate conductivities and electrode reactions. Together with the relative permittivity, that is responsible for the number of charge carriers per unit volume of the solution, the solvent

viscosity, η, are among the bulk properties that are responsible for the differences of the conductivities of electrolytes in different solvents.

A solvent, in addition to permitting the ionic charges to separate and the electrolyte solution to conduct an electrical current, also solvates the discrete ions, by ion–dipole or ion-induced dipole interactions and by more direct interactions, such as hydrogen bonding to anions or electron-pair donation to cations. Lewis acidity and basicity of the solvents affect the latter. The redox properties of the ions at an electrode depend on their being solvated, and the solvation effects electrode potentials or polarographic half-wave potentials.

Additional solvent effects, like ion pairing, occur in not-so dilute solutions. At higher concentrations in solution with bulky solvents, a lack of sufficient solvent dilution may take place. Neighboring ions will share solvent molecules.

3.5.8 Solvation Effect on Kinetic Rate Constant

Chemical reactions at supercritical conditions are good examples of solvation effects on rate constants. While the most compelling reason to carry out reactions at (near) supercritical conditions is the ability to tune the solvation conditions of the medium (chemical potentials) and attenuate transport limitations by adjustment of the system pressure and/or temperature, there has been considerable speculation on explanations for the *unusual* behavior (occasionally referred to as *anomalies*) in reaction kinetics at near and supercritical conditions. True near-critical anomalies in reaction equilibrium, if any, will only appear within an extremely small neighborhood of the system's critical point, which is unattainable for all practical purposes. This is because the near-critical anomaly in the equilibrium extent of the reaction has the same near-critical behavior as the internal energy. However, it is not as clear that the kinetics of reactions should be free of anomalies in the near-critical region. Therefore, a more accurate description of *solvent effect* on the kinetic rate constant of reactions conducted in or near supercritical media is desirable (Chialvo et al., 1998).

It has been suggested that the experimental isothermal kinetic rate constants of some reactions at near and supercritical conditions could not be explained solely by the thermodynamic pressure effect, but from the combination of local composition enhancement and density augmentation around reactants.

Although these variations on the TS theory argument have often been successful in providing qualitative agreement with experimentally observed trends, they have not yielded quantitative predictions of the solvation effect on the reaction rate.

The use of physical properties and fluid behavior from molecular thermodynamics can lead to better decision-making in the design of substitute solvents and can greatly reduce the expense and time required to find substitutes compared to designing substitute solvents by experiment. A previously cited paper (Zhao and Cabezas, 1998) systematically discusses the equilibrium and dynamic properties and the fluid behavior, which are important for designing substitute solvents. For each property, it discusses the rationale for using the property, the current level of understanding from molecular thermodynamics, the general methodology for estimating the property for single chemicals, and suggested methods for liquid mixtures. In addition to bulk physical solvent properties such as viscosity, other solution properties such as activity coefficients are also important for designing substitute solvents.

3.6 Solvent Roles

Although water is the most abundant liquid on this planet, and is essential for living systems, nonaqueous liquids are widely used as solvents. Most chemists routinely use solvents other than water in their work. The summary of these applications is shown below (and expanded in chapter 1).

- Synthetic chemistry
- Analytical chemistry
- Spectroscopy
- Chromatography
- Crystallography
- Electrochemistry

3.6.1 Examples of Solvent Roles

Let's look at a few examples of how solvents affect the outcome of chemical processes. The effect of arm molecular weight (MW), temperature, solvent composition, and divinylbenzene (DVB) concentration on the development of multiarm star-branched polyisobutylenes was studied. The rate of star formation and the weight-average number of arms per star polymer scaled inversely with MW. The star formation was faster at −80°C than at 23°C, regardless of solvent composition. Some reactions containing chloromethane were immediately warmed to 23°C after DVB addition. The strong influence of the initial chloromethane content on the rate of star formation persisted throughout the star-forming reaction, even when the solvent was immediately converted to 100% hexane. The fraction of unlinked arms was higher at higher temperature and at lower solvent polarity (Storey and Shoemake, 1998).

3.6.1.1 Ionic Liquids

Ionic liquids are a class of solvents and they are the subject of keen research interest in chemistry (Freemantle, 1998). Hydrophobic ionic liquids with low melting points (from −30°C to ambient temperature) have been synthesized and investigated, based on 1,3-dialkyl imidazolium cations and hydrophobic anions. Other imidazolium molten salts with hydrophilic anions and thus water-soluble are also of interest. NMR and elemental analysis have characterized the molten salts. Their density, melting point, viscosity, conductivity, refractive index, electrochemical window, thermal stability, and miscibility with water and organic solvents were determined. The influence of the alkyl substituents in 1, 2, 3, and 4(5)-positions on the imidazolium cation on these properties has been scrutinized. Viscosities as low as 35 cP (for 1-ethyl-3-methylimidazolium bis((trifluoromethyl)sulfonyl)amide (bis(triflyl)amide) and trifluoroacetate) and conductivities as high as 9.6 mS/cm were obtained. Photophysical probe studies were carried out to establish more precisely the solvent properties of 1-ethyl-3-methylimidazolium bis((trifluoromethyl)sulfonyl)amide. The hydrophobic molten salts are promising solvents for electrochemical, photovoltaic, and synthetic applications (Bonhote et al., 1996).

Molten sodium tetrachloroaluminate (a 1:1 mixture of NaCl and $AlCl_3$) is a good reaction medium for the Friedel-Crafts acylation reaction given in fig. 3.3 (Wade et al., 1979). Whereas the classical procedure for the synthesis of 1-indane from 3-phenylpropanoic acid consists of three reaction steps with a total reaction time of ca. six hours (Gattermann et al., 1982), the molten salt reaction is finished in five minutes and gives an even better yield (Wade et al., 1979).

A 1:2 mixture of 1-methyl-3-ethylimidazolium chloride and aluminum trichloride, an ionic liquid that melts below room temperature, has been recommended recently as solvent and catalyst for Friedel-Crafts alkylation and acylation reactions of aromatics (Boon et al., 1986), and as solvent for UV/Vis- and IR-spectroscopic investigations of transition metal halide complexes (Appleby et al., 1986). The corresponding 1-methyl-3-ethylimidazolium tetrachloroborate (as well as *n*-butylpyridinium tetrachloroborate) represent new molten salt solvent systems, stable and liquid at room temperature (Williams et al., 1986).

Organic molten salts such as tris-*n*-butyl-dodecylphosphonium halides (melting point below 40°C) have been used as reaction media for nucleophilic aromatic substitution of aryl tosylates by halide ions (Fry and Pienta, 1985).

3.6.1.2 Supercritical Fluids

A third example can be taken from analytical chemistry. Absorption and resonance Raman spectra of phenol blue were measured in liquid and supercritical solvents to determine the solvent dependence of absorption bandwidth and spectral shifts. Good correlation between absorption peak shift and resonance Raman bands and between Raman bands and bandwidth of C-N stretching mode were observed while anomalous solvent effect on the absorption bandwidth occurred in liquid solvents. Large bandwidths of absorption and resonance Raman spectra were seen in supercritical solvents as compared to liquid solvents. This was due to the small refractive indices of the supercritical solvents. The large refractive index of the liquid solvents only make the absorption peak shifts without broadening the absorption spectra (Yamaguchi et al., 1997).

A paper by Poliakoff highlights some of the properties of supercritical fluids, especially supercritical CO_2, which offer particular advantages for the handling of poly-

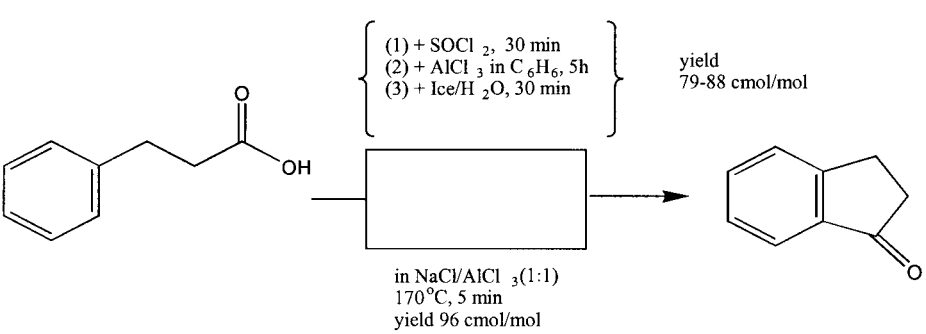


Figure 3.3 Friedel-Crafts acylation.

mers, metal complexes, and the environmentally more friendly synthesis and manufacture of chemicals (Poliakoff et al., 1999). The paper includes some of his research from the University of Nottingham and a number of recent reviews, which together provide a comprehensive introduction to this important field.

3.6.1.3 Catalysis

As we will see later in the book, a great deal of research in green chemistry pertains to catalysis. Recent work in lanthanide catalysis in aqueous media is an area of heightened interest. The use of Ln(OTf)(Otf-triflate) in organic reactions, including aza-Diels-Alder reaction, reactions of indole with aldehydes, and catalysis on solid support was discussed in a recent article by Zhang. An emphasis is placed on the synthetic applications and their contribution to green technology by using environmentally friendly solvents (Zhang et al., 1999).

3.7 Solvent Effects and Green Chemistry

To go from experimental observations of solvent effects to an understanding of them requires a conceptual basis that, in one approach, is provided by physical models such as theories of molecular structure or of the liquid state. For instance, although all chemists share intuitive notions of the concept of polarity, based on the expected ability of a solvent to solvate (stabilize) a charged species, the exact meaning of polarity is unspecified. Thus, we can readily agree that the solvents water, ethanol, acetonitrile, and cyclohexane are listed in order of decreasing polarity, although we might be unable to agree on a ranking of acetic acid, *t*-butyl alcohol, diethyl ether, and acetone.

Ultimately physical theories should be expressed in quantitative terms for testing and use, but because of the complexity of liquid systems this can only be accomplished by making severe approximations. For example, it is often necessary to treat the solvent as a continuous homogeneous medium characterized by bulk properties such as dielectric constant and density, whereas we know that the solvent is a molecular assemblage with short-range structure. For an example of this tool with supercritical fluids see Ting et al., 1993.

3.7.1 Empirical Correlations

Another method for studying solvent effects is the extrathermodynamic approach. For example, we might seek a correlation between log (k_A/k_A^{o}) for a reaction A carried out in a series of solvents and log (k_R/k_R^{o}) for a reference or model reaction carried out in the same series of solvents. A linear plot of log (k_A/k_A^{o}) against log (k_R/k_R^{o}) is an example of a linear free energy relationship (LFER). As an example of this tool, the reader can see de Sainte Claire (de Sainte Claire et al., 1997). As with structure-reactivity relationships, these solvent-reactivity relationships can be useful to us, but they have limitations.

The benefit of such LFERs is that they establish patterns of regular behavior, isolating apparent simplicity and defining normal or expected reactivity. The essential

weakness of the correlation approach is that it lacks a "linkage" to molecular events. A correlation is not a cause-effect relationship. Such an LFER was used by Stevenson (Stevenson et al., 1991) to probe a linear free energy relationship for an equilibrium isotope effect.

3.7.2 Green Solvents

The possibilities within green chemistry are as numerous as those in chemistry in general. Barry Trost succinctly described this in a recent book (Trost, 1998). If establishing the safety of the final end use compounds is important, this has to become an integral part of the process of developing new products. On the other hand, developing the chemical processes by which the end-use products are made has not been a generally recognized part. This is now recognized as important. Making chemical manufacturing more environmentally benign by design must now become an integral part of the product development process. There are many dimensions to this issue. The development and use of solvents that pose reduced hazard to mankind and the environment is one facet of this issue. Using raw materials more efficiently and generating less waste is another. For example in synthesis, the utilization of solvents in reactions that yield simple products, which are the sum of the reactants with anything else needed only catalytically becomes a goal. To realize such a goal, the repertoire of synthetically useful solvents must be greatly increased.

Note

1. Chemometrics has been defined as the application of mathematical and statistical methods to chemical measurements, in particular in providing maximum chemical information through the analysis of chemical data. Because of the enormous increase in generating analytical data, analytical chemists were among the first to use chemometrical methods extensively.

4

Green Solvents in Green Chemistry

4.1 Definition of Green Solvents

The criteria for what determines a green solvent will depend upon the use and ultimate fate of the solvent during the chemical process. Likewise, the determination of what constitutes appropriate solvent usage in green chemistry might include any of the following actions.

- Redesign of the exact chemical nature of the solvent via synthesis;
- Identification of equally useful but less toxic substitutes of another chemical class for use instead of a "traditional" solvent; or
- Reduction/elimination of the use of solvents in particular chemical processes.

The discussion of green solvents will include chemistry, ecology, and philosophy. The choice of solvents will include new criteria in addition to the traditional considerations of synthesis yield (if we are dealing with reactions), perfect product recovery (separations), or commercial usefulness.

What, then, constitutes an appropriate solvent for green chemistry? Fundamentally, it must be a solvent, which allows completion of the task, but in an environmentally conscious manner. Environmental toxicity is a key factor affecting choice of solvents. These chemicals should be minimally toxic to human health and the environment, and should not contribute to pollution (DeVito, 1996a). The considerations for what constitutes a safe solvent might be summarized as follows:

- It must have reduced human and environmental absorption.
- Its environmental toxicity should be understood.
- Its environmental fate is understood.

The environmental toxicology of a solvent is affected by many factors. The chemical structure of the solvent could lead to bioavailability or metabolism, or could enhance the reactivity of the parent molecule. Structure-activity data available for many classes of commercial chemical substances can be used as a rational approach for choosing or designing new, less toxic commercial chemical substances. This data is growing and being supported by empirical data. With qualitative structure-activity relationships, it may then be possible to predict a relationship between structure and toxicity and then identify the least toxic members of a class of compounds as possible commercial alternatives to the more toxic substances.

The grouping of solvents into classes with common characteristics can be useful in focusing attention on features that may play a role in experimental solvent effects. Reichardt's review of classification schemes is thorough (Reichardt, 1988). It is remarkable that solvent classification correlates strongly with the chemist's intuition. The new direction of the science demands that new properties be incorporated into mundane practices. These will include safety properties and environmental properties, as well as chemical properties.

4.1.1 Criteria and Functions

Toxicophoric or toxicogenic substituents, or information pertaining to a toxic mechanism, will guide solvent selection and usage in the twenty-first century. The article by Stephen DeVito explains clearly the toxicological considerations for chemists (DeVito, 1996a). Through the use of well-known toxicophoric or toxicogenic substituents, it might be possible to be alerted to the avoidance of certain solvents or to the substitution of more friendly ones. There are instances, however, in which the toxicity of a substance is unknown and the toxic mechanism is not apparent or predictable from its structure; no obvious or known toxicophoric or toxicogenic substituents may be present.

Environmental toxicity considerations for choice of solvents include the degree of absorption reported in the literature, exploration of toxic mechanisms, and the use of Structure-Activity Relationships (SAR). The relative seriousness of the toxic effect depends upon the extent of exposure to the substance, its bioavailability, and the importance of the physiologic process that the substance has disrupted (DeVito, 1996a). Over this information must be laid the physical parameters of the solvent's use (i.e., amount, state, reaction environment, etc). This requires a basic understanding of the processes involved in chemical toxicokinetics and toxicodynamics.

To incorporate the green chemistry paradigm into a methodical framework, chemists must expend efforts to understanding the mechanisms of desired reactions (both existing and future), and simultaneously evaluate the steps and chemical components in terms of environmental cost/benefits. This modus operandi (MO) is novel and it has not been rigorously or universally applied to the conscious choice of solvents or design of new reactions. To achieve such a rigorous methodology we can begin by looking at the following:

- "External" considerations—Reduction of exposure or accessibility
  A. Properties related to environmental distribution/dispersion
  B. Properties related to uptake by organisms

C. Consideration of routes of absorption by man, animals, or aquatic life
D. Reduction/elimination of impurities

- "Internal" considerations—Solvent performance
  A. Facilitation of solution
  B. Reactivity of solvated species
  C. Avoidance of undesired side reactions

4.1.2 Environmental Toxicology

Toxicology is traditionally defined as the study of the harmful effects of drugs, chemicals, and chemical mixtures on living organisms. Within the past two decades the environmental branch of toxicology has assumed a wider meaning. The survival of humanity depends on the survival of other species (plants and animals alike); on the availability of clean water, air, and soil; and on the availability of energy. Moreover, although preservation of our local and regional environment is vital to our survival, global problems such as the increasing CO_2 content in the atmosphere and depletion of stratospheric ozone are also critical.

Contemporary toxicology has evolved into a study with three branches:

- *Clinical toxicology* is concerned with the effect of drugs on human patients.
- *Forensic toxicology* is concerned with the detection, for judicial purposes, of the unlawful use of toxic agents.
- *Environmental toxicology* is concerned with the effects of toxins, whether purposely applied (such as pesticides) or derived from industrial processes, on health and the environment.

Environmental toxicology is a multidisciplinary science involving many widely diverse areas of study (Zakrzewski, 1991):

- Chemistry (the characterization of toxins)
- Pharmacology (the mode of entry and distribution of toxins in the body)
- Biochemistry (the metabolism and interaction of toxins with cell components)
- Physiology (the effect of toxins on body organs)
- Biology (the effect of toxins on the environment)
- Genetics (the effect toxins can have on the reproductive system and on future generations by altering genetic codes)
- Epidemiology (the effect on the population as a whole number of chronic exposure to small quantities of suspected agents)
- Law (regulation of the use or release into the environment of toxic substances)
- Economics (evaluation of the environmental cost versus benefit of economic development and the determination of tradeoffs among economy, health, and the environment)

4.1.3 Determination of Toxicity

To determine the toxicity of a compound for a biological system, an observable and well-defined end effect must be identified. Turbidity or acid production, reflecting the growth or growth inhibition of a culture, may be used as an endpoint in bacterial

systems. In some cases, such as in the study of mutagenesis, colony count may be used. The most readily observable endpoint with in-vivo experiments is the death of an animal, and this is frequently used as a first step in evaluating the toxicity of a chemical. Inhibition of cell growth or death of animals are not the only concerns of toxicology.

4.1.4 Reversibility of Toxicity

Another aspect to be considered is the reversibility of a toxic effect. In most cases, toxicity induced by a chemical is essentially reversible. Unless damage to the affected organs has progressed too far, so as to threaten the survival of the organism, the individual will recover when the toxin is removed by excretion or inactivated by metabolism. However, in some cases the effect may outlast the presence of the toxin in the tissue. A typical example of such an effect is intoxication with organophosphates, which bind essentially irreversibly to acetylcholine esterase.

In some cases, although no irreversible inactivation of an enzyme occurs, the action of a toxin may deprive an organism of a vital substance and recovery has to await resynthesis of this substance. Such is the case with reserpine, which acts by depleting sympathetic nerve endings of catecholamine; the time required to replenish the reserves of catecholamine is longer than the persistence of reserpine in the tissue.

4.1.5 Concept of Receptors

Some chemicals, such as strong aids and bases, exert their toxic action in a nonspecific way simply by denaturing protein and dissolving the tissue. Such lesions are referred to as chemical burns. In most cases, however, toxins act by interacting with specific components of the tissue, thus perturbing normal metabolism. Early in the twentieth century Paul Ehrlich proposed the concept of specific receptors (Ehrlich, 1913). He postulated that a chemical, in order to exert biological action, must reach a specific target area and fit into a receptor site.

Many receptors have been identified; in all cases they are proteins. Some of the proteins have enzymatic activity. Some receptors serve as "transport vehicles" across the cellular membranes, as is the case with the receptors for steroid hormones (Baxter and Forsham, 1972).

4.2 Specific Health and Environmental Requirements

4.2.1 Toxic Chemicals

A green solvent should not be toxic to humans. A solvent is considered to be toxic if:

- Oral $LD_{50} \leq 50$ mg/kg;
- Inhalation $LC_{50} \leq 200$ ppm of vapor or 2 mg/L of mist or dust;
- Dermal $LD_{50} \leq 200$ mg/kg.

The toxicity tests should at a minimum meet the requirements put forth by the Consumer Product Safety Commission in 16 CFR 1500/3(b)(6) I and 16 CFR 1500.40.

For purposes of demonstrating compliance with this requirement, the testing prescribed by the regulations is not required for the product mixture if sufficient information exists concerning the toxicological properties of each of the ingredients of the product to demonstrate that the product mixture complies. It is assumed that the toxicity of the individual component compounds is additive. Data from the *Registry of Toxic Effects of Chemical Substances* (RTECS) and from the Hazardous Substances Data Bank will be helpful in completing this assessment, as peer-reviewed primary data.

4.2.2 Carcinogens and Reproductive Toxins

The chemical should not contain any chemicals that are a carcinogen or that are known to cause reproductive toxicity. Carcinogens are defined as those chemicals listed in the current edition of the *Annual Report on Carcinogens*, U.S. Department of Health and Human Services, National Toxicology Program. Chemicals known to cause reproductive toxicity, for example, are defined as those listed by the state of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (California Code of Regulations, Title 22, Division 2, Subdivision 1, Chapter 3, Sections 1200, et seq.)

4.2.3 Flammability

The solvent should not be flammable (i.e., the flashpoint for the compound should be above 100°F). The flashpoint will be determined using the test procedures put forth in 16 CFR 1500.43, 1500.43a, and 1500.44.

4.2.4 Photochemical Smog and Ozone Production

The solvent should not contain substances that contribute significantly to the production of photochemical smog and troposphere ozone. The volatile organic content of the product, as used, should not exceed 50 g/L. None of the components of the product will have a maximum incremental reactivity (MIR) exceeding 1.9 g O_3/g of compound (the MIR for toluene). MIR values can be obtained from the maximum incremental reactivity list found in Appendix VII of the California Air Resources Board's *California Exhaust Emission Standards and Test Procedures for 1988 and Subsequent Model Passenger Cars, Light-Duty Trucks and Medium-Duty Vehicles* as amended on September 22, 1993.

4.2.5 Ozone Depletion

The solvent, if a blend, should not contain any Class I or Class II ozone-depleting substances as listed in Title VI of the Clean Air Act (Sect. 602) or any chemical with an ozone-depletion factor of 0.2 or greater (CFC 11 = 1).

4.2.6 Toxicity to Aquatic Life

The product should not be toxic to aquatic life as measured by performance in the following tests found in 40 CFR PART 797, Subpart B:

- Acute LC_{50} daphnia or fish ≥ 100 mg/L;
- Acute LC_{50} algae ≥ 100 mg/L;
- Chronic EC_{50} daphnia ≥ 10 mg/L.

For the purposes of estimating the potential toxicity of the chemical mixture, it is assumed the toxicity of the individual component compounds is additive. Data from the *Registry of Toxic Effects of Chemical Substances* (RTECS) and from the Hazardous Substances Data Bank will be accepted, as well as peer-reviewed primary data.

4.2.7 Biodegradability

The organic ingredients should be readily biodegradable in accordance with 40 CFR, Part 796, Subpart D. The biodegradability of the finished product should be determined using the Shake Flask Method given in 40 CFR 796.3100. The compound should meet the requirements of a minimum of 80% biodegradation based on DOC concentration or 70% of theoretical maximum CO_2 production. In the absence of data generated via this methodology, BOD measurements taken at lesser time intervals can be used.

4.2.8 Eutrophication

The product should not contain any ingredients that can cause eutrophication of receiving waters. As such, the following ingredients will be excluded:

- Sodium phosphate
- Sodium pyrophosphate
- Sodium tripolyphosphate

4.3 Solvents in Terms of Life-cycle Analysis

The extraction of raw materials, manufacturing processes, use/reuse, and disposal represent the basic stages of a solvent's life cycle. Each stage of a solvent's life cycle generates a variety of environmental burdens. Environmental-impact evaluation qualitatively assesses the life-cycle stages for chemical solvents. The goal of this evaluation is to select environmentally preferable solvents that can best minimize these life-cycle impacts.

Life-cycle assessment (LCA) is part of a special section on the trends and challenges of the new environmental landscape. Another area seen as a priority is that of exposure estimations and the elucidation of the biological mechanisms of chemicals. Pollution prevention, which aims to deal with problems before they occur, is clearly becoming a salient approach to industrial ecology (*Environmental Science & Technology*, 1996; Anastas and Lankey, 2000).

The benefits of using economy input-output life-cycle analysis (EIO-LCA) to estimate economy-wide discharges are significant. LCA is a systematic tool that is used to provide information on the consequences of alternative products and processes, thereby facilitating effective environmental decision-making. This is generally achieved

by tracing pollution discharges and resource use through the chain of producers and consumers (Wang, 1993).

Process and product models are commonly used for performing LCAs of the environmental impacts of materials and products through different stages of fabrication, use, and end-of-life options. In a recent article, it was shown that these models can be represented as process flow diagrams or as matrices of process interactions. Matrix representations are advantageous if application cost, feedback flow, or speed of analysis is important. They are also useful in conjunction with comprehensive, general equilibrium models in which the system boundary of the problem (e.g., an LCA of a product) being analyzed is on the level of the national economy (Hendrickson et al., 1998). Rich communities bear a responsibility to pioneer a path toward sustainable consumption (Myers, 1997).

Authors have stressed the importance of LCAs for comparing environmental and energy impacts, outlined the difficulties encountered in conducting such assessments, and provided examples of past LCAs. They addressed additional issues and also examined the usefulness of LCAs in formulating public policy. When a given pollutant arises at multiple sites, life-cycle impact analysis is often replaced by life-cycle inventory analysis (Graedel et al., 1995).

4.4 Life-cycle Assessment

4.4.1 Introduction

LCA is a powerful engineering systems approach to understanding the flow of materials and wastes throughout the life cycle of a product or system, from raw materials acquisition to final disposition (i.e., from "cradle to grave"). Originally developed in the 1960s as a tool for understanding potential energy and material efficiency opportunities, LCA was conceptually expanded in 1990 (beyond the engineering inventory/mass balance phase) to include methodologies for identifying potential environmental impacts and improvement opportunities (Veroutis et al., 1996).

Corporate competitiveness traditionally has been achieved through new product development, quality performance, and cost control. Competitiveness in the twenty-first century will require extending these traditional elements to include the life-cycle environmental impacts of materials and final products. Three forces are driving this evolution. The forces driving life-cycle accountability are

- Government regulations gradually moving in direction of life-cycle accountability;
- Emerging international standards with life-cycle requirements affecting access to, and competitiveness in, the global marketplace;
- Environmental "preferability" emerging as a key criterion in both consumer markets and government procurement guidelines.

Collectively, these developments have fostered a burgeoning corporate interest in the concepts of life-cycle design (LCD)—the application of life-cycle assessment (LCA) concepts to determine what a product contains, how it was produced, how it

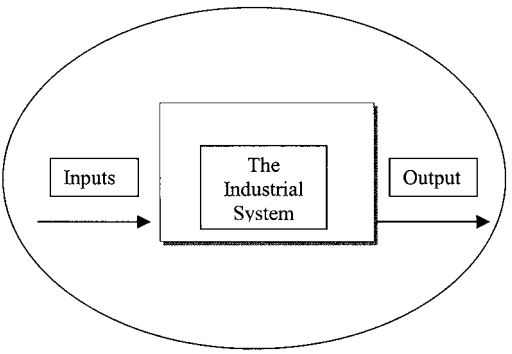


Figure 4.1 The industrial system. *Source:* SETAC, 1991.

will perform, and what will be left after its useful life is expired. This is the same for solvents.

Any industrial system can be represented by a system boundary that encloses all the operations of interest. The region surrounding this boundary is known as the *system environment* (fig. 4.1). The inputs to the system are all raw materials taken from the environment, and the outputs are waste materials released back into the environment.

4.4.2 The LCA Model

LCA is defined as a phased approach (fig. 4.2), comprising three interrelated components: inventory, impact, and improvement assessments.

4.4.2.1 Components of the Life-cycle Assessment

LCA activity has three components as defined by the Society of Environmental Toxicology and Chemistry (SETAC): life-cycle inventory, life-cycle impact assessment,

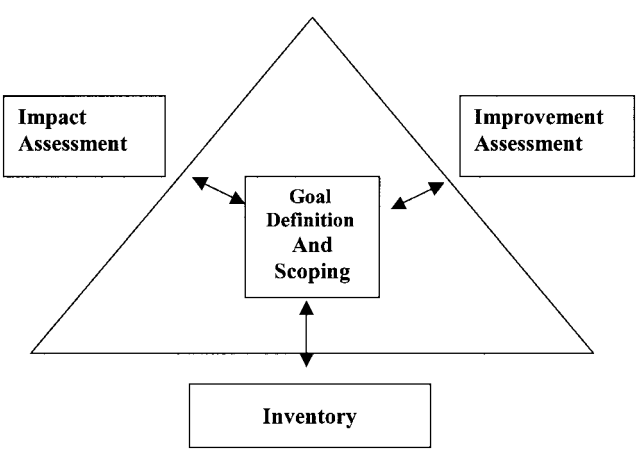


Figure 4.2 The LCA conceptual model. *Source:* SETAC, 1993.

and life-cycle improvement assessment (Fava, 1990). At the front end of this description should be added the goal definition of the LCA study (table 4.1). As suggested by Osnowski and Rubik, environmental LCA might be seen as part of a more comprehensive assessment of products including environmental, consumer safety, cost, and other aspects (Osnowski and Rubik, 1987).

To establish the goal discussions take place between different participants and technological information is needed about product alternatives that can be significantly compared with each other in relation to the goal of the study. For example, does the goal of the assessment refer to the improvement of a given solvent, the design of a new solvent, the publishing of product information, the granting of an ecolabel, or the exclusion or admission of products from or to the market? The type of intended application will influence the sequence of and the choices to be made within the different components.

In the inventory phase the boundaries between the inputs from and the outputs to the environmental system and the boundaries between the product system under study and other product systems are specified. In this stage three elements may be distinguished: the definition of the processes of the product system; the specification of all processes and their data; and the compilation of the inventory tables.

The second stage of life-cycle assessment may be complex in practice but is conceptually straightforward. The third stage, impact assessment, is more conceptually difficult, because it ultimately involves making choices among different impacts on the environment. Several techniques for impact assessment of specific products have been proposed; none has yet seen general use (Graedel and Allenby, 1995). The basic principles for impact assessment are: (1) the assessment should focus on specific concerns or categories, and (2) the process should be a stepwise exercise separating three different operations, shown in table 4.2 (Fava et al., 1992).

The inventory and impact assessment phases of LCA have different end results. The inventory component quantifies energy use, the masses of inputs, and the mass loadings of products, wastes, and releases on a systemwide basis. In contrast, the extrapolation of these mass-loading data generates a diverse spectrum of qualitative

Table 4.1. Components of Life-Cycle Assessment.

Component	Description
Life-cycle goal definition	The reason(s) for undertaking the individual assessments in the LCA.
Life-cycle inventory	Objective, data-based process of quantifying energy and raw material requirements, air emissions, and all other environmental releases incurred throughout the life cycle of a product, process, or activity.
Life-cycle impact assessment	Technical, quantitative, and/or qualitative process to characterize and assess the effect of the environmental loading identified in the inventory component.
Life-cycle improvement assessment	Systematic evaluation of the needs and opportunities to reduce the environmental burden associated with energy and raw materials use and waste emissions throughout the whole life cycle of a product process or activity.

Table 4.2. Stepwise operations in an impact assessment.

Component	Description
Classification	Properly select and organize inventory data into technically correct categories. Examples of such categories include climate change, eutrophication, and renewable resources.
Characterization	Model the selected inventory data to provide better perspective than simple mass loadings, for example, the total number of pounds or tons released.
Valuation	Use subjective values in an attempt to rank or to weight across different categories.

and quantitative estimates when inventory data are examined from an environmental impact perspective.

After the materials flows and environmental impacts of a product or a process have been assessed, the next step is to design a strategy for improvement. The techniques for doing so are generically called "design for environment" (DFE) (Fava et al., 1992).

LCA is a process used to evaluate the environmental burdens associated with a product, package, process, or activity. The considerations for LCAs can be useful when applied as a tool for decision-making. This has specific applicability when used to evaluate the solvent choices within a manufacturing process or any chemistry endeavor. Concretely, the decision to use a solvent (or not to use one) will involve many considerations: How best to achieve the desired results (specifications, yield, etc.), overall cost of the chemistry, and relevant environmental regulations.

Pollution prevention is another area that should be viewed with life-cycle impacts in mind. In P2 assessment, the system boundaries are drawn very narrowly around the chemical activity. Figure 4.3 shows how boundaries for pollution prevention as-

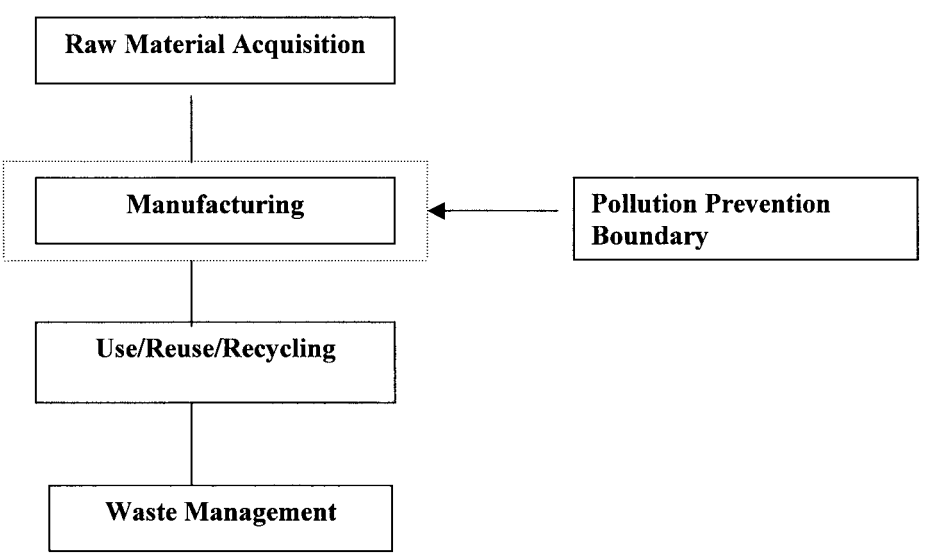


Figure 4.3 Pollution prevention assessment boundaries in the context of LCA.

sessments compare with boundaries that identify the entire system. P2 opportunities identified in this way will benefit the facility but may not always achieve reduced impacts on the environment.

Institutions, companies, and individuals have achieved competitive advantage by expanding the boundaries of their concern beyond the product life-cycle stage that they directly control. By using product stewardship and life-cycle information, coupled with business analysis, companies can successfully outperform their competitors by improving their product or product system by reducing costs, increasing revenue, reducing liabilities, and enhancing their image.

LCA and related methods have been in use for more than 25 years. Linkages between environmental impacts in the product life cycle and business issues are becoming more formal. Examples of some of these business issues are shown in table 4.3.

There is a general consensus supporting the use of life-cycle inventories and life-cycle assessments in targeting areas and identifying methods for the environmental improvement of a product. The "life-cycle thinking" perspective has allowed an establishment of commitment to environment, and being on the cutting edge of environmental considerations in product development.

Over the last 5 to 10 years, the consequences of past operating conditions, disposal practices, and product usage have been realized through the traumatic and expensive experiences of many companies, municipalities, and government agencies. For example, the experience dealing with Superfund liabilities and the increased costs of solid and hazardous waste disposal illustrate the importance of understanding short- and long-term liabilities (Fava and Page, 1992). As society becomes more conscious of the limits to industrial growth, manufacturing firms are increasingly recognizing environmental stewardship as an essential business function (Fiksel and Wapman, 1994).

4.5 Life-cycle Assessment: Its Application to Solvents

4.5.1 LCA Methodology

LCA is a snapshot in time of inputs and outputs. It can be used as an objective technical tool to identify environmental impacts associated with a specific product,

Table 4.3. Examples of business issues in the product life cycle.

Stage in Product Life-Cycle	Issue
Market analysis	Customer environmental requirements
Product design R&D	Redesign for compliance
Raw materials & energy acquisition	Cost versus function versus environmental impacts
Manufacturing processing	Compliance costs resource productivity
Transportation & distribution	Palletization efficiency/space utilization
Product usage	Cost versus function versus environmental impacts
Post-use disposition	Disposal cost/potential liability

process, or activity. The LCA is a holistic approach that analyzes the entire system around a particular process. Data are used to assess the impact of energy and material uses and releases on the environment, and to evaluate and implement opportunities to achieve environmental improvements. Solvent users presently face a challenge to maintain competitiveness while creating minimal adverse impacts on the environment. The conventional concerns of product functionality, quality, and cost are further complicated by environmental considerations.

"The life-cycle concept is based on the recognition that a 'cradle to grave' perspective is critical to any evaluation" and that "an inherently integrated concept . . . is the best way to allow for the evaluation, economic, environmental, and energy dimensions of a problem at the same time," (*Workshop*, 1994). The overall goal is to incorporate life-cycle environmental thinking into corporate decision areas: environmental strategic planning, research and development, product/process design, manufacturing, decommissioning, and closure/restoration.

For our considerations, the immediate challenge is to obtain an optimum solvent or solvating medium for effective chemistry. By using product stewardship and life-cycle information, coupled with business analysis, individuals and companies can successfully achieve their results by improving their product or product system by reducing costs, increasing revenue, reducing liabilities, and enhancing their image. Life-cycle information and its use within a product stewardship management framework go beyond traditional life-cycle applications. It must be noted that changes at any stage of a process can have positive or negative effects on waste generation at any other stage.

The terms LCA and cradle-to-grave analysis indicate that it is not the products per se that are analyzed, but in fact product systems in the sense of the production-consumption-waste treatment systems (Bousead and Hancock, 1989). However, the function of the product as it is used remains the point of reference to which the environmental impacts are attributed. LCAs assist in evaluating proposed changes to product or process designs so that a tradeoff can be identified.

Let us look at the stages of an LCA, as it would apply to technologies and processes (see table 4.4). It becomes apparent that the application of the LCA methodology to solvent choices bears closer scrutiny.

We can apply the same analysis to table 4.1 (Components of an LCA) in terms of how it might be applicable to the choice and evaluation of solvents. Below we will look at the components, asking the same questions as before, and now how they might

Table 4.4. Examples of issues in the product life cycle applied to solvent use in industry.

Stage in Product Life Cycle	Issue
Market analysis	How effective or efficient is the process?
Product design R&D	Most appropriate chemical technologies
Raw materials & energy acquisition	How much does the present/future chemical stage cost?
Manufacturing processing	Time? Space?
Transportation & distribution	Congruous with current GMP and practices?
Product usage	How efficient is the process?
Post-use disposition	How much waste and what is the cost?

describe important considerations in the evaluation of these processes. Further, we can see that they might guide our systematic analysis.

- Life-cycle goal definition: "How well does the solvent work?"
- Life-cycle inventory: How much does the present process stage cost? Time? Space? How much waste and what is the cost?
- Life-cycle impact assessment: Most appropriate use in chemistry and chemical technologies? Congruous with current GMP and practices? How efficient is the process?
- Life-cycle improvement assessment: What will be the cost of the future scaling-up?

It must be emphasized that this is not a strict LCA method, rather it is the use of the methodology to address key issues in the industries that utilize solvents. Because of the large amount of data required by a full LCA, a lot of attention has been directed toward developing a streamlined LCA approach. The goal of streamlining LCA is to reduce the time and cost of doing an LCA without sacrificing the credibility of the results. A streamlined approach would make LCA more applicable by more users, especially smaller companies that may be limited in resources and unable to conduct LCAs (Curran, 1996).

Streamlining in these applications refers to some method of shortcutting the LCA method. Such a shortcut method may require the user to make decisions about what to exclude from the study in order to "shrink" the boundaries and minimize the amount of data that must be gathered. Of course, this must be done with extreme caution and without jeopardizing the accuracy of the results.

Another way to view streamlining is through the application of the cradle-to-grave nature of LCA to look at products, processes, and activities in a more qualitative manner. This approach is also called *using the life-cycle concept* or *life-cycle thinking*. Life-cycle thinking requires the user to look upstream and downstream of the operation being studied, perhaps in an approach that combines quantitative and qualitative information.

We can summarize streamlining the LCA for solvent development:

What is the problem?

- Too much waste/garbage/cost/pollution/etc.
- Regulatory pressures
- Quality

What is the goal?

- Reduce waste, etc.
- Achieve compliance
- Improve quality

Alternate and augmentative solutions

- What can firms relate to/accommodate the best?

4.5.2 Initiating an LCA: Cross-functional Teamwork

Before we attempt to rigorously analyze the solvent usage from an LCA perspective, we need to add one further condition to the method. From the outset an LCA must be

Table 4.5. Collaborative inputs into the components of solvent selection.

Life-cycle goal assessment	***Life-cycle inventory***
Accounting	Accounting
R & D	Workers
Workers	Marketing
Marketing	Process technicians
Upper management	Environmental scientists
	Plant managers
Life-cycle impact assessment	***Life-cycle improvement assessment***
Accounting	Accounting
Industrial ecologists	R & D
Environmental scientists	Workers and plant managers
Marketing	Marketing
Upper management	Upper management

rooted in a cross-functional teamwork approach. It has been documented that "most of the responsibility for environmental assessments falls in the hands of the health, safety, and environment group," (Huang and Hunkeler, 1995/1996). During the goal definition, discussions should take place between different participants such as purchasing agents, workers, consumers, R & D, and LCA scientists. In addition, technological information is needed about product/process alternatives that can be significantly compared with each other in relation to the goal of the study.

The use of cross-functional teamwork can enhance the benefits that can be realized during each component of the LCA process. This underscores the fact that the life-cycle assessment is a dynamic and iterative process of evaluation. In order for this dynamism to be fostered, the LCA must encompass as much of the life cycle of the product, process, or activity, as possible. This will necessarily include total cost of raw materials, manufacturing, transportation, and distribution; use/reuse/maintenance; recycling, and final disposal (Fava and Page, 1992).

Table 4.5 suggests the individual areas of expertise necessary to make a strong analysis of solvent selection, using LCA principles. As previously emphasized, the areas impacted by the chemical process must be represented during the evaluation. There will be a direct correlation between the quality/composition of the cross-functional team and the quality of the conclusions reached.

4.6 A Proposed LCA Approach to Solvent Selection

4.6.1 Initial Requirement: A Change in Mindset

Realizing Benefits Requires Change in Mindset

From compliance	→	To prevention
From facility oriented	→	To division
From single issue	→	To systems approach (product life-cycle based)
From legally-driven	→	To market-driven standards

From cost of doing business → To opportunities to improve competitiveness
From "end-of-pipe" controls → To value-added management systems and processes

4.6.2 Goal Establishment

This sets the necessary direction for an LCA. When this is done for evaluation of solvents, it will indicate the direction of the process. Some possible goals might result from the following considerations. Typically LCI and LCA studies are performed in response to specific questions.

A solvent user may be deciding whether to fund or promote a new process, a new product, or a different type of package for the product. Determining what choices are available helps determine what the purpose and scope of the LCI and LCA should be.

Information sought in LCA includes:

- Energy use
- Resource productivity
- Environmental abatement costs
- Marketing feedback on customer concerns
- Stakeholder issues analysis
- Regulatory compliance costs at each stage of the product life cycle
- End-of-life management issues

4.6.3 LCA Inventory

The core of LCA is a cradle-to-grave life-cycle inventory analysis that is fundamentally an engineering exercise describing a chemical, material, and energy accounting balance for the entire product system. The various inputs and outputs are collected or inventoried for each unit operation in the defined system (see fig. 4.4). A key qualifier in the figure is the definition of the *system boundary*, as it will directly affect the quality of the final results and conclusions. The inventory practice and methods are relatively well defined.

Industry use of LCA as a tool to improve environmental performance is increasing. An LCA quantifies energy and resource inputs and outputs at all stages of a life cycle, and then determines and weighs the associated impacts to set the stage for improvements.

Information, which will be important for completing the inventory, can be found in table 4.6. These will affect the quality of the results from this component of the LCA.

4.6.4 How to Decide What to Measure and What to Track

It is not usually practical for a solvent user to track all possible types of process stewardship/life-cycle information. There are a number of criteria that should be used to determine which life-cycle information should be tracked including those listed in table 4.6.

Understanding where the opportunity for competitive advantage lies is half the battle. Finding effective measures to achieve the desired results is the other half. A

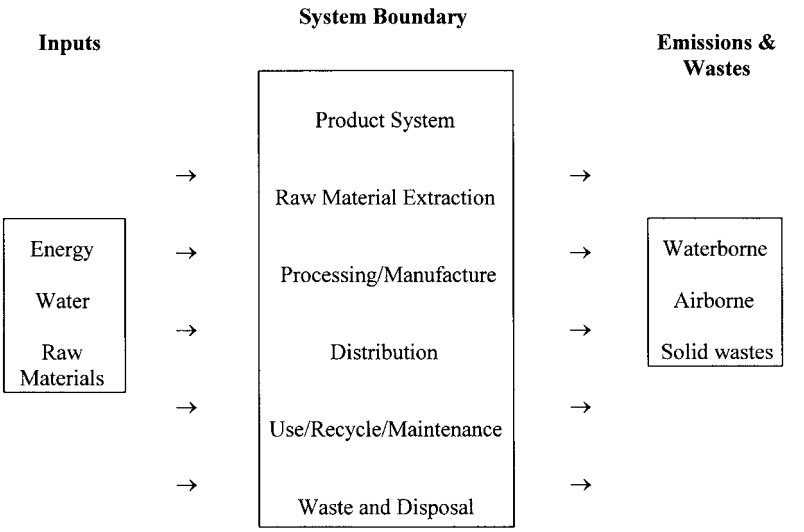


Figure 4.4 Elements of a life cycle inventory analysis.

decision support tool can often be helpful in identifying opportunities for enhancing competitiveness during this stage of the product life cycle.

To construct a decision support tool, one needs to have a focus of evaluation:

- Identify business issues for the organization;
- Evaluate areas for focusing improvement efforts for a specific product line;
- Change a currently existing process;
- Benchmark competitive products, to identify areas in which there is a competitive advantage to be achieved.

Once the areas for improvement have been identified, the details of data collected can be increased according to the requirements of the improvement and measurement effort. In some instances, decisions to track and measure product stewardship information (e.g., supplier performance) may be based on nonbusiness criteria, such as responsible care compliance.

Table 4.6. Issues for consideration.

Determining Information to Track: Issues to Consider
Potential cost savings
Potential business impacts on customer perceptions/sales
Severity of environmental impact consequences
Potential corporate liability
Cost of collecting data
Ease of using the information for decision-making

4.6.5 Efficiently Collecting Process Life-cycle Information

When collecting process life-cycle information, increased information collection costs will negatively affect efforts to achieve competitive benefits. Therefore, efficient collection methods should be sought.

4.7 Proposed Checklist for Solvent Use Evaluation

In the lists that follow will be compiled initial considerations for an individual or company attempting to use an LCA-based analysis of their solvent use. The categories are broad and they illustrate the necessity of the cross-functional teamwork.

General Information:

- No. of employees at facility
- SIC code
- Annual Sales
- Affiliation with other corporations (parent co., etc.)
- Current product lines

Current process description:

- Types of manufacturing process
- Support processes (vehicle maintenance, etc.)
- Shipping & receiving details
- Operating schedule (shifts, weekends, etc.)
- Labor description

Waste Description:

- Type, origin, and quantity of all waste streams
- Waste collection and handling procedures
- Waste tracking procedures
- Relationship between wastes and production units
- Efforts to separate/avoid mixing of wastes
- Waste treatment procedures
- Explanation of waste-handling accounting procedures (environmental department versus individual production/process departments)
- Description of facility emissions
- Off-site waste transportation and disposal arrangements
- Waste storage procedures

Present process and process change opportunities:

- Process information

1. Process description
2. Quality requirements
3. Raw materials usage for each process (types, quantities, purity)
4. Equipment used in each process
5. Labor requirements including maintenance and clean-up

6. Efficiency of process
7. Solid-waste generation including off-spec product, scrap material, packaging, trash, etc.

- Production information

1. Production schedule
2. Raw material inventory information (including ordering procedures, shelf-life of material)
3. Raw material usage—cleaners, machine oils, etc.

- Maintenance/housekeeping

1. Facility maintenance schedule
2. Maintenance products—cleaners, paints, paint removers, etc.
3. Estimate of wastes generated during a unit shutdown/clean-out

- Economic information

1. Product, utility, water, sewer, and raw material costs
2. Operating and maintenance costs
3. Departmental cost accounting reports
4. Waste disposal costs—account for waste costs?

4.8 Practical Approach to Life-cycle Evaluation of Solvent Usage

4.8.1 Industrial Ecology

The relatively new field of industrial ecology provides a useful organizing framework for DFE (Lowe, 1993). Design for Environment (DFE) is the terminology for the third component of the LCA: life-cycle improvement assessment. The principle of sustainable development suggests that companies or individuals should try both to minimize the consumption of virgin natural resources and to minimize the generation of waste material that has no productive use.

4.8.2 Integrating LCA with Economics to Monitor Process/Product Performance

The life-cycle concepts presented above and the process of working through an assessment provide a tool to identify and evaluate opportunities to improve solvent selection and use from cradle to grave. Using a quantitative life-cycle assessment of processes and potential processes, the impacts of the process during its entire life cycle can be determined and attributed quantitatively to the functioning of product as far possible. To make LCA an acceptable tool for product/process-oriented environmental management, the general methodological framework described above will prove beneficial (Guinée et al., 1993).

4.8.3 Life-Cycle Cost Management

While LCA focuses on assessing environmental releases and impacts, the emerging field of life-cycle cost management (LCCM) is aimed at helping individuals and com-

panies achieve the dual goals of environmental stewardship and increased global competitiveness (Cohan et al., 1992). Using a LCCM approach, individuals and companies can make business decisions that fully reflect environmental impacts and costs throughout the life cycle. Under conventional accounting methods, it is often difficult to justify the costs of environmental quality improvement, since their benefits are not directly quantified. Recent work has shown that when savings associated with reduced energy use, reduced waste management expenses, and salvage values of recycled materials are taken into account, environmental improvement projects become much more financially attractive (White et al., 1992).

LCCM builds on and extends certain aspects of LCA and life-cycle costing (LCC), which share a life-cycle perspective. In practice, LCA has addressed broad environmental impacts, but has had few applications to real business decisions; in contrast, LCC has seen some operational use at individual firms, but has typically ignored environmental costs. LCCM bridges this gap by explicitly recognizing the environmental costs associated with business activities, while maintaining a pragmatic focus on business decisions. The LCCM approach starts by identifying the classes of design or operating decisions to be addressed and the life-cycle information required to enable good choices. An efficient decision analysis process is then used to evaluate alternatives given the available life-cycle information, with sensitivity analysis techniques identifying when additional information or analysis is required.

4.9 LCA Leading to Total Quality Management (TQM)

4.9.1 Expanding the Role of Environmental Management to Incorporate Product LCA

Although corporations differ greatly in their responses to external stimuli, it is well established that those corporations that aggressively work to maintain profits by focusing on their customers are most likely to make the most forward-looking and aggressive business decisions (Graedel and Allenby, 1995). They are also somewhat more willing than average to adopt ideas and technologies developed outside their own corporations. These characteristics fit those firms that are now beginning to implement industrial ecology within their corporate structure, as opposed to those who are content to comply with regulation but to go no further.

In practice, hardly anything starts from scratch and adoption of new or modification of existing solvent usage will demand a consistent methodology to evaluate the alternatives. Inevitably, questions like the following will arise: “What is the best possible solution to my particular solvents requirements?” By following the above methodology, the answer will be more valuable because it will have resulted from a thorough evaluation of the present process and its alternatives.

It is helpful to think of industrial ecology as the sum of several focused efforts. The first, pollution prevention, is largely directed at taking current processes and products and minimizing their environmental impact. The typical time-scale for the actions and their effects is a year or two, and typical actions include leak prevention, energy conservation, and packaging improvements. The second activity, design for environment, has a longer time horizon and often deals with products and processes

prior to their introduction. Its typical action is the development of modularity, minimization of materials diversity, and process substitutions. These two thrusts, taken together, constitute the industrial ecology activities of a corporation (see fig. 4.5).

4.9.2 Promoting TQM as the Driving Force Behind LCA

The term "life-cycle framework" is used broadly to refer to any and all of the tool and programs that provide insights into and to some extent quantify a company's extended environmental concerns (Sullivan and Ehrenfeld, 1994). It would therefore include all of the considerations we used above to evaluate solvents. These extended environmental concerns are associated with activities beyond as well as at the company's own production facilities, from raw material acquisition, to component production, to recycling or disposition of a product. This is a different way of expressing total quality management, or TQM.

Environmentally conscious manufacturing (ECM) involves developing and implementing chemical processes that minimize or eliminate chemical waste, reduce scrap, or are operationally safer. The benefits include safer and cleaner factories, reduced future costs for disposal and worker protection, reduced environmental and health risks, improved product quality at lower cost, and higher productivity (Weissmann and Sekutowski, 1994).

ECM reduces the impact of manufacturing operations. The critical point is that ECM, as an integral part of TQM, is the responsible and economically sound thing to do. It decreases costs and future liability and often improves the quality of the end product because of more efficient processes that generate less waste. It is a technology for the twenty-first century.

4.10 Concluding Comments on LCA

Fundamental concerns about present LCA methodologies are that they are:

- Too complex and detailed to be useful in the real world; and
- Are limited, because they were developed for fairly simple products.

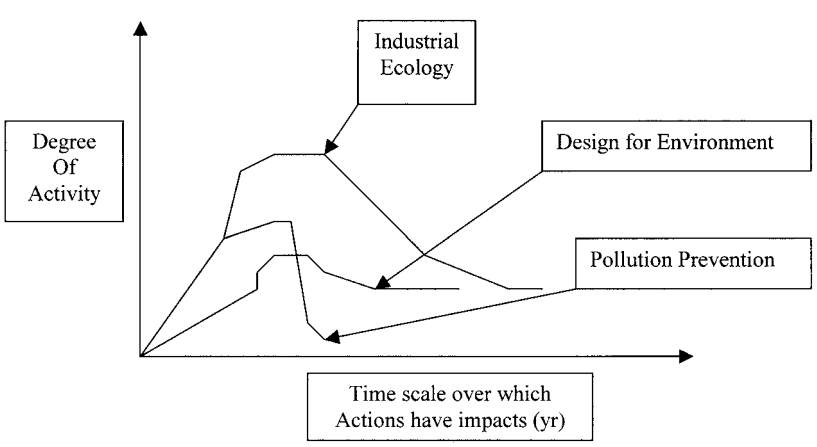


Figure 4.5 Industrial ecology as the sum of several focused efforts.

While the basic goal of business must remain economic growth, current environmental pressures are changing the course toward that goal. LCA is a viable tool in this period of time. As a direct expression of this, business has moved from a position of reacting to external pressures to one of being more efficient and competitive. It is instructive to use LCA as a tool for resolving the complex issues involved with considerations for a process change.

LCA also implies life-cycle responsibility. A combination of increasing external pressures and internal commitments requires a methodology like that embodied in LCA that will enable a company to effectively respond to the global demands for resource management (see table 4.7).

4.11 Green Solvents

With the valuable perspective afforded by the LCA methodology, let us return to our original question. What, then constitutes an appropriate solvent for green chemistry? Fundamentally, it must be a solvent which allows the chemist to accomplish his or her task, but in an environmentally conscious manner. Chemists are expected to consider toxicity as part of the key elements affecting choice of solvents, so that they are minimally toxic to human health and the environment, and disposed of in ways that do not contribute to pollution (DeVito, 1996b).

In accord with this, chemists today who have a knowledge of the environmental fate of the chemicals they use, or can obtain information pertaining to both areas, are in a much better position to respond in harmony with the mandates of green chemistry because they can envision the potential dangers particular solvents pose to the global ecology or to the individuals who will contact the chemicals directly (chemists, workers, local populace, etc.). Chemists must seek to reduce the toxicity and to influence the resultant toxicology of those chemicals while attempting to maintain the overall commercial usefulness of the substance.

Despite the structure-activity data available for many classes of commercial chemical substances, chemists have not recognized the use of structure-activity relations as a rational approach for choosing or designing new, less toxic commercial chemical substances, even though it can be an exceptionally powerful tool. With qualitative structure-activity relationships, comparing the structures of the substances in the series with corresponding effects on the toxicity makes the correlation of toxic effect and structure. Through these, it may then be possible to predict a relationship between structure and toxicity and identify the least toxic members of a class of compounds as possible commercial alternatives to the more toxic substances.

Table 4.7. Effectively using life-cycle information.

Effectively Using Life-Cycle Information: Success Factors
Demonstrate to management a clear link between information collected and business drivers.
Use existing information collection systems as much as possible.
Use simple analysis methods such as spreadsheets.
Spread the effort among a large number of people.

Using the challenges of the TQM and LCA, the current environmental revolution presents the science of chemistry with a new adaptation imperative. Incorporating the ideals of pollution prevention into all its operating paradigms will eventually open up new vistas and unexplored realms in chemical sciences. The chemist is already finding that sensitivity to the changing priorities among the world's populations will dictate a movement toward greener strategies.

The possible alternatives to ozone-depleting or otherwise environmentally challenging organic solvents for chemical processes are abundant. We can begin a review by looking at five broad categories: aqueous, ionic liquids, supercritical fluids, fluorinated solvents, or solventless processes (Illman, 1993).

4.11.1 Current Status: Introduction to Green Solvents

One way to reduce pollution at the source is to design safer chemicals. Chemicals that persist in the environment remain available to exert toxic effects and may bioaccumulate. Since microbial degradation is the major loss mechanism for most organic chemicals in soil, water, and sewage treatment, biodegradability should be included as a factor in product design along with function and economics. Biodegradability has been an important design consideration for down-the-drain consumer products like laundry detergents for more than 40 years, but not for chemicals used mainly in commerce. The relationship between molecular structure and biodegradability is generally well enough understood to make its application feasible in product design. We must extend the benign-by-design concept to commercial chemicals because

- production volume and thus release may increase with time;
- new uses may develop and with them, the potential for greater release;
- we cannot know in advance all of the possible toxic effects of released chemicals.

By designing a chemical such that it will biodegrade more readily to nontoxic product, the risks posed by the chemical to human health and the environment are reduced (Boethling, 1996). For a concise development of choosing green solvents, see this author's paper from the 1998 Green Chemistry and Engineering Conference (Nelson, 2000).

4.11.2 Water and Aqueous Systems as Solvents for Chemical Synthesis and Processes

Recent advances have demonstrated that water, both in its normal phases and in its supercritical state, can effectively be used in many processes in place of the organic solvents that are traditionally employed (Li, 2000).

Water is inexpensive, nontoxic and nonflammable. Replacing organic solvents with water may reduce volatile organic compound (VOC) emissions and CO_2 production from solvent incineration. Supercritical water is less polar than ambient water and will dissolve many organic compounds that would not otherwise be soluble (Katritzky et al., 1996). At the same time, it can act as an acid, base, or acid-base catalyst (Katritzky et al., 1996). This can eliminate the wastes generated from neutralization steps.

Water has a high boiling point, which has the potential to raise energy costs. Separations can be difficult, which can lead to contamination in aqueous effluents. Low solubility of substrates can create problems. Supercritical water is highly corrosive.

Aqueous systems have been used in separations, coatings, and synthesis. Aqueous biphasic systems have been developed for liquid–liquid extractions using water-soluble polymers such as polyethylene glycol, and inorganic salts such as ammonium chloride or potassium phosphate (Rogers et al., 1998), (Sherman et al., 1998). These systems have been investigated for use in the separation and recovery of heavy metals from mixed wastes and in the recovery of colored impurities from textile waste streams (Sherman et al., 1998).

4.11.3 Non-aqueous Ionic Liquids as Alternative Solvents

Ionic liquids are low melting organic salts that are liquids at ambient temperature. They typically contain quaternary ammonium cations such as 1-butyl-3-methylimidazolium- or N-butylpyridinium- with inorganic anions, such as tetrachloroaluminate or tetrafluoroborate (Chauvin and Helene, 1995; Freemantle, 1998). Melting points for these materials can be near −100°C, and the liquids are often thermally stable at temperatures approaching 200°C.

Ionic liquids have very low volatilities and are easily recycled. Many of these materials can act as both a solvent and a catalyst depending on their Lewis acidities and other properties. These catalytically active solvents can eliminate the need to use additional catalysts that may be toxic or may produce large amounts of wastes. Reactions in ionic liquids are usually carried out under mild conditions, and the products are often easily removed from the solvent by phase separation or low-pressure distillation from the ionic liquid.

The toxicities of ionic liquids have not been well characterized. The costs associated with the manufacture and use of large quantities of ionic liquids have not been determined. Separations may be difficult in some cases (Freemantle, 1999).

The pH-neutral ionic liquids are highly polar and noncoordinating. These liquids have potential applications as solvents for metallic and organometallic reagents in two-phase reactions, and as replacements for polar, aprotic solvents like dimethylformamide. The Lewis-acidic and superacidic ionic liquids are being investigated for use as catalytic solvents.

For further examples of work in this area, one should examine the elegant work of Professor K. R. Seddon (Earle et al., 1999; Earle and Seddon, 2000).

4.11.4 Supercritical Fluids as Solvents for Chemical Synthesis and Processes

Supercritical (sc) fluids are materials that are heated above their critical temperatures and pressurized above their critical pressures to produce single-phase condensed fluids having densities similar to liquids and viscosities similar to gases. The solubilities of substrates in supercritical fluids vary with small changes to the temperature and pressure of the system, especially near the critical point.

The ability to fine-tune the solubility properties of supercritical fluids makes them useful in a variety of applications. This property enhances the solvent selectivity and

makes separations easier. Other advantages are specific to the particular fluid used. One of the most widely used supercritical fluids, sc-CO_2, is noncorrosive, nonflammable, relatively nontoxic, recyclable, inexpensive, and won't degrade the ozone layer (Black, 1996). Further information can be found in excellent work by Tanko (Tanko et al., 1994; Tanko et al., 2000).

Supercritical fluids are becoming increasingly attractive as environmentally acceptable replacement for organic solvents in chemical reactions and material processing. A paper highlights some of the properties of supercritical fluids, especially supercritical CO_2, which offer particular advantages for the handling of polymers, metal complexes, and the environmentally more friendly synthesis and manufacture of chemicals. The paper includes some of the research from the University of Nottingham and a number of recent reviews that together provide a comprehensive introduction (Poliakoff et al., 1999). Work at the Massachusetts Institute of Technology also has led to a comprehensive examination of reactions in supercritical fluids (Tester et al., 2000).

Supercritical CO_2 is emerging as an environmentally friendly alternative solvent in various industrial and analytical processes. CO_2 becomes a supercritical fluid at pressures greater than 1,100 psi and at temperatures at or above 88°F. Supercritical CO_2 has already found use in coffee decaffeination, wastewater treatment, and chemical analysis, and it is presently being studied for use in polymer manufacturing, pharmaceutical manufacturing, and soil remediation. According to John Rankin, the three main advantages of supercritical CO_2 are speed, the inherent cleanliness of the extracts, and a substantial reduction in the volume of solvents used. The disadvantages are equipment cost and the small sample size obtained in supercritical CO_2 extraction (Black, 1996).

4.11.5 Derivatized and Immobilized Solvents

Derivatized solvents are modified solvent molecules that are designed to mimic the solubility properties of the original solvent while greatly reducing its volatility. An example is *n*-octyl tetrahydrofurfuryl ether, used as a replacement for tetrahydrofuran (THF). By taking this concept a step further, immobilized solvents are solvent molecules that are tethered to a low-molecular-weight polymer, further reducing its volatility (Sherman et al., 1998).

The potential advantages of using derivatized and immobilized solvents include reduced VOC emissions, negligible global warming potential, no ozone depleting potential, cleaner and easier separations from water, and reduced solvent contamination in aqueous waste streams.

Immobilized and derivatized solvents are expensive to produce. The life-cycle impact of using them has not been characterized. The recyclability of the solvents has not been characterized. Separations may be difficult in some cases.

The use of derivatized and immobilized solvents is still in the early stages of development. Now that their use has been demonstrated, further work in this field will expand the utility of this new class of solvents. The potential applications extend beyond synthesis to cleaning and separations processes. Work is currently underway to develop derivatives of other solvents, such as dichloromethane and ketones.

4.11.6 Nonaqueous Solvents

The concept of fluorous biphasic catalysis (FBC) represents a new paradigm for the separation of homogeneous catalysts from their substrates and the products emanating from these reactions. Since its published inception four years ago, FBC has been demonstrated in a variety of catalytic reactions that encompass hydroformylation, hydrogenation, hydroboration, hydride reduction, alkene epoxidation, and alkane and alkene functionalization. The common theme in all these homogeneous catalysis reactions, accomplished under FBC conditions, is the modification of the homogeneous catalyst with long-chain fluoroponytails to render them soluble in the fluorous phase; most hydrophobic substrates, and, to a large extent, hydrophilic products, are relatively insoluble in fluorocarbon solvents. The fact that fluorocarbon solvents are apparently nontoxic provides the FBC concept with a possible entry to the new green chemistry regime of being environmentally friendly, and therefore potentially attractive in a wide variety of industrial processes for the catalytic production of important organic chemicals worldwide (Fish, 1999), (Vincent et al., 2000).

4.11.7 Solvent-free Reactions and Processes

New developments in microwave-accelerated solventless organic syntheses are appearing in the literature. This expeditious and solvent-free approach involves the exposure of neat reactants to microwave irradiation in conjunction with the use of supported reagents or catalysts which are primarily of mineral origin (Varma, 1999).

Solvent-free processes make use of neat or solid-state materials. Solvents or diluents that do not become incorporated into a final product are not used.

Solvents are often the largest sources of wastes in chemical syntheses and processes. Eliminating the use of solvents can dramatically reduce the amount of waste and volatile organic compound (VOC) emissions that are produced in a process. Many solvents are themselves toxic, flammable, and explosive. Eliminating their use reduces safety and storage hazards. Eliminating the need to purchase and then treat large amounts of solvent may also provide substantial economic benefits.

Solvent-free processes can be energy-intensive. Applications can be limited by viscosity concerns and other physical constraints. Solvent-free syntheses sometimes yield lower-purity products than do traditional syntheses.

Successful solvent-free chemical syntheses have been reported for a variety of small molecules, both with and without the use of microwave irradiation, and for some polymer preparations (Varma, 2000). Solvent-free coatings formulations have also been developed.

5

Criteria for Selection and/or Design of Green Solvents

5.1 The Need for Green Solvents

Converting waste into products, as Holtapple does, is one way to enhance "greenness." Another approach is "source prevention," which Roger L. Garrett believes is the ultimate goal in the field of green chemistry. If you want to avoid the toxic effects of a substance, he said, "don't generate it in the first place" (Wilkinson, 1997).

The use of solvents in the chemical industry and in the chemical-related industries is ubiquitous. Beyond "chemical industries," solvent use has become an integral part of life in the twenty-first century. In 1991, the production of the 25 most commonly used solvents was more than 26 million tons per year. According to EPCRA section 313 data, of the chemicals and chemical categories tracked by the program in 1994, five of the top 10 chemicals released or disposed of were solvents, and included methanol, toluene, xylene, methyl ethyl ketone, and dichloromethane. The total quantity of these chemicals released or disposed of was over 687 million pounds, which accounts for 27% of the total quantity of TRI-listed chemicals released and disposed of in that year (Sullivan, 1997).

Because solvents are required in such high volumes compared to all other materials used in a synthetic transformation, hazards associated with solvents and safety issues associated with their use have always been a consideration in the development and selection of solvents. Some of the earliest and most obvious hazards, that if solvents were found to possess would cause them to be selected against, include properties such as high flammability or explosivity. With the greater understanding of the health and environmental effects that could be caused by other hazardous properties that solvents may possess or by their use in such large volumes, alternative solvents are

being carefully scrutinized for all hazardous properties, and new solvent systems are being developed to be more environmentally benign.

5.1.1 Exposure-Level Effects in Solvent Selection

Many solvents used in large volumes for many decades have been found to posses serious toxic or otherwise hazardous properties. Halogenated solvents such as carbon tetrachloride, perchloroethylene, and chloroform, for example, have been implicated as potential and/or suspect carcinogens, while other classes of solvents have demonstrated neurotoxicological effects. Concern for the use of hazardous solvents is compounded by the fact that the level of exposure to solvents can be extremely high. By design, many solvents have high vapor pressures. Although this property is often a highly desirable property for solvents to possess, this coupled with the high volumes often required of solvents can result in sufficient exposure to humans to cause harm.

5.1.2 Environmental Effects in Solvent Selection

In addition to hazards to human health, solvents should also be assessed for potential effects on the environment due to other hazards that they may possess or to their large use volumes. The use of solvents has, more than the use of any other type of chemical, caused damage to the environment on both a local and global scale. Until recently, chlorofluorocarbons (CFCs) were used in high volumes as refrigerants and in other applications. Recent discovery of their role in stratospheric ozone depletion resulted in a global phaseout of the substance from virtually all uses. The use of other VOCs as solvents has generated concern regarding their ability to elevate atmospheric ozone levels. Other substances used as solvents have been found to possess significant global warming potential and have been postulated to contribute to the overall greenhouse gas loading in the environment.

5.1.3 Additional Criteria to Evaluate Solvents

The solvent can be toxic itself, but it may also facilitate the toxicity of solutes. On gaining information from structure-activity relationships (SAR), it is possible to minimize the hazard while maintaining efficacy of function. Designing safer chemicals can be accomplished through several different strategies, the choice of which is largely dependent on the amount of information that exists on the substance of interest.

5.1.3.1 Determining Mechanism of Action

There is the great potential to design a chemical that is safer to human health and the environment when the mechanism of action of a hazardous property of a chemical is known. In order to avoid or reduce toxicity, a goal should be to elucidate the pathway that chemical follows in the body or environment that results in a toxic or otherwise hazardous effect.

5.1.3.2 Evaluating Structure-activity Relationships

For many chemicals the mechanism of action may not be known. For these cases detailed correlations and structure-activity relationships should be used to select safer solvents. As long as a chemical's structure and its hazard can be correlated empirically, then structure-activity relationships can be a powerful tool in designing and selecting safer solvents.

5.1.3.3 Selecting Against Toxic Functional Groups

Certain structural features, including whether it contains functional groups such as aldehydes, ketones, nitriles, or isocyanates, often define a class of chemicals. If information on the mechanism of action of a hazardous property of a chemical is not known, or if variances in the chemical's hazard through structural modification cannot be determined, then the assumption that certain chemically reactive functional groups can react similarly with the body or in the environment is often a good starting point in the process of evaluating the safety of solvents.

A conflict arises if a toxic functionality is wholly or partially responsible for the properties that are required for the chemical to perform in a desired way in its intended use. In these cases, options still exist to minimize the hazardous property and include masking the functional group by converting it to a less hazardous form (and only converting the less hazardous derivative back to the parent form when necessary) (DeVito, 1996).

5.1.3.4 Reducing Bioavailability

If through the above methods the elements of a chemical's structure that need to be modified in order to make the chemical less hazardous cannot be determined, then there is still the option of making the substance less bioavailable. If the substance is unable, due to structural redesign, to reach an environment in which it is hazardous, and then it has been rendered, in effect innocuous. Reducing bioavailability can be accomplished through a manipulation of the hydrophilicity/lipophilicity relationships that often control the ability of a substance to pass through biological membranes including skin, lungs, and the gastrointestinal tract. The same principle applies when designing safer chemicals for the environment including chemicals that are not, for example, ozone depleting. In order for a substance to have significant ozone-depleting potential, it must be able to both reach the appropriate altitudes in the atmosphere and have a sufficient lifetime at those altitudes in order to cause damage.

5.1.3.5 Designing for Innocuous Fate

A property often designed into chemical substances is robustness, or designing the chemical to last as long as possible. This practice has resulted in legacy wastes, persistent and bioaccumulative substances, and accumulation of landfills and lingering toxic-waste sites. It is now more desirable not to have substances persist in the environment, but to design them to degrade after their useful life is over. Furthermore, it is important that chemicals be designed to degrade into smaller, nontoxic, nonpersistent

substances. The design of safer chemicals therefore cannot be limited to an assessment of the hazards associated only with the manufacture and use of that chemical, but also must include a consideration of any hazards associated with its disposal and the end of its life cycle.

5.2 Criteria to Evaluate Solvents

5.2.1 Review of Pharmacological Concepts

Chemists in general need to be attuned to critical properties and structural features that could make a particular substance more environmentally sound. For example, compounds that are either highly lipophilic or particularly hydrophilic are less well absorbed from the human digestive tract than substances with properties between these two extremes (Wilkinson, 1997).

Once inside the body, extremely hydrophilic compounds tend to be excreted more readily by the kidney. That could be useful, because it lowers toxicity. Additionally, chemical classes and functional groups known to be toxic—as well as those that can be bioactivated into toxic substances—should be avoided when designing chemical products. Chemicals can also be designed to shield active toxic sites or to facilitate metabolic degradation to nontoxic metabolites.

Many chemical substances or mixtures exert a whole spectrum of activities, ranging from beneficial to neutral to lethal. Their effect depends not only on the quantity of the substance to which an organism is exposed, but also on the species and size of the organism, its nutritional status, the method of exposure, and a number of other related factors.

If the biological effect of a chemical is related to its dose, there must be a measurable range between concentrations that produce no effect and those that produce the maximum effect. The observation of an effect, whether beneficial or harmful, is complicated by the fact that apparently homogeneous systems are, in fact, heterogeneous. Even an inbred species will exhibit marked differences among individuals in response to chemicals. An effect produced in one individual will not necessarily be repeated in another one. Therefore, any meaningful estimation of the toxic potency of a compound will involve statistical methods of evaluation.

5.2.2 Determination of Toxicity

Modern toxicology is composed of three subdisciplines (Hughes, 1996).

- *Descriptive toxicology* involves toxicity testing of chemicals.
- *Mechanistic toxicology* examines the biochemical processes by which identified toxicants have an impact on the organism.
- *Regulatory toxicology* is concerned with assessing the data from descriptive toxicology and mechanistic toxicology in an attempt to determine the legal uses of specific chemicals, as well as the risk posed to the ecosystem by the marketing of those chemicals.

Many disciplines contribute an understanding of toxicology (see table 5.1). Forensic toxicology is concerned with the medical and legal questions relating to the harm-

Table 5.1. Selected disciplines that contribute to a more complete understanding of toxicology.

Ecotoxicology	Industrial toxicology
Forensic toxicology	Risk assessment
Genetic toxicology	Environmental toxicology
Teratology	Biochemical toxicology
Cancer research	Immunotoxicology
Pesticide toxicology	Food toxicology
Analytical toxicology	Clinical toxicology
Veterinary toxicology	Vasculotoxicology
Hepatotoxicology	Pulmonotoxicology
Pharmacology	Industrial hygiene
Biochemistry	Epidemiology
Pathology	Medicine
Environmental law	Atmospheric sciences
Marine biology	Ecology
Soil sciences	Genetics
Cytology	Molecular biology
Cellular physiology	Physiology

ful effects of known or suspected toxicants, and industrial (or occupational) toxicology studies the disorders found in individuals who have been exposed to harmful materials in their place of work.

To determine the toxicity of a compound for a biological system, an observable and well-defined end effect must be identified. The most readily observable endpoint with in-vivo experiments is the death of an animal, and this is frequently used as a first step in evaluating the toxicity of a chemical. Inhibition of cell growth or death of animals is not the only concerns of toxicology. Many other endpoints may be chosen, depending on the goal of the experiment.

Because the toxicity of a chemical is related to the size of the organism exposed, *dose* must be defined in terms of concentration rather than absolute amount.[1] Weight units (milligram, microgram, nanogram, etc.) per milliliter of maintenance medium or molar units (millimolar, micromolar, nanomolar)[2] are used with in-vitro systems. In animal experiments doses are expressed in weight or molecular units per kilogram of body weight or per square meter of body surface area.

5.3 Reversibility of Toxicity

Another aspect to be considered is the *reversibility* of a toxic effect. In most cases, toxicity induced by a chemical is essentially reversible. Unless damage to the affected organs has progressed too far, so as to threaten the survival of the organism, the individual will recover when the toxin is removed by excretion or inactivated by metabolism. However, in some cases the effect may outlast the presence of the toxin in the tissue. This happens when a toxin irreversibly inactivates an enzyme, and thus deprives the organism of vital functions. In such a case, although no free toxin can be

detected in the body, the recovery of the organism will not occur until enough of the affected enzyme has been newly synthesized. A typical example of such an effect is intoxication with organophosphates, which bind essentially irreversibly to acetylcholine esterase.

In some cases, although no irreversible inactivation of an enzyme occurs, the action of a toxin may deprive an organism of a vital substance and recovery has to await resynthesis of this substance. Such is the case with reserpine, which acts by depleting sympathetic nerve endings of catecholamine; the time required to replenish the reserves of catecholamine is longer than the persistence of reserpine in the tissue.

5.4 Concept of Receptors

Some chemicals, such as strong aids and bases, exert their toxic action in a nonspecific way simply by denaturing protein and dissolving the tissue. Such lesions are referred to as chemical burns. In most cases, however, toxins act by interacting with specific components of the tissue, thus perturbing normal metabolism. Early in the twentieth century Paul Ehrlich (Ehrlich, 1913) proposed the concept of specific receptors. He postulated that a chemical, in order to exert biological action, must reach a specific target area and fit into a receptor site.

Many receptors have been identified; in all cases they are proteins. Some of the proteins have enzymatic activity. For instance, dihydrofolate reductase is a receptor for antifolates and acetylcholine esterase is a receptor for organophosphates. Some receptors serve as "transport vehicles" across the cellular membranes, as is the case with the receptors for steroid hormones (Baxter and Forsham, 1972). Specific receptors may be confined to certain tissues or may be distributed among all the cells of an organism.

5.5 Mode of Entry of Toxins

From the environmental point of view, the three principal routes of entry of xenobiotics into the human body are percutaneous, respiratory, and oral. In multicellular animals, the extracellular space is filled with interstitial fluid. Thus, regardless of how a compound enters the body (with the exception of intravenous administration), it enters interstitial fluid after penetrating the initial cellular barrier (such as skin, intestinal mucosa, or the lining of the respiratory tract). From the interstitial fluid, the compound penetrates the capillaries and enters the bloodstream, which distributes it throughout the body.

5.5.1 Percutaneous Route

The skin forms a protective barrier that separates the rest of the body from the environment. In the past it was thought that chemicals did not penetrate the skin. In view of more recent research, this view no longer holds. Although penetration of the skin by most substances is slow, this route of entry plays an important role with regard to human and animal exposure to toxic chemicals.

Three possible routes of percutaneous absorption are

- diffusion through the epidermis into the dermis;
- entry through sweat ducts; and
- entry along the hair follicle orifices.

The main obstacle to percutaneous penetration of water and xenobiotics is the outermost membrane of the epidermis. This is called the stratum corneum. All entry of substances through the stratum corneum occurs by passive diffusion across several cell layers. The locus of entry varies, depending on the chemical properties of xenobiotics. Polar substances are believed to penetrate cell membranes through the protein filaments; nonpolar ones enter through the lipid matrix. Hydration of the stratum corneum increases its permeability for polar substances. Electrolytes enter mainly in a nonionized form, and thus the pH of the solution applied to the skin affects permeability. Many lipophilic substances, such as carbon tetrachloride and organophosphate insecticides, readily penetrate the stratum corneum. Pretreatment of the skin with solvents, such as dimethyl sulfoxide, methanol, ethanol, hexane, acetone, and, in particular, a mixture of chloroform and methanol, increases permeability of the skin (Loomis, 1978).

Permeability of skin is not uniform. It varies between species and even within species, depending on the diffusivity and the thickness of the stratum corneum (Klaassen, 1986).

Percutaneous absorption is a time-dependent process, with passage through the stratum corneum as the rate-limiting reaction. Therefore, duration of exposure to a xenobiotic is critical. It follows that the quick removal of spills is of the utmost importance.

5.5.2 Respiratory Route

The respiratory system consists of three regions: nasopharyngeal, tracheobronchial, and pulmonary.

- The *nasopharyngeal canal* is lined by ciliated epithelium through which mucous glands are scattered. The role of this region is to remove large inhaled particles and to increase the humidity and temperature of inhaled air.
- The *tracheobronchial region* propels foreign particles from the deep parts of the lungs to the oral cavity, where they can be either expelled with sputum or swallowed.
- The *pulmonary region* concerns exchanging gases with the cells of the body.

Another important factor affecting diffusion rate is the solubility of the gas in blood. When the solubility of the gas in blood is large, the diffusion rate is fast and the gas is removed quickly from the alveoli. In this case, the limiting factor in delivery of gas to the blood is the rate of supply of gas to the alveoli. When this solubility is small, the diffusion rate is slow; thus blood flow (i.e., cardiac output) rather than minute volume becomes the rate-limiting factor in toxicity.

5.5.3 Oral Route

The absorption of compounds taken orally begins in the mouth and esophagus. However, in most cases the retention time in this area is so short that no significant absorption takes place.

In the stomach, compounds are mixed with food, acid, gastric enzymes, and bacteria. All of these can alter the toxicity of the chemical, either by influencing absorption or by modifying the compound. It has been demonstrated that there are quantitative differences in toxicity, depending upon whether compounds are administered with food or directly into the empty stomach (Worden and Harper, 1963).

Most food absorption takes place in the small intestine. The gastrointestinal tract possesses specialized carrier systems for certain nutrients such as carbohydrates, amino acids, calcium, and sodium. Some xenobiotics use these routes of passage through the cells, while others enter through passive diffusion.

Lipid-soluble organic acids and bases are absorbed by passive diffusion only in nonionized form. Equilibrium on both sides of the cell membrane is established only between the nonionized forms (Klaassen, 1986).

A percentage of xenobiotics absorbed in the gastrointestinal cells may be biotransformed prior to entering the circulatory system; the balance is transported as the parent compound. The absorbed compounds may enter the circulation either via the lymphatic system, which eventually drains into the bloodstream, or via the portal circulation, which carries them to the liver.

5.6 Translocation of Xenobiotics

To arrive at the receptor site in the target cell, the blood must transport the absorbed xenobiotic. The time to the onset of toxicity depends on how quickly plasma levels of the toxic compound may be achieved. In contrast, the time to reach peak plasma concentration of the toxin is significantly longer after oral administration.

Lipophilic compounds diffuse easily through capillary walls. Their diffusion velocity is related to their lipid–water partition coefficient (Goldstein et al., 1974).

The entry of a compound into the bloodstream does not necessarily ensure that it will arrive unchanged at its specific receptor. As mentioned before, xenobiotics absorbed from the gastrointestinal tract are carried by the portal vein to the liver. The liver has a very active xenobiotic-metabolizing system in which chemicals may or may not be altered before being released through hepatic veins into the general circulation. Alternatively, they may be excreted into the bile and returned to the gastrointestinal tract. From there they may be excreted, all or in part, or reabsorbed and carried back to the liver.

5.6.1 Cellular Uptake

It is believed that four mechanisms of passage through the cell membrane are possible (Zakrzewski, 1991). Water and small organic and inorganic molecules diffuse through relatively few very small (0.2–0.4 nm) pores in the membrane. Lipid-soluble molecules diffuse easily through the lipid bilayer in the direction of the concentration gradient. Certain molecules are transported across the membrane by specialized enzymatic processes that exhibit saturation kinetics. When this process is energy-independent and the transport occurs in the direction of the concentration gradient, it is called *facilitated diffusion*. If transport occurs against the concentration gradient and therefore requires energy input, it is called *active transport*.

At the capillary subdivision, solutes are freely exchangeable between plasma and the interstitial fluid; thus the concentration of a xenobiotic in tissue is proportional to that of the free xenobiotic in plasma.

The entry of toxins into the brain and central nervous system (CNS) is frequently more difficult than into other tissues. The function of this blood–brain barrier is related to impaired permeability of the blood capillaries in brain tissue, the necessity for toxins to penetrate glial cells, and the low protein content of the CNS interstitial fluid (Klaassen, 1986). Lipid solubility of a toxin is an important factor in the penetration of the blood–brain barrier.

5.7 Storage of Chemicals in the Body

An important factor to be considered is the ability of certain chemicals or their metabolites to be stored in the body.

In general, a compound will accumulate in the body after repeated intake if its elimination or biotransformation is slower than the frequency of uptake. The best example of this phenomenon is the accumulation and persistence of alcohol in the blood after prolonged drinking. The human body metabolizes, on the average, one drink (a 12-oz can of beer, a 5-oz glass of wine, or one shot of 86-proof liquor) per hour. For a person weighing 140–160 pounds, the blood alcohol level rises 20-mg% per drink per hour. Therefore, to maintain legally safe levels of alcohol in the blood while driving (less than 50-mg%), it is recommended that one consume no more than one drink per hour.

Some compounds are stored in the body in specific tissues. Such storage effectively removes the material from circulation and thus decreases the toxicity of the compound. Repeated doses of a toxic substance may be taken up and subsequently stored without apparent toxicity until the storage receptors become saturated; then toxicity suddenly occurs. In some cases, the stored compound may be displaced from its storage receptor by another compound that has an affinity for the same receptor. Examples of this phenomenon are the displacement of antidiabetic sulfonylureas by sulfonamides and the ability of antimalarial drugs such as quinacrine (atabrine) and primaquine to displace each other (Loomis, 1978). A special danger in such cases is that compounds may have escaped detoxifying metabolism while stored in the body, and that their toxicity may be potent and prolonged when released.

Lipophilic compounds (such as halogenated hydrocarbons, DDT, PCBs, etc.) may be stored in fat without apparent harm to the exposed organism. However, these toxins tend to accumulate in the food chain. Eventually the storage capacity of an organism at the end of the food chain may be exceeded, and toxin may be released into circulation. Another danger is that during a period of starvation, as frequently happens to wild animals in winter, fat deposits are mobilized for energy. Stored toxins are then released, causing sickness or death.

In addition to a possible lasting inactivation of xenobiotics due to storage in various tissues, living organisms are partially protected by their reserve functional capacity. Some organs (such as the lungs, liver, and kidney) may withstand a certain amount of injury without any demonstrable symptoms.

5.8 Interpretation of Toxicity

The first problem in interpretation of the probable ecotoxicity of a given chemical is selecting those species and possible effects, which are most significant (Duffus, 1986). This requires a knowledge of ecosystems at risk together with an ability to assess the likely toxicity of the chemical from its chemical and physical properties and mammalian effect data that are usually available.

In the natural environment, chemicals are transported to the affected organisms through air, water, or soil and can pass between these media depending upon their physicochemical properties such as volatility, solubility, stability, biodegradability, and their tendency to be adsorbed by environmental components. The fate of a chemical in the natural environment is also profoundly affected by bioaccumulation. Substances which are readily taken up by living organisms and lost only slowly can reach very high concentrations in the exposed organism. If the exposed organism is part of a food web, bioaccumulation may be observed to occur subsequently in predators above it in the web. Food web bioaccumulation may lead to a disproportionately large uptake of xenobiotics by predators (biomagnification) because one predator may consume many prey organisms.

Interpretation of ecotoxicity is still more of an art than a science. Perhaps the greatest advances in this area will come from increasing understanding of the structure-activity correlations for chemicals. However, at the present time, further effort is necessary to integrate the wide range of different types of assessment currently employed, which range over almost every scientific discipline. In the strictest sense, the laboratory methods described can permit only comparative evaluation of chemicals under the test conditions. Extrapolation from laboratory results to predict what will happen when chemicals enter the natural environment must be improved.

5.8.1 Biodegradation

Biodegradation of chemicals by living organisms, especially micro-organisms, plays a major part in removing the chemicals from the natural environment (Duffus, 1986). Many factors can affect the nature and kinetics of biodegradation. Water and soil must contain in assimilable form adequate concentrations of all the nutrients needed for relevant micro-organisms to flourish. Such nutrients include nitrogen, phosphorous, sulphur, calcium, potassium, other elements in trace quantities, growth promoters, and for aerobic metabolism, oxygen.

Not all organic molecules are equally susceptible to biodegradation. The following generalizations have been proposed:

- Aliphatic chains are broken down more rapidly than aromatic or polycyclic compounds.
- Straight chains are more rapidly degraded than branched chains.
- The presence of heteroatoms in a ring structure and of halogenated or nitrated substituents greatly reduces biodegradability.
- The presence of double bonds favors biodegradation.
- Polymers break down slowly or not at all, but the corresponding monomers can usually be degraded more readily.

Assessment of the biochemical oxygen demand (BOD) of chemicals in suitable test systems gives a measure of the capacity of micro-organisms to metabolize these chemicals in the presence of oxygen and also of the potential of the chemical to cause oxygen depletion in water to which it is discharged. A measure of chemical oxygen demand (COD) gives a figure for the amount of oxygen required to oxidize the chemical completely or nearly so. The ratio of the value for COD to that for BOD gives an indication of the ease with which a chemical may be biodegraded.

5.8.2 Bioaccumulation, Bioconcentration, and Biomagnification

Bioaccumulation is defined as the uptake of xenobiotics and their retention by living organisms. Bioconcentration is the term applied to the uptake and retention of xenobiotics by organisms from their immediate environment. Biomagnification is the term applied to uptake and retention of xenobiotics from food.

5.9 Methodology to Evaluate Green Solvents

In this section we will present considerations that can be used to evaluate the environmental compatibility of solvents. The considerations are based on the Aberdeen/Green Seal Standard for Certification of Cleaning/Degreasing Agents for Steel and Aluminum, which was promulgated in the spring of 1999. While the standard is applicable to the cleaning industry, it rivets our attention to appropriate areas in which to evaluate solvents and solvent use.

5.9.1 Evaluation of Solvents

5.9.1.1 Scope

These recommended considerations should be used to weigh environmental requirements for solvents used in any chemical activity.

5.9.1.2 Definitions

The following terms will be understood to mean:

- ASTM: American Society for Testing and Materials
- CPSC: Consumer Product Safety Commission
- HSDB: Hazardous Substances Data Bank
- Ingredient: Any constituent of a product, whether intentionally added or not, including any impurities
- ISO: International Organization for Standardization
- OECD: Organization for Economic Cooperation and Development
- RTECS: Registry of Toxic Effects of Chemical Substances

5.9.1.3 Product-specific Performance Requirements

The solvent should function as required in the chemical process in which it is used. Some solvent-use applications may need to be systematically evaluated in order to determine if a particular solvent meets their specific requirements.

5.9.1.4 Product-specific Health and Environmental Requirements

5.9.1.4.1 Toxic Compounds The product should not be toxic to humans. A product is considered to be toxic if any of the following criteria apply:

- Oral $LD_{50} \leq 5{,}000$ mg/kg
- Inhalation $LC_{50} \leq 20{,}000$ ppm of vapor or gas or 500 mg/L of mist, dust, or fume
- Dermal $LD_{50} \leq 2{,}000$ mg/kg

The toxicity testing procedures must follow the protocols put forth in the OECD Guidelines for the Testing of Chemicals. These protocols include the following: Acute Oral Toxicity Test (TG 401), Acute Inhalation Toxicity Test (TG 403), and Acute Dermal Toxicity Text (TG 402). For purposes of demonstrating compliance with this requirement, the testing is not required for the product mixture if sufficient information exists concerning the toxicological properties of each of the ingredients of the product to demonstrate that the product mixture complies. It is assumed that the toxicity of the individual component compounds is additive. Data from the *Registry of Toxic Effects of Chemical Substances* (RTECS) and from the Hazardous Substances Data Bank (HSDB) should also be consulted, as well as peer-reviewed primary data.

5.9.1.4.2 Carcinogens and Reproductive Toxins The solvent should not contain any chemicals that are a carcinogen or that are known to cause reproductive toxicity. Carcinogens are defined as those chemicals classified by the International Agency for Research on Cancer (IARC) as Group 1 (carcinogenic to humans), Group 2A (probably carcinogenic to humans), or Group 2B (possibly carcinogenic to humans) agents. Chemicals known to cause reproductive toxicity are defined as those listed by the state of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (California Code of Regulations, Title 22, Division 2, Subdivision 1, Chapter 3, Sections 1200, et. seq.)

5.9.1.4.3 Corrosivity and Causticity The pH, if applicable, of the solvation media should be less than 11.0 but greater than 2.5.

5.9.1.4.4 Skin and Eye Irritation The solvent should not be a skin or eye irritant. A product is considered to be a skin irritant if it has a mean score of 2 or more for either erythema and eschar formation or edema formation, based on the OECD dermal scoring system (OECD, TG 404). A product is classified as an eye irritant if it causes significant ocular lesions, in any type of ocular tissue (i.e., cornea, iris, or conjunctivae) within 72 hours after exposure and which persist for at least 24 hours.

5.9.1.4.5 Flammability and Ignitability The concentrated product will not be ignitable (i.e., the flashpoint for the compound will be above 140°F). The flashpoint of the solvent should be determined using either the Cleveland Open Cup Tester (ASTM D92-97) or a Tag Closed Tester (ASTM D56-97).

5.9.1.4.6 Photochemical Smog and Oxidant Production The compound must not contain substances that contribute significantly to the production of photochemical smog and tropospheric ozone. The volatile organic content of the product, as used, will not exceed 50 g/L. None of the components of the product will have a maximum incremental reactivity (MIR) exceeding 1.9 g O_3/g of compound (the MIR for toluene). MIR values can be obtained from the MIR list found in Appendix X of the California Air Resources Board's *California Exhaust Emission Standards and Test Procedures for 1988 and Subsequent Model Passenger Cars, Light-Duty Trucks and Medium-Duty Vehicles* as amended on September 22, 1993.

5.9.1.4.7 Ozone Depletion The product will not contain any ozone depleting substances. An ozone depleting substance is any compound with ozone depletion potential greater than 0.01 (CFC 11 = 1.0).

5.9.1.4.8 Toxicity to Aquatic Life The product will not be toxic to aquatic life. A compound is considered not toxic to aquatic life if it meets one or more of the following criteria:

- acute LC_{50} daphina or fish ≥ 100 mg/L
- acute LC_{50} algae ≥ 100 mg/L
- chronic EC_{50} daphina ≥ 10 mg/L

Acute toxicity tests for these solvents must follow the appropriate protocols put forth in the International Organization for Standardization (ISO) Determination of the Acute Lethal Toxicity of Substances to a Freshwater Fish—Part 2 (ISO 7346-2); Determination of the Inhibition of the Mobility of Daphia magna Straus—Acute Toxicity Test (ISO 6341); and/or Fresh Water Algal Growth Inhibition Test with *Scenedesmus subsicatus* and *Selenastrum capricarnutum* (ISO 8692; 1989). The chronic Daphnia toxicity test must follow the procedures given in the ISO guidance, Determination of Long Term Toxicity of Substances to Daphnia magna Straus (ISO 10706).

For the purposes of estimating the potential toxicity of the chemical mixture, it is assumed that the toxicity of the individual component compounds is additive. Data from the RTECS and from the HSDB will be accepted, as well as peer-reviewed primary data.

Exception to this standard can be made for products that have LC_{50} and EC_{50} values that are greater than the solubility of the product in water.

5.9.1.4.9 Aquatic Biodegradability The organic ingredients will be readily biodegradable in accordance with 40 CFR Part 796, Subpart D. The biodegradability of the finished product should be determined using the Shake Flask Method given 40 CFR Part 796.3100. The compound should meet the requirements of a minimum of 80% biodegradation based on dissolved organic content concentration or 70% of theoretical maximum CO_2 production within 28 days. Exception to this standard can be made for products that are practically insoluble, that is, solubility less than 10 mg/L.

5.9.1.4.10 Eutrophication The product shall not contain any ingredients that can cause eutrophication of receiving waters.

5.9.1.4.11 Disposal The manufacturer should either take back unused or spent solvent for recycling or disposal, or provide the user with specific recycling and disposal instructions, which must comply with these recommendations and with all applicable federal and state regulations.

5.10 Presently Available Solvents

Solvents are substances that are liquid (or fluid in the case of supercritical fluids) 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. So many substances conform to this definition—practically all those that can be liquefied under some conditions—that it is not very helpful, unless the word "application" is stressed, meaning that the solvents and the solutes in them ought to be applicable for some purpose. This leaves a host of organic and many inorganic substances that are liquid at or near ambient conditions, which could be considered to be solvents under the present definition. Of these, a limited number are selected (Marcus, 1998).

The solvents that are included in the extensive compilation of physical and chemical properties shown in this book have been selected so as to cover the major classes of solvents, and bring several examples of each class. The properties of solvents that have not been included, but that belong to these classes in particular isomers or higher members of homologous series, can often be inferred from the reported data at least to some extent. One criterion according to which solvents have been selected for inclusion in the table is that most of their physical chemical properties, among those considered here, should be known. Solvating ability can be characterized by so-called solvatochromic parameters or similar indices of solvation ability, and some, at least, of the most commonly used of these parameters, ought to be known for inclusion of the solvent in the list.

Water, being the most abundant, extensively employed, and a very useful solvent, has always been accorded very wide attention by chemists of all disciplines who have been studying solutions. Inorganic solvents have long been considered to be the typical "non-aqueous solvents," as is manifested in the titles of several books dealing almost exclusively with them. In the last few decades a large number of organic, in particular dipolar aprotic, solvents have been dealt with extensively in this context of "nonaqueous solvents" almost to the exclusion of the traditional inorganic ones.

A classification scheme for solvents needs, therefore, to reflect to some extent the uses for which the solvents are put. Many classification schemes have been proposed, and a single major property, that may form the basis for the usefulness of solvents for certain applications, can often be employed in order to classify solvents. On the other hand, a few selected properties may advantageously be used to form the basis for the classification. Various solvent classification schemes have been presented (Reichardt, 1988) and a common solvent classification scheme is:

- Nonpolar solvents (such as hexane and tetrachloromethane);
- Solvents of low polarity (such as toluene);
- Aprotic dipolar solvents (such as acetone and N,N-dimethylformamide);
- Protic and protogenic solvents (such as ethanol and nitromethane);

- Basic solvents (such as pyridine and 1,2-diaminoethane); and
- Acidic solvents (such as 3-methylphenol and butanoic acid).

Some other classification schemes are provided in a work by Kolthoff (Kolthoff, 1974). It is according to the polarity and is described by the relative permittivity (dielectric constant) ε, the dipole moment μ (in 10^{-30} C.m), and the hydrogen-bond donation ability E^{N}_{T}. Another suggested classification (Parker, 1969) stresses the acidity and basicity (relative to water) of the solvents. A third one (Chastrette, 1979), stresses the hydrogen-bonding and electron-pair donation abilities, the polarity, and the extent of self-association. A fourth is a chemical constitution scheme (Riddick et al., 1986). The differences among these schemes are mainly semantic ones and are of no real consequence. Marcus presents these clearly (Marcus, 1998).

Table A1 in the appendix shows the solvents on the list of green solvents found in the USEPA's Green Chemistry Expert, which is utilized in the following sections of the chapter. An ordinal number in the first column identifies the solvent.

Many solvents have quite common synonyms that are in widespread use, but such synonyms are not listed in table A1 (see the appendices).

A further aid in the location of the solvents and their exact specification is the Chemical Abstracts (CAS) Registry Number, shown in the second column. The Chemical Abstracts name may be the same as the commonly used one or may differ from it considerably, so that it is not always easy to find the solvents in these Chemical Substance Indexes of the Chemical Abstracts. For instance, "benzene, methyl" is a fairly transparent name for toluene, and "methanol, phenyl" a slightly less one for benzyl alcohol, but one has to become familiar with the systematics of Chemical Abstracts nomenclature in order to search for diethyl ether or any other more complicated compound. It is expected that with all this information available in table A1 the solvents listed are definitely specified and readily found in the Abstracts and other compilation of information and data.

The list of green solvents is given below. This list may be found at http://www.epa.gov/greenchemistry/tools.htm. Many of the solvents on the list are commercial and industrial solvents. The list also includes many solvents that are hardly of any industrial interest, but still may be useful in laboratory situations or interesting from a theoretical point of view.

5.10.1 Solvent Purity and Purification Methods

Absolute purity cannot be achieved for any material, but high purity can and it is generally desirable and often mandatory for the applications intended for solvents. Commercially available solvents can be obtained in several categories of purity and the desired or required purity depends on the envisaged application. It is, therefore, impractical to specify a solvent that is "pure" for all possible applications.

There are three aspects of the question of solvent purity that have to be considered: the specification of the purity of the given solvent; its further purification, if necessary; and the testing of the actual purity of the original or purified solvent.

Distillation, and in particular fractional distillation, is the most commonly employed method for the purification of solvents. In order to avoid decomposition at elevated temperatures, distillation at a reduced pressure is often resorted to. It is the

usual practice to discard the first and last fractions of the distillate collected and use only the middle fraction, which may constitute no more than some 50–80% of the total amount. The distillation, however, is often the last step that is applied after more specific purification procedures have been applied as described (Perrin et al., 1980).

An important earlier step in the purification is commonly the removal of the ubiquitous impurity: water. This is present both from its formation in the synthetic procedure during the manufacture of the solvent and because of its ready absorption from the laboratory air. Due to its low molar mass, a millimolar concentration of water may result from only 20 ppm of this impurity. Various drying agents can be used, but porous aluminosilicates known as molecular sieves (e.g., the 4A type) have found universal use. They must be thermally activated, that is, predried, for most efficient use. In their pellet-like form they can be kept in the bottom of the storage bottle of a solvent to keep it dry without contaminating it. Also they can be used, as well as other drying agents such as calcium hydride for basic solvents, or phosphorus pentoxide for acidic solvents, in the still pot in the final distillation step. Another fairly universal purification method to remove water and other protic impurities from low-polarity solvents is to pass the solvent through a long column of activated alumina or silica gel (Trusell and Diehl, 1963).

Table A2 (see the appendices) lists briefly the purification methods applicable to many of the solvents listed. It is, however, often advisable to guard solvents, once their bottles have been opened, from the absorption of moisture from the atmosphere, and in the case of basic solvents, also from the absorption of carbon dioxide. If purification is deemed to be necessary and no method is specified in table A2, then usually a method noted for a chemically similar solvent can be employed.

Organic solvents ought to be stored in properly sealed glass bottles, since they are not apt to dissolve silica from the glass as water does, when stored over extended periods. When light sensitivity is known or suspected, brown bottles are to be used, or else the bottle should be wrapped in opaque paper. Bottles made of plastic materials are better avoided for storage, since the solvent is capable of leaching a plasticicizer out from the bottle. For rapid transfer, however, polyethylene or -propylene pipettes, measuring cylinders, and so on, can be used with apparently no detrimental effects.

5.10.3 Toxicity and Other Hazards of Solvents

Special attention must be given to the hazards involved in the use of solvents, and there is a general tendency to replace solvents that are hazardous, but have long been in use for historical reasons, with less dangerous solvents. For instance, benzene, a very useful solvent but known carcinogen, ought to be and actually often is replaced by the less hazardous toluene or xylene. Table A3 (see the appendices) provides some information concerning the toxicity of solvents on the table as well as their inflammability and the explosive limits of their vapor in air.

The *permissible exposure limit*, PEL in table A3, is given in ppm in the air for an ordinary work shift in the laboratory in industry (Kirk-Othmer, 1978). This quantity is also called the threshold limit (Riddick et al., 1986). Concentrations that are *of immediate danger to life or health*, called IDLH in table A3, in ppm in the air, may be much higher than the PEL and be tolerated for short periods of time, say 30 min.

It must be stressed that the information summarized in tables A1, A2, and A3 is not exhaustive, and where no information is given, this does not mean that a solvent is not toxic or flammable. While some solvents are relatively nontoxic regarding their concentrations in the air (at least those having very low vapor pressures), they may still be quite toxic on ingestion or be a strong irritant on skin or eye contact.

The toxic effects on ingestion are commonly reported in terms of LD_{50} in mg kg^{-1} body weight, meaning the lethal dose for 50%, or with some other specified subscript, of the organisms, usually rodents, treated. However, the mode of introduction of the toxic solvent: orally or by subcutaneous or intravenous injection, the duration: acute or chronic, and if the latter, over what time period, and the species of the test animal: whether mice, rats, or rabbits, among other factors, strongly affect the numbers. Such quantities have, moreover, been reported very nonsystematically and some of those available are shown in table A3 (Riddick et al., 1986). For no solvents are the minimal lethal doses reported nor are the LD_{100} values. Handbooks on toxicology ought to be consulted in this respect. Evidently, total avoidance of ingestion is to be the rule. Harmful effects on skin contact can be expected from strong acids or strong bases or such solvents that can readily hydrolyze to become such materials. Acetic acid, acetic anhydride, benzoyl chloride, and phosphorus oxychloride can be cited in the latter category.

Further hazards arise from the ability of solvents to ignite or of their vapor to form flammable and even explosive mixtures with air. The flashpoint is defined as the temperature below which the liquid solvent cannot be ignited, and is reported in the tables in the appendix in °C. The reported flashpoints, however, depend somewhat on the mode of ignition, and inconsistencies between the sources of the data have been noted. Solvents also have an autoignition temperature generally well above 200°C (see tables in the appendix, e.g., some ethers), above which rapid combustion in air takes place even without supply of external heat (Riddick et al., 1986), (Kirk-Othmer, 1978). Exceptions are polyhalogenated small hydrocarbons, but these may decompose in a fire fed by other materials to yield very toxic compounds: phosgene and dioxane. Care must, therefore, be used when employing organic solvents at elevated temperatures and even in their storage, when a nearby source could cause ignition.

The vapors of many solvents form with air explosive mixtures, when present at certain concentrations in the air. The lower and upper explosive limits are reported in tables in the appendix in percent by volume of the vapors in air, pertaining generally to room temperature (Kirk-Othmer, 1978). It should again be stressed that the information provided here is for general guidance only, and that more specific and binding recommendations concerning the hazards involved and precautions to be taken against them should be obtained from the specific regulatory authorities.

Notes

1. In medical literature and in pharmacokinetics, the total amount administered is frequently referred to as the total dose.
2. M always stands for moles per liter and is pronounced as molar. Thus, mM is millimolar, µM is micromolar, and nM is nanomolar.

6

Green Solvents for Academic Chemistry

6.1 Environmental Concerns for Educational Institutions

Environmental chemistry is generating considerable interest. Hardly a week goes by without some chemical aspect of the environment making it into the news within the academic community; environmental chemistry is a hot topic. But environmental issues and the standard chemistry curriculum do not correlate exactly. Many environmental subjects require understanding chemical principles that are not taught until fairly advanced courses. Teaching both environmental issues and basic chemistry to nonscience students requires making choices in emphasis: to teach mainly environmental topics with chemical "facts" introduced when necessary, to teach mainly basic chemistry with environmental "points" interjected when possible, or to integrate the two subjects so that both are taught simultaneously. Reciprocally, education provides the initial vantage from which chemistry is critically evaluated.

The process of communicating green chemistry is more complex and less direct than it appears. The meaning of the ideas and concepts yields an interpretation that is heavily dependent on the structure of language, on where information is situated relative to other information. Context is critical. It allows us to make sense out of information by selecting among competing interpretations.

The need for connection pertains not only to the lectures, but also to the laboratories and problem sets as well. Students arrive at their understanding of a subject by actively constructing it using the material at hand. When that material is not integrated, when the linkages between the different parts of the course are not explicit, students are forced to spend much of their energy simply figuring out how the different parts of the course fit together (Swan and Spiro, 1995).

Table 6.1. Selected environmental laws and regulations.

Clean Air Act	Control air pollution
Clean Water Act	Control water pollution
Environmental Clean-up Responsibility Act (ECRA)	Clean-up of environmental pollution
Resource Conservation Recovery Act (RCRA)	Chemical Disposal
Superfund Amendments Re-authorization Act (SARA)	Extremely hazardous chemical quantitative reports

Education for green chemistry must show that chemical processes that carry environmental negatives can be replaced with less polluting or nonpolluting alternatives. The strategic goals in research must be long term and both patience and persistence is needed to achieve them. Professors in their teaching must incorporate green goals into courses without compromising the integrity of chemical knowledge. It is realistic to anticipate that green chemistry will lead to successful products and a large marketplace (Collins, 1995).

- We must define goals for green research and to consider evaluation criteria for green reagents.
- We must identify target technologies that realistically might be replaced by green technologies and to ponder the alternatives.

An ever-expanding list of occupational and environmental laws and regulations affect schools and colleges. The corresponding responsibilities require school administrators and staff to not only be aware of the various hazardous chemical regulations, but also to expend substantial time and dollars to assure that liabilities are minimized. Compliance with many of these regulations can be simplified, or at least, effectively focused and prioritized, if hazardous chemical and product information is readily available (Forum for Scientific Excellence, 1990).

Many of these laws were primarily enacted to regulate the chemical industry (i.e., manufacturers, distributors, and *user companies*). However, since educational institutions also utilize chemicals in their facilities, the "user company" definitions in these laws typically include schools and colleges. Schools and colleges must provide information to their employees through material safety data sheets (MSDS); training programs (written and/or oral), and labels. The philosophy behind this regulation based upon an employee's "right-to-know" information about hazardous chemicals to which they may be potentially exposed. This OSHA health and safety standard requires that the hazards of all chemicals produced or imported by chemical companies be fully evaluated.

In a similar fashion, many environmental laws and regulation originally intended to curtail pollution and contamination by industry have also affected academic institutions (see table 6.1). Schools and colleges are occasionally cited for releasing hazardous materials into the air from their incinerators. Water pollution by educational institutions is not uncommon and can occur as a result of sewer-system contamination, septic-system misuse, dumping of hazardous materials on institution-owned property, and/or accidental discharges. Inappropriate and illegal hazardous chemical disposal by schools and colleges is also fairly common.

The ever-expanding list of occupational and environmental laws and regulations makes it increasingly necessary for academic institutions to have access to comprehensive hazardous chemical data and assessments. Health and physical hazard data for pure chemicals can readily lead to an understanding of the composite hazards for the mixtures of these chemicals found in the diverse products with educational facilities. Increased hazardous chemical awareness is the first step toward effectively fulfilling regulatory requirements, reducing liability risks and establishing responsible chemical policies and procedures.

6.1.1 Why Academic Institutions?

Let us put chemistry education in context, as it plays a major role in solvent selection and usage. A longitudinal study of 250 students following the context-led Salters Advanced Chemistry (SAC) course explored changes in students' thinking about basic chemical ideas. Students at schools and colleges completed the same diagnostic test at the start, after 7 months and 16 months of their 20-month course. Questions probed a range of chemistry topics, including conservation of mass in closed- and open-system chemical reactions, and reacting mass reasoning. Data suggest that many students begin studies with a wide range of misunderstandings about chemical reactions. However, students' understanding improves steadily as the course progresses. More direct and explicit teaching may accelerate this. This suggests a continuing need to review teaching approaches (Barker and Millar, 1999).

To determine how best to present green chemistry to students, it would be best to look at attitudes. A study reports on the relationship between attitudinal factors and student academic success in first-year chemistry courses. The study includes a comparison of attitudes toward chemistry of first-year medical students at two universities. Students from these two institutions differ considerably with respect to educational backgrounds. In the investigation, attitudes toward science (particularly chemistry) were correlated not only with students' academic achievement, but also with personal demographic data, such as matriculation results, parents' educational level, and location of high school. The students' responses to an opinion survey suggest a substantial relationship between attitudes and academic achievement. The results also suggest that academic achievement in chemistry is more dependent on attitudes toward science than aptitudes of students (Cukrowska et al., 1999).

Looking at the issue in a broader context, the purpose of another study was to ascertain the views of 2 groups of college-bound high school students concerning meaning and action in cultural context. What does it mean to understand and to succeed in introductory chemistry? A focus group of students from each school and the two teachers were interviewed and participated in informal conversations. Students explained understanding in at least two ways, one practical and task oriented, while the other definition was theoretical and epistemological. Success associated with the latter understanding was elusive, yet considered more meaningful (Rop, 1999). This must be developed in green chemistry.

The conception of sustainable resource development worked out under the initiative of the United Nations (U.N.) actualizes ideas for improving the health of people and the environment. The needs of people are to be addressed and, simultaneously, natural resources preserved. Chemical education in schools has to support a change in the

Table 6.2. Steps for evaluation and execution of green chemical processes.

Steps
Identify a suitable goal or target molecules;
Identify the current technology used to attain this goal;
Identify the starting material or feedstock, utilizing the most environmentally benign feedstock that will accommodate the existing technology;
Execute the chemical process by the best means available;
Incorporate green chemistry developments into the process: 1. to introduce greater selectivity and efficiency; 2. to replace solvents with more environmentally benign solvating media or eliminate solvent use; and 3. minimize the toxicity of the entire process (from starting materials through waste-stream);
Reduce the number of steps necessary to complete the process;
Evaluate the total environmental load of the process (analyze all areas of feedstocks, auxiliary reagents, solvating media, products, and wastes (e.g., byproducts));
Introduce additional green techniques;
Improve the synthesis in an iterative and multigenerational effort.

way of thinking and many concrete subjects can be connected with the problems of sustainable development (Karik, 1996).

6.2 Green Chemistry Alternatives

In an insightful chapter entitled "Green chemistry alternatives for the processing of aromatic compounds. Tandem strategies in biocatalysis and synthesis," Hudlicky listed the logical progression of steps that are necessary for the execution of truly efficient syntheses (Hudlicky, 1998). The steps enumerate the systematic analysis/execution of a synthesis, but it may have general applicability throughout chemistry. We have adapted them to fit the broader approach to chemistry in general, and would like to list the steps here, as a prelude to the discussion of academic solvents (see table 6.2).

This table assumes the existence of chemistries that are in current usage. The enterprise of green chemistry will have tremendous impact in both the development of new technologies that are tools in pollution prevention (the raison d'être of green chemistry) and in the renovation of existing chemistry practices so that they become more "green."

The decision to replace solvents with more environmentally benign solvating media or eliminate solvent use altogether is not a trivial task. It can be as challenging as inventing an entirely new synthetic route! In order to properly employ solvents and reaction media, their role must be appreciated (see chapter 3 in this book), and the available alternatives must be easily accessible and readily evaluated.

6.3 Early Chemistries: Elementary Through High School

6.3.1 Background

Chemistry and chemical laboratories have effects on the students and faculty. An example of this influence is provided by Crump et al. (1996). To assess whether high school chemistry teachers had higher urinary mercury concentrations than other high

school teachers did, 24 high school teachers from nine schools were studied. The median adjusted urinary mercury concentration in the 12 chemistry teachers was 4.6 μg/g creatinine (range 2.2–8.2 μg/g creatinine) and it was 6.3 μg/g creatinine in the 12 nonchemistry teachers. All classroom air samples contained mercury levels below detection limits. No evidence was provided that high school chemistry teachers are at increased risk of chronic mercury exposure from their teaching activities compared to other high school teachers. In this case knowledge of the toxicity of chemicals is shown to be beneficial. Often, as this example implies, our information regarding the chemicals (especially solvents) used in primary and secondary schools comes via the results of their usage.

Another article reported an investigation of the intuitive scientific ideas and understandings of 321 preservice elementary-teacher–education students enrolled in a three-year program. The sample completed a physical science concept challenge instrument by responding, in writing, to open-ended questions about the concepts of floating/sinking, the nature of matter, air pressure and its effects, and the balance beam. The results reveal that the majority of subjects, with the exception of a high proportion of those who had a successful senior high school background in physics and chemistry, have misunderstandings in these basic concept areas. It is argued that teachers should have a sound conceptual knowledge base in order to implement effective problem-solving strategies in the elementary science classroom. The importance of teaching science in elementary schools is widely acknowledged, therefore teacher educators must identify and implement more effective strategies for science instruction in preservice teacher education courses that will enable all students to construct scientifically accurate concept knowledge (Ginns and Watters, 1995).

The Ginns and Watters work indicates that science education throughout the education process is critical to honing the problem-solving skills of students. The use of laboratory courses augments this necessary dimension in education.

The low popularity of chemistry at our secondary schools has various causes; for example, a too-extensive curriculum and unsatisfactory selection of the teaching material. Teachers often neglect experiments. There is no clear boundary between the chemistry teaching at primary and secondary schools. It seems indispensable to bring the program of chemistry education at the both types of school closer to everyday life, including a reasonable proportion of the theory at secondary schools (Pacak, 1994).

6.3.2 Solvent Use in Education

In outline form with references (below) we demonstrate various subject areas of physical science (chemistry, physics, and others) where the use of solvents is invaluable. (This will become the mode of reference presentation during the remainder of the book.) Reading these references, the seminal value of early educational experiences involving concepts and exposure to chemical practice are clear, and it is a short conceptual step to link these with solvent usage.

1. Acids and Bases
   a. A study to investigate whether student teachers at a university and a college of education hold any misconceptions about acids and bases was conducted. The study was based on the understanding that any erroneous

knowledge that the student teachers may have is likely to be transmitted later in teaching careers (Bradley and Mosimege, 1998).

2. Demonstrating Electron Transfer
   a. A simplified solar cell fabrication procedure was presented. It used natural anthocyanin or chlorophyll dyes extracted from plants. This procedure illustrates how interdisciplinary science can be taught at lower division university and upper division high school levels for an understanding of renewable energy, as well as basic science concepts (Smestad, 1998).
3. Construction of the Chemical Reaction Concept during Secondary Education
   a. The outcomes show how pupils reorganize their conceptual domain and proceed to the construction of the chemical reaction concept in three distinct stages (Stavridou and Solomonidou, 1998).
4. Integrating High School Chemistry with Environmental Studies and Research (Randall, 1997)
5. How Teacher's and Students Study
   a. The data presented documents that what goes on in classrooms reflects and recreates societal attitudes toward work, in general, and teachers' work, in particular. The teacher in this study reduces his demands for academic work in return for students' cooperation. Students, in turn, are concerned about the academic credentials that lead to success in the college and employment arenas (Costa, 1997).
6. Incorporating Nuclear Chemistry as an Education Tool in the Undergraduate Chemistry Curriculum
   a. The authors propose to address this problem by "educating the educators." Two advantages of this approach are: (1) it will generate scientists with a basic understanding of this field, and (2) as teachers incorporate nuclear topics, many students will have the opportunity to reflect on the role of science in a technological society (Kleppinger and Robertson, 1997).
7. Development and Implementation of Two Industrial Chemistry Case Studies
   a. It is suggested that in-service teacher training courses include a broad spectrum of instructional techniques, which will enable teachers to vary their classroom procedures and to plan new strategies for classroom implementation of industrial chemistry case studies (Kesner et al., 1997).
8. STS Interactions and the Teaching of Physics and Chemistry
   a. The absence of science-technology-society (STS) interactions and its consequences in the basic teaching of science are analyzed. This article proposes the introduction of STS interactions in physics and chemistry classes in conjunction with the teaching/learning model of science as research (Solbes and Vilches, 1997).
9. From Student to Scientist—An Experiential Approach to Science Education
   a. This article provides a rationale for exploring ways in which science educators can structure learning activities that more accurately reflect the scientific inquiry processes used by practicing research scientists (Tuss, 1996).
10. Topic of Redox Reactions—Actions
    a. Teachers' scientific expertise is an important source of difficulties when

teaching redox reactions or chemistry in general. Improvement of current chemistry classroom practice and content-related teacher training are offered (Dejong et al., 1995).

11. Applying the Concept of Conjugation to the Bronsted Theory of Acid-Base Reactions
    a. The result suggests that these problems be addressed in chemistry textbooks and in the classroom teaching of chemistry. If teachers are more aware of students' misconceptions, they will be better able to remove them (Schmidt, 1995).
12. Analogies in Chemistry Textbooks
    a. Sixty-two analogies were identified which described abstract chemical concepts such as atomic structure and collision theory. Authors contended that they were cautious about including analogies in textbooks, as analogies require a flexibility not available when they are set in print (Thiele and Treagust, 1995).
13. Effects of Teacher Talk in a High School Science Classroom
    a. This paper argues that high school classrooms can be considered speech communities in which language may be selectively used as a means of fostering academic speech community identification (Moje, 1995).
14. Analysis of Essential Drugs by Visual Methods
    a. A method for rapidly screening pharmaceuticals by thin-layer chromatography has been designed for use in areas with limited resources and by operators with limited training (Kenyon et al., 1995).
15. What College Chemistry Instructors and High School Chemistry Teachers Perceive as Important for Incoming College Students
    a. College professors universally identified student personal attributes as significantly more important for incoming students to possess over specific knowledge and skills included in the ACS-NSTA Achievement Examination. Conversely, high school chemistry teachers regard the knowledge and skill items to be more important for college preparation than personal attributes (Razali and Yager, 1994).
16. A Cross-Age Study of the Understanding of Five Chemistry Concepts
    a. The amount of experience with the concepts (grade level) and reasoning ability (developmental level) were examined as possible sources of variation in student understanding. Differences in understanding with respect to grade level were found to be significant for the concepts of chemical change, dissolution of a solid, conservation of atoms, and periodicity (Abraham et al., 1994).

6.4 Undergraduate/Graduate Schools

6.4.1 Background

Recent unparalleled changes in our society, in science, and in the economy are contributing to a redefinition of what a college education in chemistry should look like. The educational goal of knowing the "structure of the discipline" is being subsumed

by more holistic and integrative coursework that often is built around socially driven research projects; for example, analysis of food additives, stoichiometry of industrial reactions, and water-quality monitoring. Environmental chemistry, which combines the application of chemical principles with an effort to maintain and enhance environmental quality, is representative of these changes.

The world's leadership demands of the chemistry community the often-competing outcomes of the continued development and production of massive amounts of chemicals that improve the human standard of living; and the responsible management, reduction, treatment, and disposal of chemicals.

The various subdisciplines of chemistry will necessarily incorporate new paradigms. Environmental chemistry tends to minimize the barriers between conventional chemistry courses because it cuts across all subdivisions of chemistry to include organic and physical chemistry, biochemistry, geochemistry, photochemistry, and chemical analysis (Aram and Manahan, 1995).

The education and research system in the sciences is tremendously vital. The scientific community must exert more leadership if this vitality is to continue, for both science education and research are prone to a common inertia. For example, in the education arena, why do medical schools require two semesters of organic chemistry but no cell biology, when the center of biomedical research has shifted to cell biology? And why do so many graduate schools continue to send a strong message to their science students that there is only one really successful career path—the one leading to academia—when most Ph.D. students cannot expect to become professors? Inertia in research can be seen in the trend for scientists to train researchers just like themselves, which means that the many opportunities to use new techniques to address important problems in science are likely to be missed. A solution to such problems is to design funding mechanisms that promote more adventuresome research. As a bottom line, our research system must support the independence of our best young scientists and encourage them to take the risks inherent in highly creative endeavors (Alberts, 1994).

The relative coverage of the major content categories for general chemistry courses at some educational institutions in the United States in 1996 is summarized in table 6.3. The range is fairly typical (Abraham et al., 1997).

Generalizing from the data, one notes the following not unexpected results: about 10% of the course is devoted to the introductory concepts of stoichiometry and chemical equations; more than 20% of the course is devoted to the study of structure of matter and chemical bonding; acids and bases (Bronsted-Lowry) and equilibrium are the most extensively covered topics among the remaining content areas.

In table 6.3 we see the amount of time devoted to solutions (5.6%). The critical role of solvents is recognized. The challenge remains to integrate this into the environmental, technical, and regulatory drivers (Nelson, 1998).

6.4.2 Laboratory

In recent years there has been renewed interest in renovating general chemistry courses in colleges and universities. Much of this interest has focused on the laboratory. Laboratory experience is an essential part of learning chemistry. It helps students comprehend concepts and develop skills to a degree that cannot be accomplished by

Table 6.3. Percentage of topics covered in general chemistry courses.

Topic	Percent Coverage
Stoichiometry & chemical equations	10.1
Atomic theory & structure of atoms	10.9
Chemical bonding	11.6
Properties of gases & kinetic-molecular theory	5.5
Liquid & solid states	4.7
Solutions	5.6
Acids, bases, and salts	7.7
Chemical equilibrium	12.2
Oxidation-reduction & electrochemistry	7.5
Chemical kinetics	6.6
Chemical thermodynamics	9.2
Descriptive chemistry	7.8

lecture or demonstration methods alone. The role of the laboratory has been an ongoing interest of chemistry educators.

According to a survey, the development of concepts is considered the most important outcome of a laboratory program and learning factual information is the least important (Abraham et al., 1997). Even given that, the exposure of undergraduate students to solvents and their use is a critical link to the goals of green chemistry (see table 6.4).

6.4.3 Solvent Use in Higher Education

1. Introducing Green Chemistry in Teaching and Research
   a. The article describes a course called "Introduction to Green Chemistry" (Collins, 1995).
2. Curricula For Environmental Chemistry
   a. Curricula for environmental chemistry have become established, not only recently in the United States, but also in European countries. Students can make their choice among four possibilities: (1) full-time studies in environmental sciences, (2) a classical chemistry program followed by

Table 6.4. Average rank of laboratory goals.

Goal	Average Rank
Concepts	2.12
Laboratory skills	2.43
Scientific processes	2.49
Positive attitudes	3.71
Learning facts	4.31

an environmental supplementary program, (3) a classical chemistry program with a mandatory choice between environmental or ecological chemistry, (4) a classical introductory chemistry followed by a major course of studies in environmental subjects (Lenoir and May, 1997).

3. The Nature and State of General Chemistry Laboratory Courses
   a. Discusses laboratory courses offered in the United States (Abraham et al., 1997).
4. The Development of Chemical Engineering in German Industry and Universities
   a. Chemical engineering is taught at German universities in three different types of curricula: chemical engineering proper, process engineering ("Verfahrenstechnik"), and industrial chemistry ("Technische Chemie"). Industrial chemistry is an essential component of chemistry course at most technical universities and an optional subject at several classical universities (Onken, 1997).
5. First-Year Chemistry Practicals at Universities in England and Wales—Organizational and Teaching Aspects
   a. The practical classes consist, as a rule, of a series of discipline-bound courses, sometimes preceded by a general techniques course. The assessment is almost entirely based on outcomes: quality and quantity of products and reports (Meester and Maskill, 1995).
6. Role of the Universities in Scientific Research Education
   a. The universities have a leading role and responsibility in the scientific education of future professionals. Scientific research training should be considered essential in the teaching of professionals in areas such as biology, chemistry, physics, mathematics, and medicine. Students should be stimulated to participate in these research projects by receiving preferential scores when their elective activities are devoted to it (Reyes, 1995).
7. Laboratory Safety Course in the Chemistry Curriculum
   a. Although laboratory safety is considered an important component of undergraduate training, less than 5% of U.S. colleges and universities offer a required course for chemistry majors. A successful one-credit Laboratory Safety Course has been instituted with the objective to develop skills and attitudes for working with chemicals in a safe and responsible way. Outcomes of the course include positive student evaluations, and an increased student awareness for applying safety practices in the laboratory (Senkbeil, 1994).

6.5 Organic Chemistry

6.5.1 A Green Reaction in Aqueous Media

Examples of organic reactions in green solvents abound. One example is described in the oxidation of cyclohexenes with 30% hydrogen peroxide (Sato et al., 1998). Currently, the industrial production of adipic acid uses nitric acid oxidation of cyclohexa-

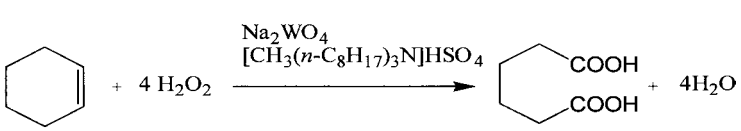
nol or a cyclohexanol/cyclohexanone mixture. The nitrous oxide emission from this process measurably contributes to global warming and ozone depletion. Therefore, the development of an adipic acid production process that is less damaging to the environment is an important subject in chemical research. Cyclohexene can now be oxidized directly to colorless crystalline adipic acid with aqueous 30% hydrogen peroxide under organic solvent- and halide-free conditions.

Adipic acid is an important chemical whose production is necessary for the manufacture of nylon-6,6, which is used in carpet fibers, upholstery, tire reinforcements, auto parts, apparel, and other products. Most industrial processes of adipic acid production use nitric acid oxidation of cyclohexanol, cyclohexanone, or both, which are accessible from benzene (Davis and Kemp, 1991). The worldwide industrial adipic acid production of up to 2.2 million metric tons per year (Thiemens and Trogler, 1991) relies on a refined technology that minimizes the emission of nitrous oxide (N_2O), an inevitable stoichiometric waste (Thiemens and Trogler, 1991) that is commonly thought to cause global warming and ozone depletion (Dickinson and Cicerone, 1986) as well as acid rain and smog. Despite the efficient recovery or recycling of N_2O, ~400,000 metric tons are still emitted each year, which corresponds to 5 to 8% of the worldwide anthropogenic emission of N_2O.

Aqueous H_2O_2 is an ideal clean oxidant if the oxidation reaction is achieved with a $[H_2O_2] < 60\%$. The authors developed practical oxidation methods with aqueous 30% H_2O_2 in the presence of small amounts of Na_2WO_4 and $(CH_3(n\text{-}C_8H_{17})_3N)HSO_4$ as a phase transfer catalyst (PTC) (Sato et al., 1997). This aqueous, organic biphasic reaction enables the high-yield epoxidations of olefins, either terminal or internal, as well as the oxidation of primary and secondary alcohols under conditions that are entirely free of organic solvents and halides. The high catalytic efficiency can be obtained only by using a quaternary ammonium hydrogen sulfate rather than conventional chlorides as the PTC.

When a mixture of cyclohexene (1, fig. 6.1), 30% H_2O_2, $Na_2WO_4 \cdot 2H_2$, and $(CH_3(n\text{-}C_8H_{17})_3N)HSO_4$ as the PTC (the olefin : PTC molar ratio is 100 :1:1) was stirred in air at 1000 rpm and at a temperature of 75°C to 90°C for 8 hours, adipic acid **(2)** was formed in 93% yield (as determined by gas chromatographic (GC) analysis). The collection of the crystalline product by filtration followed by drying in air produced colorless, analytically pure **2** in 90% yield. The aqueous phase of the reaction mixture can be reused with a renewed PTC and 30% H_2O_2 to produce **2** in 78% yield.

This solvent- and halide-free oxidation of cyclohexene and cyclopentene is clean, safe, and reproducible, with conditions that are less corrosive than those of the nitric acid oxidation. No operational problems are foreseen for a large-scale version of this "green" process, and technical refinement should further increase the synthetic effi-



1 2

Figure 6.1 Synthesis of adipic acid

ciency. The worldwide chemical industry is directing extensive efforts toward the efficient production of H_2O_2 as a clean, selective oxidant (Arends et al., 1997).

The synthetic efficiency compares favorably with existing methods that largely use quaternary ammonium halides and chlorohydrocarbon solvents (Arends et al., 1997). Sato and co-workers (Sato et al., 1997) provide several tables of primary and secondary alcohols that were successfully oxidized with aqueous hydrogen peroxide.

A major concern in H_2O_2 oxidation is the alcohol/olefin chemoselectivity (Rao, 1991). This biphasic oxidation was initially developed for olefin epoxidations but with an (aminomethyl)phosphonic acid additive for high selectivity (Rudolph et al., 1997). Now, the removal of this additive has been found to significantly increase the rate and selectivity of alcohol oxidation.

6.5.2 Supercritical Carbon Dioxide

Supercritical CO_2 has emerged as an environmentally friendly alternative solvent in various industrial and analytical processes (Tanko et al., 2000). CO_2 becomes a supercritical fluid at pressures greater than 1,100 psi and at temperatures at or above 88°F. Supercritical CO_2 has already found use in coffee decaffeination, wastewater treatment, and chemical analysis, and it is presently being studied for use in polymer manufacturing, pharmaceutical manufacturing, and soil remediation. Advantages of supercritical CO_2 include speed, the inherent cleanliness of the extracts, and a substantial reduction in the volume of solvents used. Disadvantages of equipment cost and the small sample size obtained in supercritical CO_2 extraction are diminishing (Black, 1996).

Interactions between solute and solvent in supercritical fluids (SCFs) are of fundamental importance because small changes in pressure or temperature near the critical point may alter reactivity in chemical and biochemical processes. Ester synthesis has been done from acyl donors and terpene alcohols catalyzed by *Candida cylindracea* (CCL) lipase in supercritical carbon dioxide. In the near-critical region, (S)-(-)-terpene esters were stereoselectively synthesized from acyl donors and a primary alcohol such as (I)-citronellol. In a very limited pressure range near the critical point, interactions between carbon dioxide and enzyme molecules greatly increased with consequent drastic conformational changes in the enzyme, causing active sites to emerge to catalyze stereoselective synthesis. Therefore, supercritical carbon dioxide medium in the near-critical region should trigger the activation of the enzyme by causing movement of its surface groups and creating active sites.

High-pressure FT-IR spectroscopy has been used to clarify (1) the rotational isomerism of molecules, (2) characteristics of water and the water-head group, and (3) RSO_3^- Na+ interactions in reverse micellar aggregates in supercritical ethane. This work demonstrates interesting pressure, temperature, and salt effects on an enzyme-catalyzed esterification and/or maintenance of a one-phase microemulsion in supercritical fluids from practical and theoretical points of view (Ikushima, 1997).

Martyn Poliakoff has presented work on transition metal catalysis using supercritical CO_2 as an environmentally benign solvent. Supercritical hydrogenation can be controlled with high precision because the solvent, organic compound, and the hydrogen are all in a single phase. For example the hydrogenation of isophorone (see fig. 6.2) is effective with large production in a small reactor. Poliakoff has also discussed

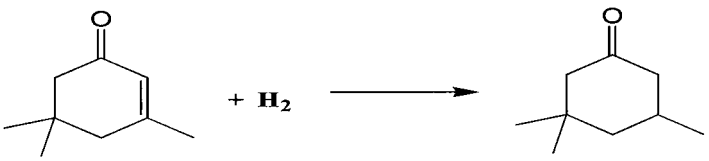


Figure 6.2 Hydrogenation of isophorone

the generation of synthetic bone material from calcium hydroxylapatite and biodegradable polymers in supercritical CO_2 (Poliakoff et al., 1999).

6.5.2.1 SCFs as Solvents for Chemical Synthesis and Processes

In recent years, fluids have been exploited as solvents up to 100K above their critical temperatures and pressures, and the term supercritical fluids has been coined to describe these media. Although environmental considerations are often the main motivation, more fundamental advantages of supercritical fluids arise because they can have properties somewhere between those of typical gases and liquids. Any advantage has to be weighed against the cost of the higher pressures needed, and so supercritical fluids are utilized in particular areas: extraction, chromatography, crystallization and particle formation, cleaning and dyeing, and chemical reactions. Apart from the environmental factor, the more basic motives for carrying out reactions in supercritical fluids include control of phase behavior, diffusion effects, control of products, and obtaining continuously varying properties for mechanistic studies.

Supercritical fluids possess properties that make them attractive as media for chemical reactions. Conducting chemical reactions at supercritical conditions provides opportunities to manipulate the reaction environment (solvent properties) by manipulating pressure, to enhance the solubilities of reactants and products, to eliminate interphase transport limitations on reaction rates, and to integrate reaction and separation unit operations. Supercritical conditions may be advantageous for reactions involved in fuels processing, biomass conversion, biocatalysis, homogeneous and heterogeneous catalysis, environmental control, polymerization, materials synthesis, and chemical synthesis. Moreover, supercritical fluids can be used profitably in fundamental chemical investigations of intermolecular interactions and their influence on chemical processes (Savage et al., 1995).

Other work on supercritical fluids covered include:

- the production of hydrogen peroxide in CO_2 with the recovery of the product without depressurization;
- drawing poly(ethylene terephthalate) fibers in CO_2;
- building products from supercritical CO_2 and fly ash.

6.5.2.2 General References on $SCCO_2$

1. Manufacturing in compressed carbon dioxide is nearing the marketplace (McCoy, 1999).
2. Remarkable tuning of reaction rates has been achieved for the isomerization of several dye molecules in supercritical fluid solvents (Dillow et al., 1998).

3. CO_2 is an inert, nonhazardous solvent, and leads to easy disposal of organic liquid wastes. Separation of CO_2 from the reaction mixture is easily achieved. Differences in diffusivity, miscibility, and solubility between sc-CO_2 and other solvents can also be used to improve certain reactions (Wai et al., 1998).
4. Solid-fluid equilibria are important for supercritical fluid processing design (Bush and Eckert, 1998).
5. The solubility of naphthalene in supercritical carbon dioxide fluids has been evaluated by means of the integral equation method (Tanaka and Nakanishi, 1994).
6. The hard-sphere expansion (HSE) theory is incorporated in the Kirkwood-Buff fluctuation integral to predict solubilities of solids in supercritical carbon dioxide and ethylene (Kwon and Mansoori, 1993).

6.5.2.3 Supercritical Fluid Extraction with CO_2

Supercritical extraction has been used increasingly in recent years for specialized processes. These processes include separation of drugs from plants, oils from vegetable seeds, impurities from labile materials, and chemical feedstocks from coal and petroleum residual. The utility of supercritical extraction processes stems principally from the enhanced solubility characteristics of CO_2 near its critical point and the ease with which the solvent can be recovered for recycle.

In a supercritical extraction process a solvent is contacted with a solute at conditions near a critical point of the solvent plus solute mixture. The mixture may exhibit multiphase behavior invoving vapor, liquid, and solid phases, depending on the mixture composition and temperature and pressure conditions.

It is valuable to use fundamental thermodynamics and particularly classical phase behavior information in understanding supercritical extraction phenomena and in designing processes utilizing supercritical extraction. Judicious choices for operation conditions and solvent to solute ratio are possible when the phase behavior for the system is established. For most supercritical extraction processes, the best operating conditions generally are as near as possible to the critical point of the mixture and are supercritical with respect to the mixture critical point, irrespective of the solvent critical point. The design of any process must take economics into account, but it is believed that the technical basis for the design would be enhanced by the type of information discussed above (Starling et al., 1985).

Carbon dioxide has moved from some marginal applications to being the major solvent for supercritical fluid (SCF) extraction. For most products, the extraction plant is operated on a batch production basis using supercritical fluid. By moving to supercritical conditions, the thermophysical properties are changed to give much better characteristics for extraction than in the liquid phase. The improvement in performance from going to supercritical conditions greatly outweighs the increases in engineering costs associated with going from a plant with design pressures of up to 100 bar to a 500 bar plant (Hurren and Berger, 1999).

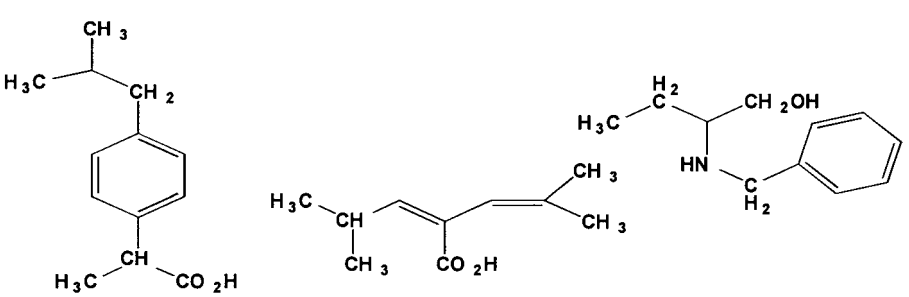
As a solvent, carbon dioxide does have a number of advantages over more conventional techniques. Because the critical point is only at 304 K (i.e., 31°C), temperature sensitive substances can be extracted without any degradation. This is particularly

important for production of plant extracts both for use in foodstuffs and for the pharmaceutical industry. For food and essential oil applications it also means that natural products can be recovered without any loss of aroma. As a solvent, carbon dioxide is more environmentally friendly than hydrocarbons.

One recent development by Messer in Germany has been for the recycling of cutting oils. Within the metals industry there is a substantial production of oil-bearing sludges. In Germany alone the annual production is in excess of 150,000 tons of sludge. This sludge is classified as a special waste and its disposal is becoming increasingly difficult and expensive as landfill restrictions increase. Conventional disposal techniques consist of oil recovery using pressing or centrifuges. This can reduce the oil content to between 10 and 15%. If the oil is extracted using supercritical carbon dioxide, then the oil content of the sludge can be reduced to less than 1%. The recovered cutting oil is of sufficient purity that it can be re-utilized in the machining process. The metal powder can also be recovered, resulting in an overall recovery of almost 100% from what had previously been a waste product (Hurren and Berger, 1999).

Extraction of 25 different binary mixtures of racemic acids (2-(4-isobutylphenyl)-propionic acid **(1)**, and *cis*- and *trans*-chrysanthemic **(2)**), and various chiral bases with supercritical carbon dioxide permitted the conclusion that molecular chiral differentiation in a supercritical fluid is more efficient than in conventional solvents. In the majority of cases, however, complete separation could not be achieved. In five cases, remarkable partial resolutions were realized (30–75% *ee*) and resolution was possible on a preparative scale. The pair *cis*-chrysanthemic acid and (S)-(+)-2-(benzylamino)-1-butanol **(3)** was studied in detail. Pressure, temperature, and time, as well as the molar ratio of base and acid, had a marked influence on the quantity and quality of the products. Increasing pressure or decreasing temperature resulted in higher ee values. (-)-*cis*-Chrysanthemic acid in 99% ee was obtained from the raffinate in a single extraction step. Multiple extractions produced the (+)-*cis*-acid in 90% ee (see fig. 6.3) (Simandi et al., 1997).

6.5.2.3.1 Applications for SCF Extraction Supercritical fluid extraction has been mainly used for the extraction of natural extracts for aromatic substances and essences, and for various active substances for pharmaceuticals. Alternative possibilities include



1 2 3

Figure 6.3

material recovery for recycling and the extraction of unreacted monomers and ligands from high-quality polymer products.

It is the potential to produce particles with a very narrow size distribution and with dimensions in the range of 1μm to 10μm which is generating the most interest in using carbon dioxide as a supercritical fluid. The technique using $SCCO_2$ allows precise control of the crystallization process, and is capable of generating very small and uniform particles (Hurren and Berger, 1999).

Additional references for SCF extraction include the following:

1. $SCCO_2$ fractionation of fish oil ethyl esters was employed to prepare ethyl esters of two omega-3 fatty acids. The triacylglycerol products were isolated using supercritical fluid fractionation (Nilsson et al., 1989).
2. SCFE of lipids from two freeze-dried microalgae species were studied (Polak et al., 1989).
3. Phenol, a common priority pollutant, was extracted from two environmental matrices, soil and water, using near-critical and supercritical carbon dioxide (Roop et al., 1989).
4. Quantitative extraction of di- and tributyltin compounds from aqueous matrices is demonstrated for the first time (Alzaga and Bayona, 1993).
5. The solubilities of soybean oil in neat supercritical carbon dioxide (SC-CO2) and CO_2 with entrained helium were measured (King et al., 1995).
6. Extraction of metal ions from liquid and solid materials by supercritical carbon dioxide (Laintz et al., 1992).
7. A comparison of extraction methods for primary aromatic amines including 1,4-phenylenediamine, 2,4-diaminotoluene, benzidine, 4,4′-methylenebis (2-chloroaniline), 3,3′-dimethylbenzidine, and 3,3′-dichlorobenzidine from solid matrices was conducted. Supercritical fluid extraction (SFE) was evaluated and compared with the classical method, sonication extraction (Oostdyk et al., 1993).
8. Measurements of solubilities in supercritical CO_2 corroborated the hypothesis that the nonpolar character of a series of tetraalkylammonium dialkyldithiocarbamate ion pairs was influenced
   a. primarily by the chain length of the alkyl substituent on the carbamate nitrogen; and
   b. to a lesser extent, by the chain length of the alkyl substituent(s) on the ammonium counterion (Wang and D., 1994).
9. The recovery of chlorobenzenes (di- to hexachloro) and hexachlorocyclohexane (HCH) isomers from supercritical carbon dioxide by trapping in cold solvent was studied (Wenclawiak et al., 1994).
10. Supercritical carbon dioxide effectively extracts the nonpolar compounds from all soil types. The extraction of more polar compounds, such as chlorophenols and some pesticides requires that a polar compound, such as a short-chain alcohol is added to the carbon dioxide. Supercritical carbon dioxide extraction is used by environmental analysis laboratories as a more efficient, occupationally more acceptable method for analyzing contaminated soils (Laitinen et al., 1994).

11. Lipids that contain polyunsaturated fatty acids (PUFA) have therapeutic value. Supercritical CO_2 extraction was chosen as an alternative method to recover these valuable compounds from the lower fungus, *Pythium irregulare* (Walker et al., 1999).
12. An automated supercritical fluid extraction and in-line clean-up system has been developed for organochlorine and organophosphate pesticide residues contained in fats (Hopper, 1999).
13. The efficacy of supercritical fluid extraction (SFE) for the recovery of 16 common organochlorine pesticides (OCPs) from liquid whole eggs was investigated by employing supercritical carbon dioxide (SC-CO2) without the use of a solvent modifier to minimize interfering coextractives (Fiddler et al., 1999).
14. Application of supercritical fluid extraction (SFE) for selective isolation of organophosphorus pesticides from a real-world matrix (wheat flour) (Kim et al., 1998).
15. Examines the supercritical extraction of dry tobacco powder using supercritical carbon dioxide (SC-CO_2) as solvent (Rincon et al., 1998).
16. Development of a method for semicontinuous extraction using supercritical carbon dioxide (Andersson et al., 1997).
17. The extraction of pentachlorophenol (PCP) from pressure-treated wood wafers with supercritical carbon dioxide (SC-CO_2) was studied in a continuous-flow extractor (Sahledemessie et al., 1997).
18. A supercritical fluid extraction (SFE) method for the determination in strawberries of a number of commonly used organochlorine insecticides, organophosphorus pesticides, and dichloroanilide fungicides (Pearce et al., 1997).
19. Description of extraction of grape seed oil by means of liquid and supercritical carbon dioxide as solvent (Gomez et al., 1996).
20. The solubility of a *tert*-butyl-substituted dibenzobistriazolo-crown ether in methanol (5 mol %) modified CO2 has been determined to be in the order of 1×10^{-3} M at 60°C and 200 atm (Wang et al., 1995).

6.5.3 SC-CO_2 as a Reaction Solvent

There are several potential advantages which may be realized with the use of supercritical carbon dioxide as a solvent for chemical reactions (Tanko et al., 1994):

- Important solvent properties of SC-CO_2 (e.g., dielectric constant, solubility parameter, viscosity, density) can be altered via manipulation of temperature and pressure. This unique property of a supercritical fluid could be exploited to control the behavior (e.g., kinetics and selectivity) of some chemical processes.
- The supercritical state of CO_2 is relatively easily attained ($T_c = 31°C$, $P_c = 74$ bar). This feature of SC-CO_2 implies that the "cost" (e.g., energy, apparatus, and materials) will not be prohibitive with the conversion to SC-CO_2.
- Finally, CO_2 is nontoxic and "environmentally benign."

Another factor to be considered in the use of SC-CO_2 as a reaction solvent deals with the possible effect of pressure on reaction rate (and selectivity). A dramatic

variation of rate with pressure just above the critical point (as seen with the Diels-Alder reaction) is attributed to a phenomenon referred to as "clustering" in which solvent molecules are believed to aggregate (cluster) about the solute (Roberts et al., 1992).

SC-CO_2 represents an inexpensive, environmentally benign alternative to conventional solvents for chemical synthesis. It can be a viable substitute solvent for many synthetic reactions. When used in conjunction with suitable catalysts, homogeneous catalytic reactions can be run (Morgenstern et al., 1996). The most important constraints on synthetic chemistry are those imposed by the solvation properties of supercritical CO_2. The regime of interest to the synthetic chemist interested in pollution prevention is likely to be that which provides maximum solubility (densities above 0.8 g/mL) while using minimal cosolvent (solvent replacement). In this regime, the solubility properties of $SCCO_2$ are similar to those of hexane, although CO_2 has some hydrogen-bond acceptor capabilities, as well as some dipole selectivity. Thus, nonpolar organic species below molecular weight 400 are generally highly soluble, including alkanes, alkenes, aromatics, ketones, and alcohols. Highly polar compounds such as sugars and amino acids are generally quite insoluble. Polysiloxanes and fluoropolymers are quite soluble, but most other polymers are not. Limitations on polymer solubility can sometimes be overcome via the use of phase stabilizers or emulsifiers, which typically contain a "$SCCO_2$-philic" fluorinated component along with a hydrocarbon portion (Morgenstern et al., 1996).

Supercritical fluids (SCFs) have many unusual properties. Homogeneous molecular catalysts, which have far greater control over selectivity than heterogeneous solid catalysts, are now being tested in SCFs, and early results show that high rates, improved selectivity, and elimination of mass-transfer problems can be achieved. More than simply substitutes for nonpolar solvents, SCFs can radically change the observed chemistry. Supercritical carbon dioxide is also an excellent medium for its own fixation, as demonstrated by studies of its hydrogenation (Jessop et al., 1995). Also, there is a growing body of studies of organometallic reactions in SCFs (Darr and Poliakoff, 1999), many of which have contributed to our understanding of solvation and solvent effects on reactions in SCFs.

Brennecke and Chateauneuf drew several conclusions regarding reactions in supercritical fluids (Brennecke and Chateauneuf, 1999):

- The primary influences on reaction rates, selectivities, and mechanisms are the bulk physical properties of the fluid, which can be varied continuously from gas-like to liquid-like.
- Local solvation in the form of local density augmentation and local composition enhancements can influence reactivity, but this depends on the relative time-scales of the reaction and solvation processes.
- The specific mechanism of the reaction is very important in determining how both bulk properties and local phenomenon might influence the reaction rate or selectivity.
- There is tremendous opportunity for conducting all types of chemistry in SCFs.

Further examples of SCF in chemical reactions can be found in the following:

1. A maximum is found in the ratio of endo- to exo-products versus, density in the Diels-Alder reaction between cyclopentadiene and methyl acrylate in supercritical carbon dioxide (Clifford et al., 1997).
2. Promotion of Lipase-Catalyzed Esterification of N-Valeric Acid and Citronellol in Supercritical Carbon Dioxide in the Near-Critical Region (Ikushima et al., 1996).
3. Esterification between oleic acid and oleyl alcohol, catalyzed by the *Mucor miehei* immobilized lipase in a batch-stirred tank reactor with supercritical carbon dioxide as solvent produced higher reaction rates at supercritical conditions than in the solvent-free system (Knez et al., 1995).
4. Reactions in Supercritical Carbon Dioxide (Kaupp, 1994).
5. The study of enzymatic esterification by an immobilized lipase in supercritical carbon dioxide ($SCCO_2$) and in *n*-hexane (Marty et al., 1994).
6. The pressure effect on the bimolecular rate constants for the esterification of phthalic anhydride with methanol in supercritical carbon dioxide (Ellington et al., 1994).
7. Homogeneous molecular catalysts, which have far greater control over selectivity than heterogeneous solid catalysts, are now being tested in SCFs, and early results show that high rates, improved selectivity, and elimination of mass-transfer problems can be achieved (Andrew et al., 1995; Birnbaum et al., 1999).

6.5.3.1 Free Radical Reactions

Free radical brominations can be conducted effectively in SC-CO_2 as solvent. The high product yields and selectivities usually found for brominations in conventional solvents are not compromised by the use of this nontoxic, less environmentally threatening medium. The results demonstrate that supercritical fluid solvents retain virtually all of the "chemical" advantages associated with conventional organic solvents (Tanko et al., 1994).

Direct bromination of toluene and ethylbenzene form the corresponding benzyl bromides in high yield. The observed selectivity in SC-CO_2 is similar to that observed in conventional organic solvents. Also, SC-CO_2 is an effective alternative to carbon tetrachloride for use in the classical Ziegler bromination with N-bromosuccinimide. Reaction yields are high, side products are minimized, and bromine-atom selectivities are observed. Thus, SC-CO_2 must be useful as a viable, environmentally benign substitute for many of the solvents typically used for free-radical reactions (Tanko and Blackert, 1994).

The chlorine atom cage effect was used as a highly sensitive probe for studying the effect of viscosity and the possible role of solvent clusters on cage lifetimes and reactivity for reactions carried out in supercritical fluid solvents. The results of these experiments provide no indication of an enhanced cage effect near the critical point in SC-CO_2 solvent. The magnitude of the cage effect observed in SC-CO_2 at all pressures examined is well within what is anticipated on the basis of extrapolations from conventional solvents (Fletcher et al., 1998).

6.5.3.2 Diels-Alder Reactions

Besides being of considerable commercial interest, Diels-Alder reactions are clean, well-characterized reactions that generally proceed in a single step through a pseudo-aromatic transition state. There have been studies on the pressure effect on ionic reactions in SCFs by Zhang et al. (1996) who measured the rates of arylmethyl cation ion-neutral reactivity in SCF.

The regioselective course of the Diels-Alder reaction in supercritical carbon dioxide was investigated. The analysis failed to confirm the previously reported dramatic effect of reaction conditions on Diels-Alder regiochemistry. The results highlighted the importance of verifying phase behavior when sampling CO_2 reaction mixtures and the utility of a view-cell reactor that allows direct monitoring of phase behavior (Renslo et al., 1997).

For the Diels-Alder reaction between isoprene and methyl acrylate (see fig. 6.4) in supercritical carbon dioxide at 323 K, the solubility parameter of the activated complex was determined in order to study the nature of the complex and the effect of the solvent on the reaction (Ikushima et al., 1994).

6.5.3.3 Polymerizations

Supercritical carbon dioxide has been used as a dispersing medium for the manufacture and processing of polymeric materials. The process allows for the synthesis of high molar mass acrylic polymers in the form of micrometer-sized particles with a narrow size distribution. This procedure represents an environmentally responsible alternative to aqueous and organic dispersing media for heterogeneous dispersion polymerizations (Fox, 1994).

Conventional heterogeneous dispersion polymerizations of unsaturated monomers are performed in either aqueous or organic dispersing media with the addition of interfacially active agents to stabilize the colloidal dispersion that forms. Successful stabilization of the polymer colloid during polymerization results in the formation of high molar mass polymers with high rates of polymerization. Supercritical carbon dioxide (CO_2) is used in conjunction with molecularly engineered free radical initiators and amphipathic molecules that are specifically designed to be interfacially active in CO_2. Conventional lipophilic monomers, exemplified by methyl methacrylate, can be quantitatively (> 90 percent) polymerized heterogeneously to very high degrees of polymerization (> 3000) in $SCCO_2$ in the presence of an added stabilizer to form kinetically stable dispersions that result in micrometer-sized particles with a narrow size distribution (Desimone et al., 1994; Quadir et al., 1998).

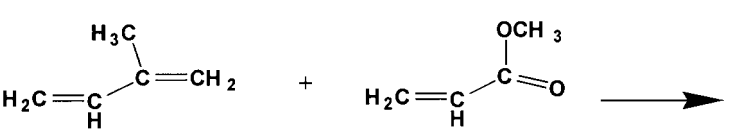


Figure 6.4

The high-pressure phase behavior of polymer-solvent-supercritical carbon dioxide systems was investigated experimentally The polymers used were poly(methyl methacrylate), polystyrene, polybutadiene, and poly(vinyl ethyl ether) at concentrations ranging from 5 to 10% in mixtures with toluene or tetrahydrofuran. The experiments were conducted for temperatures from 25 to 70°C and pressures up to 2200 psi in a high-pressure cell (Kiamos and Donohue, 1994).

Supercritical carbon dioxide was found to be a suitable substitute for halogenated organic solvents in its copolymerization with propylene oxide. The system was studied utilizing a heterogenous catalyst, zinc glutarate. The polymers were analyzed for selectivity in polycarbonate linkages by ^{1}H NMR spectroscopy and for molecular weight by gel permeation chromatography (Darensbourg et al., 1995).

Previous major advances have occurred in the synthesis of a variety of polymeric materials in carbon dioxide. At the same time, complementary studies have successfully elucidated the physical behavior of a range of polymers in carbon dioxide solution (Cooper and DeSimone, 1996).

The dispersion polymerization of styrene in supercritical CO_2 using amphiphilic diblock copolymers to impart steric stabilization has been investigated. Lipophilic, CO_2-insoluble materials can be effectively emulsified in carbon dioxide using amphiphilic diblock copolymer surfactants. The resulting high yield (> 90%) of polystyrene is obtained in the form of a stable polymer colloid comprised of submicron-sized particles (Canelas et al., 1996).

Dispersion polymerizations of methyl methacrylate utilizing poly(1,1,-dihydroperfluorooctyl acrylate) as a steric stabilizer in supercritical CO_2 were carried out in the presence of helium. Particle size and particle size distribution were found to be dependent on the amount of inert helium present. Particle sizes ranging from 1.64 to 2.66 μm were obtained with various amounts of helium. Solvatochromic investigations using 9-(α-perfluoroheptyl-β,β-dicyanovinyl)julolidine indicated that the solvent strength of CO_2 decreases with increasing helium concentration. This effect was confirmed by calculations of Hildebrand solubility parameters (Hsiao and DeSimone, 1997).

The proton and fluorine chemical shifts of *n*-hexane, perfluoro-*n*-hexane, and 1,1-dihydroperfluorooctylpropionate dissolved in supercritical carbon dioxide have been studied using high-pressure, high-resolution nuclear magnetic resonance. The CO_2 density differentially influences ^{1}H and ^{19}F chemical shifts, which, in turn, suggest specific solute–solvent interactions between CO_2 and fluorinated compounds. The density-dependent proton chemical shifts are exclusively governed by changes in the bulk susceptibility of CO_2; these shifts exhibit only slight temperature dependence (Dardin et al., 1998).

6.5.3.4 Miscellaneous Reactions in $SCCO_2$

The efficient production of formic acid (HCOOH) from carbon dioxide (CO_2) has been reported. HCOOH was produced in a supercritical mixture of CO_2 and hydrogen containing a catalytic ruthenium(II)-phosphine complex. An initial rate of reaction of up to 1,400 moles of HCOOH per mole of catalyst per hour was achieved, giving a final yield of 3,700 moles HCOOH per mole of catalyst after several hours. The rate of reaction in the supercritical fluid was 18 times faster than that in tetrahydrofuran

(THF) under otherwise identical conditions. Supercritical fluids therefore represent a promising medium for homogeneous catalysis (Johnston, 1994).

The rapid and efficient methylation and extraction of organic acids from aqueous solution using supercritical carbon dioxide containing methyl iodide and tetrahexylammonium hydrogen sulfate was shown to be analogous to similar reactions in conventional liquid–liquid extractive alkylation systems. The presence of methanol modifier in the supercritical carbon dioxide was deleterious to recovery of the methyl esters. A method in which the derivatizing reagent was continually supplied to the extraction vessel was found to be more demanding of reagents and equipment and gave less repeatable results than a simpler static reaction system (Croft et al., 1994).

Cyclohexane oxidation has been studied in supercritical carbon dioxide medium for homogenizing the initial reaction mixture to produce cyclohexanone and cyclohexanol as the chief reaction products. Conversions obtained are low compared to the liquid phase oxidation because of dilute concentrations of the reactants. Cyclohexanone is more selectively formed and favored by both pressure and temperature. Results suggest that the reaction in supercritical CO_2 medium can be greatly manipulated (Srinivas and Mukhopadhyay, 1994).

Homogeneous molecular catalysts, which have far greater control over selectivity than heterogeneous solid catalysts, are now being tested in SCFs, and early results show that high rates, improved selectivity, and elimination of mass-transfer problems can be achieved. Supercritical carbon dioxide may be an ideal replacement medium for nonpolar or weakly polar chemical processes. More than simply substitutes for nonpolar solvents, SCFs can radically change the observed chemistry (Jessop et al., 1995).

Catalytic hydrogenation in supercritical carbon dioxide has been studied. The effects of temperature, pressure, and CO_2 concentration on the rate of reaction are important. Hydrogenation rates of the two double bonds of an unsaturated ketone on a commercial alumina-supported palladium catalyst were measured in a continuous gradient-less internal-recycle reactor at different temperatures, pressures, and CO_2-to-feed ratios. The accurate control of the organic, carbon dioxide, and hydrogen feed flow rates and of the temperature and pressure inside the reactor provided reproducible values of the product stream compositions, which were measured on-line after separation of the gaseous components (Bertucco et al., 1997).

$SCCO_2$ is a reaction medium for highly efficient rhodium-catalyzed hydroformylation reactions. Olefinic substrates can be hydroformylated in $SCCO_2$ at 40–65°C to give the corresponding aldehydes in practically quantitative yields. The reaction course of the hydroformylation of 1-octene in $SCCO_2$ was analyzed in detail by online-GC monitoring. With unmodified catalysts, the hydroformylation rates are considerably higher in $SCCO_2$ than in organic solvents or liquid CO_2 under otherwise identical conditions. Modified catalytic systems formed with perfluoralkyl-substituted triarylphosphine and triaralyphosphite ligands lead to higher regioselectivities than those found in conventional solvents. Olefin isomerization, which is a typical side reaction for phosphite-modified systems in conventional solvents, was effectively suppressed in $SCCO_2$ (Koch and Leitner, 1998).

The three-phase catalytic hydrogenation of an unsaturated ketone using supercritical carbon dioxide as a solvent was studied in order to simulate the performance of a semi-industrial trickle-bed reactor. It is shown that supercritical CO_2 strongly increases the reaction rate (Devetta et al., 1999).

6.5.3.5 Metals and Textiles/Dyeing in Supercritical CO_2

German scientists believe that "supercritical" carbon dioxide can be used instead of water as a medium for dyeing, thus solving the problem of how to remove color from wastewater. Another advantage of this process is that supercritical carbon dioxide readily dissolves dyes without the additional chemicals required to improve dye solubility in water (Houlton, 1993).

The quenching of 9,10-bis(phenylethynyl)anthracene (BPEA) fluorescence by carbon tetrabromide (CBr_4) is investigated in supercritical carbon dioxide as a function of densities. Fluorescence lifetimes of BPEA at different CBr_4 concentrations are determined using the time-correlated single photon counting method. While the fluorescence decays adhere closely to single-exponential functions and the CBr_4 concentration dependence follows the Stern-Volmer relationship, the quenching of fluorescence lifetime is unusually efficient at near-critical densities. The results are in support of a solute–solute clustering mechanism in which the enhanced bimolecular reactions are attributed to a higher local quencher concentration than the bulk under near-critical solvent conditions (Toews et al., 1995).

Extraction behaviors of U(VI) and selected fission product elements from HNO_3 solution into a supercritical CO_2 fluid containing tributylphosphate (TBP) were studied under equilibrium and dynamic extraction conditions. Uranium(VI) was found to be extracted in the supercritical CO_2 phase. The distribution ratio of U(VI) increased with an increase of HNO_3 concentration (0.1–6 M) or TBP (0.1–0.3 M), along with a decrease of pressure at 60°C, and with an increase of the temperature (40–80°C) at 15 MPa. A salting-out effect enhancing the distribution of U(VI) was observed by addition of a fairly high concentration of $LiNO_3$ to the aqueous phase. Results of dynamic extraction using a continuous flow of supercritical CO_2-TBP through the aqueous nitric acid solution showed that > 98% of U(VI) could be extracted from 3M HNO_3+3 M $LiNO_3$ solution into supercritical CO_2-0.08 M TBP (60°C, 15 MPa). Main fission product elements such as lanthanides, Cs, Sr, Ba, Zr, Mo, and Pd were hardly extracted into the supercritical CO_2 phase under this condition, which suggests that the supercritical CO_2 extraction is a feasible method for the separation and recovery of uranium from these elements (Meguro et al., 1996).

Monomeric compounds of the type Cp_2M (e.g., M = Fe, Co, Ni) are soluble in liquid or supercritical CO_2 without any reaction with the solvent. The polymeric compounds zincocene or manganocene form with CO_2 insoluble CO_2 insertion products. $Fe(CO_5)$ reacts photochemically in this solvent to Fe-2(CO_9) and thermically to Fe-3(CO_{12}). The highly reactive (cdt)Ni(0) (cdt: cyclododeca-1,5,9-triene) is soluble in liquid CO_2. A reaction with the solvent could not been observed. CpCo(cod) catalyzes slowly the cyclo-cooligomerization of hex-3-yne with acetonitrile to form 2,3,4,5-Tetraethyl-6-methylpyridine. The catalytic oxidation of cyclooctene to form cyclooctenoxid with t-BuOOH using Titan(IV)-isopropylate as soluble catalyst proceeds less selectively. However, in the presence of $Mo(CO_6)$ the epoxide is formed in good yields and in a highly selective reaction (Kreher et al., 1998).

A series of complexometric extractions were performed to optimize the mobilization/purging of metallic ions from samples of processing condensate of chromated copper arsenate (CCA). Whereas Cr(VI) and Cu(II) were rapidly mobilized into isobutylmethyl ketone-amended $SCCO_2$ after reaction with dithiocarbamate or alkylxan-

thate, Cr(III) was appreciably less reactive under these conditions. In feasibility trials with CCA suspension that had been diluted 10-fold, optimized extraction procedures resulted in the mean removal of 99.9% Cu, 96.8% Cr, and 86.0% As from the aqueous phase. Similar procedures with the undiluted suspension were approximately equally efficient (100% Cu, 98.7% Cr, and 80.9% As). Although the solvent-assisted complexometric extraction was virtually quantitative for Cu and efficient for Cr, the mobilization of As would necessitate a subsequent treatment to remove residues of these ions (Ager and Marshall, 1998).

A study of the reactivity of the halogenated porphyrins tetrakis(pentafluorophenyl)porphyrinato iron(III) chloride (Fe(TFPP)Cl) and beta-octabromo-tetrakis(pentafluorophenyl)porphyrinato iron(III) chloride (Fe(TFPPBr$_8$)Cl) with dioxygen and cyclohexene was executed in $SCCO_2$. A lower limit for the solubility of the iron porphyrins was determined in $SCCO_2$. Both halogenated metalloporphyrins were active catalysts for oxidation of cyclohexene to epoxide and allylic oxidation products in $SCCO_2$. Selectivity for epoxidation with Fe(TFPPBr$_8$)Cl is higher in $SCCO_2$ than in organic solvents, with up to 34% cyclohexene oxide produced (Birnbaum et al., 1999).

6.5.3.6 Biocatalysis and Microemulsions in Near-critical and Supercritical Fluids

Supercritical fluids represent a unique class of nonaqueous media for biocatalysis and bioseparation. The inherent gas-like low viscosities and high diffusivities of supercritical fluids increase the rates of mass transfer of substrates to enzyme. Conversely, the liquid-like densities of supercritical fluids result in higher solubilizing power than those observed for gases. Unlike the behavior of gases and liquids, the physical properties of a supercritical fluid can be adjusted over a wide range by a relatively small change in pressure or temperature. In a supercritical fluid, the careful regulation of the density enables reactant and product solubility to be controlled, thus simplifying downstream separations. The use of supercritical fluids as a dispersant for biocatalysis was first described in 1985, and there is a growing trend in using supercritical fluids as reaction media for enzymatic catalysis. The advantages of using enzymes in supercritical fluids include the following:

- Synthesis reactions in which water is a product can be driven to completion;
- The solubilities of hydrophobic materials are increased relative to those in water;
- The thermostability of biomolecules in supercritical fluids is greater than in water;
- The solvent can be readily recycled;
- Biochemical reactions and separations can be integrated into a single step.

Among potentially interesting solvents for enzymatic catalysis, carbon dioxide is the most widely used supercritical fluid. However, there is a growing interest in using other supercritical fluids (e.g., ethylene, fluoroform, ethane, sulfur hexafluoride, and near-critical propane) (Kamat et al., 1995b).

It has been demonstrated that the activity of the lipase (*Candida cylindracea*) catalyzed transesterification reaction between methylmethacrylate and 2-ethylhexanol in

supercritical carbon dioxide is comparatively low. The same reaction was run in supercritical carbon dioxide with a special emphasis on determining the extent of any interaction between the enzyme and carbon dioxide. Transesterification reaction rates in hexane and supercritical carbon dioxide were compared. In supercritical carbon dioxide, temperature was found to have no significant effect on reaction rate in the range of 40 to 55°C. Above 55°C, however, the reaction rate increased significantly as a function of temperature. The effect of bubbling carbon dioxide and/or fluoroform on the reaction rate in hexane at different temperatures suggests that the enzyme undergoes shear inactivation in hexane (Kamat et al., 1995a).

The addition of a dispersed droplet phase (forming a microemulsion) provides a convenient means of solubilizing highly polar or ionic species into the low polarity environment of the SCF phase. Hence, the combination of supercritical solvents with microemulsion structures provides a new type of solvent with some unusual and important properties of potential interest to a range of technologies. These droplets have high diffusion rates in SCF and the properties of the continuous phase can be readily controlled by manipulation of system pressure (Beckman et al., 1995).

It is quite common to add small amounts of cosolvents to SCFs (especially CO_2) to increase the solubilities of heavy organic solutes. Unfortunately, not much seems to dissolve in CO_2 (Gwynne, 1996). In order to extend its use in drug research and in the food and paper industries, microemulsions are formed in CO_2. As the amount of water in the system increases, the microemulsions, called micelles, swell up to the point that the water they contain effectively resembles bulk water.

To design a supercritical fluid extraction process for the separation of bioactive substances from natural products, a quantitative knowledge of phase equilibria between target biosolutes and solvent is necessary. The solubility of bioactive coumarin and its various derivatives (i.e., hydroxy-, methyl-, and methoxy-derivatives) in $SCCO_2$ were measured at 308.15–328.15 K and 10–30 MPa. Also, the pure physical properties such as normal boiling point, critical constants, acentric factor, molar volume, and standard vapor pressure for coumarin and its derivatives were estimated. By this estimated information, the measured solubilities were quantitatively correlated by an approximate lattice equation of state (Yoo et al., 1997).

Potential applications of microemulsions include separation processes, reaction processes, and chromatographic applications. Chemical processes, which would benefit from the solubilization of polar substances in a nonpolar SCF are interesting candidates for this area.

6.5.4 Water-promoted Organic Reactions

6.5.4.1 Introduction

Chemical reactions, including those used in chemical manufacturing, are commonly carried out in organic solvents such as toluene or methylene chloride, but such solvents pose significant problems. They are costly, and they must be disposed of without causing environmental damage. Thus it has long been felt that it would be better to replace these organic solvents with water, if that were possible.

The biggest problem in switching to water as a solvent for chemical reactions is that the reagents may be quite insoluble in water. A second problem is that they may

react with water and be quenched before they can perform their function. Advances have demonstrated that water, both in its normal phases and in its supercritical state, can effectively be used in many processes in place of the organic solvents that are traditionally employed. The use of water as solvent in organic chemistry was rediscovered in the eighties. Many biochemical processes occur in the presence of water, and the diversity of the reactions in vivo should prompt chemists to discover the potential of water as a solvent. The hydrophobic effect, a principal force determining the folding of proteins and nucleic acids, and the binding of enzymes to substrates, was utilized for the first time in 1980 for a water-promoted Diels-Alder reaction (Rideout and Breslow, 1980).

Water is inexpensive, nontoxic and nonflammable. Replacing organic solvents with water may reduce VOC emissions and CO_2 production from solvent incineration. Supercritical water is less polar than ambient water and will dissolve many organic compounds that would not otherwise be soluble. At the same time, it can act as an acid, base, or acid-base catalyst (Katritzky et al., 1996). This can eliminate the wastes generated from neutralization steps.

Water has a high boiling point, which has the potential to raise energy costs. Separations can be difficult, which can lead to contamination in aqueous effluents. Low solubility of substrates can create problems. Supercritical water is highly corrosive.

6.5.4.2 Physicochemical Background: Structure of Water

Liquids (solvents) can be divided in two groups. In the first, molecules are held together by weak nondirectional van der Waals forces and fill space in a regular manner. In these unstructured liquids, molecules have 10–11 nearest neighbors on average. The second group concerns the structured liquids, such as water, in which molecules are held together with strong, directional bonds, such as hydrogen bonds. In this case, molecules do not fill space efficiently as a consequence structured liquids display cavities. In a two-state model, liquid water is represented as an equilibrium between such "structured water" constituted by ice-type clusters and "unstructured water" having higher entropy and density in which each molecule has many more neighbors. Temperature, pressure, and additives can influence this equilibrium. At room temperature and under normal pressure, water molecules in the pure liquid have 4.4 nearest neighbors on average as seen by neutron diffraction (Benson and Siebert, 1992).

6.5.4.3 Aqueous Solutions of Simple Molecules

Solutes can be divided into two classes according to their thermodynamic behavior (Lubineau et al., 1994). The transfer of a hydrophobic molecule from a pure state to an aqueous solution is an unfavorable process, due to the large decrease of entropy which results from the reorganization of the water molecules surrounding the solute. This effect is called hydrophobic hydration. Hydrophobic solutes are structure-making compounds. By contrast, hydrophilic solutes can bind water molecules through hydrogen bonds.

6.5.4.4 Hydrophobic Effects

The hydrophobic interaction is the tendency of apolar groups to aggregate in aqueous solutions, in order to minimize unfavorable interactions with water. This entropically

favorable interaction is a partial reversal of the entropically unfavorable hydration process. Research indicates that a hydrophobic molecule occupies preferably a cavity surrounded by a hydrogen-bonding network of water molecules.

6.5.4.5 Reactivity in Water

Solvation effects are rationalized by studying the relative solvation of the initial (reactants) and transition states. These effects include the solute–solvent interactions and the reorganization of solvent around the solute. An enthalpically dominated rate-enhancement could result from an increase of the initial state enthalpy, but it usually arises from a decrease of the transition state enthalpy. Thus the well-known S_N1 solvolysis reactions are accelerated in highly polar solvents, such as water, by strong interactions between the carbenium ions and the solvent in the transition state, the dielectric constant ε of the solvent being the critical rate-determining factor. With ε = 78, water is a solvent of choice for reactions which go through a more polar transition state. However, owing to the hydrophobic interaction, one must keep in mind that the entropic term must play a special role.

Whereas the polarity effect is ascribed to the dielectric constant, the hydrophobic effect is a consequence of the high cohesive energy density (c.e.d.) of water, resulting from a unique hydrogen-bonding network (Lubineau et al., 1994). Given table 6.5, which compares the cohesive energy density and the dielectric constant of selection of common solvents at 25°C, there is no correlation between the structuralization and the polarity of the solvents.

What occurs when two hydrophobic molecules, susceptible to reaction, are put together in aqueous solution? Due to the hydrophobic interaction, they have a tendency to aggregate, but this association is not sufficient to explain the rate enhancement. Noteworthy is the high surface tension of water (72 dynes/cm), a consequence of its high c.e.d. (550 cal/cm^3 or 22000 atm), which tends to induce a diminution of the surface of contact between hydrophobic and water molecules. This process is facilitated by a decrease of the volume of the reactants along the reaction coordinate,

Table 6.5. Cohesive energy density and ε for some common solvents.

	c.e.d. (cal/cm^3)	ε
Water	550	78
Formamide	376	109
Methanol	209	32.7
DMSO	169	47
Ethanol	161	24.5
Nitromethane	159	36
DMF	139	37
1-butanol	114	17
Dioxane	95	2
Acetone	94	21
THF	87	7.6
Chloroform	85	4.8
Diethyl ether	60	4.3
Hexane	52	1.9

which means that it should be enhanced for reactions with a negative volume of activation (Blokzijl et al., 1991). To take advantage of this effect, the reactants must be, at least partially, dissolved in water and since they are hydrophobic, this could be the cornerstone of the method. But besides the fact that small nonpolar molecules are fortunately soluble in water to some extent, a possibility to induce water solubility lies in grafting the hydrophobic moiety onto a hydrophilic residue.

Some cosolvents can diminish the hydrophobic effect of water. For example, ethanol in water increases the solubility of hydrocarbons by helping to solvate them in preference to the poor solvation by water alone.

6.5.5 Examples of Water as Solvent

Several liquid-phase extraction technologies employing environmentally benign phase- or micelle-forming polymers in aqueous solution have the potential to replace volatile organic compounds in classical solvent extraction technologies. Examples include aqueous biphasic systems, cloud-point extraction, micellar extraction, and thermoseparating polymer systems. Environmentally benign polymers in clean-separation science and technology could lead to new and better solvent extraction systems (Huddleston et al., 1999).

Aqueous systems have been used in separations, coatings, and synthesis. Aqueous biphasic systems have been developed for liquid–liquid extractions using water-soluble polymers such as polyethylene glycol, and inorganic salts such as ammonium chloride or potassium phosphate. These systems have been investigated for use in the separation and recovery of heavy metals from mixed wastes and in the recovery of colored impurities from textile waste streams (Sherman et al., 1998).

The coatings industry has developed waterborne paints and coatings that greatly reduce VOC emissions. Some applications include automotive coatings, interior latex paints, and polyurethane coatings (Sherman et al., 1998).

Several organic reactions are successfully carried out in aqueous media. In some cases, notably in the Diels-Alder reaction and in other pericyclic reactions, the hydrophobic effect accelerates the reaction and influences product selectivity. Nucleophilic addition reactions such as aldol reactions, Michael additions, and benzoin condensations can proceed faster in water using milder bases than are used in organic solvents or under phase transfer conditions. In organometallic reactions, the limitations of feedstock reactivity and insolubility can often be overcome by changing the metal, the reaction conditions, or the ligand. For example, tin, zinc, indium, and bismuth are used as alternatives to magnesium and give high yields of Grignard-type products in aqueous media. On the other hand, magnesium can be used in a Barbier-type reaction run in 0.1 N ammonium chloride. Other aqueous organometallic reactions include hydrogenations, carbonylations, and alkylations.

In contrast to supercritical carbon dioxide, water does not require pressure vessels. It is easily cleaned up after use. It remains to be seen whether manufacturing chemistry will follow the example from natural biochemistry, and use water as the solvent medium for chemical transformations.

Reviews describe several organic reactions that are successfully carried out in aqueous media (Li, 1993; Li, 2000). In some cases, notably in the Diels-Alder reaction and in other pericyclic reactions, the hydrophobic effect accelerates the reaction and

influences product selectivity (Breslow, 1998). Nucleophilic addition reactions such as aldol reactions, Michael additions, (Toda et al., 1998), and benzoin condensations can proceed faster in water using milder bases than are used in organic solvents or under phase transfer conditions (Li, 1993; Li and Chan, 1997). In organometallic reactions, the limitations of feedstock reactivity and insolubility can often be overcome by changing the metal, the reaction conditions, or the ligand. For example, tin, zinc, indium, and bismuth are used as alternatives to magnesium and give high yields of Grignard-type products in aqueous media (Li, 1996). On the other hand, magnesium can be used in a Barbier-type reaction run in 0.1 N ammonium chloride.(Li, 1998a) Under these conditions, the Barbier/Grignard product is formed quantitatively, while a similar reaction run in wet THF produces little product. Other aqueous organometallic reactions include hydrogenations, carbonylations, and alkylations (Li, 1993).

The use of water as solvent is advantageous in many respects. Using water can make many chemical processes more economical. Water is not flammable or toxic. Water-soluble substrates can be used directly. In many organic syntheses that use water as the solvent, it is possible to eliminate the need for protection and deprotection of functional groups, thus saving many synthetic steps, which contributes to an overall reduction in chemical emission and enhances pollution prevention.

The following are further examples of water in chemical reactions:

1. Barbier-type reaction (Chen and Li, 1996)
2. Aqueous reaction using In and Sn (Li and Lu, 1995)
3. Annulation methodology based on indium-mediated allylation reactions in water (Li and Lu, 1996)
4. Highly regioselective when using indium (Kim et al., 1993)
5. Barbier-Grignard reaction in water is very good (Li et al., 1996)
6. Homoallylic alcohols and allylic alcohols undergo structural reorganization (Li et al., 1995)
7. Palladium catalysed copolymerization of aryl iodides with acetylene gas in an aqueous medium provides areneethynylene polymers and oligomers (Li et al., 1997)

6.5.5.1 Pericyclic Reactions

The use of water as a solvent in organic chemistry has, for the most part, been nonexistent despite the fact that many biochemical processes occur in the presence of water at ambient temperature. Paul Grieco has shown that water can have a profound effect on the way one does organic chemistry (Grieco, 1991). Breslow described the kinetic study of the cycloaddition between two small lipophilic molecules, the poorly water-soluble cyclopentadiene (10 mM in water at 20°C) and buten-2-one (Rideout and Breslow, 1980) (see fig. 6.5). This model reaction is interesting for both its physicochemical and stereochemical aspects. Indeed, the implication of the hydrophobic effect is supported by effects of additives, such as lithium chloride, known for decreasing the water solubility of organic molecules (salting-out agent), which accelerates the reaction even more.

Another typical effect due to the use of water as the solvent for the Diels-Alder reaction is the higher endo-selectivity obtained in comparison with organic solvents

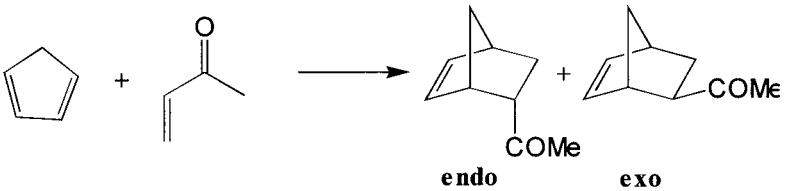


Figure 6.5

(Breslow, 1998), (Yoshida and Grieco, 1984). This effect is general and illustrates the role of the high cohesive energy density of water in these phenomena. The endoselectivity is decreased by the addition of detergents such as sodium dodecyl sulfate or cetyl trimethylammonium bromide, as well as in microemulsions (water, propan-2-ol, and toluene) or when a large excess of diene is used. Concentrated aqueous carbohydrate solutions (mono- or disaccharides) have been shown to accelerate the Diels-Alder reaction because of an increase of the hydrophobic effect (Lubineau et al., 1994).

Engberts and co-workers (Otto et al., 1996) reported a detailed study of a Diels-Alder reaction that was catalyzed by Lewis acids in water. They presented the results of the effects of Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} ions as Lewis acid catalysts on the rate and endo-exo selectivity of the DA reaction between the bidentate dienophiles 3-phenyl-1-(2-pyridyl)-2-propen-1-ones and cyclopentadiene in water (see fig. 6.6). Relative to the uncatalyzed reaction in acetonitrile, catalysis by 0.010 M $Cu(NO_3)_2$ in water accelerates the Diels-Alder reaction by a factor of 79,300. Water does not induce an enhanced endo-selectivity for this reaction.

Intramolecular ionic Diels-Alder reactions were carried out in highly polar media to afford carbocyclic ring systems. The strategy, which obviates the need for high temperatures and pressures, features in situ generation of heteroatom-stabilized allyl cations that undergo subsequent (4 + 2) cycloaddition at ambient temperature. Typically, reactions were complete within 1 hour after addition of substrate. Some cycloadducts were the result of a concerted process, whereas others were formed via a stepwise reaction mechanism (Grieco, 1996).

Aqueous hetero Diels-Alder reaction was first described by Grieco, who reported the use of water as solvent for cyclocondensations of iminium salts (Larsen and Grieco, 1985). Known as being a very energy demanding reaction, the retro Diels-Alder process is usually not considered as a competitive pathway in most Diels-Alder

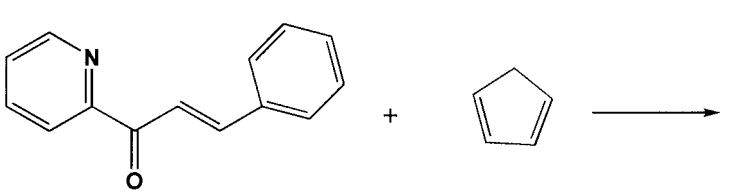


Figure 6.6

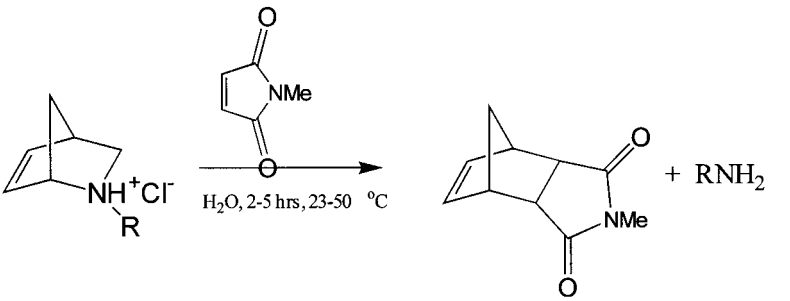


Figure 6.7

reactions. Nevertheless, Grieco has shown that the 2-azanorbornene hydrochloride (or its N-alkylated analogs) undergoes a retro (4 + 2) cycloaddition at room temperature, as proven by the trapping of the cyclopentadiene formed in the process as its adduct with N-methylmaliemide (see fig. 6.7) (Grieco and Bahsas, 1987).

6.5.5.3 Claisen Rearrangements

The hydrophobic effects between the apolar groups involved in the Diels-Alder reaction also occur when the apolar groups belong to the same molecules, and thus should also be beneficial to the Claisen rearrangement. The nonenzymatic rearrangement of chorismate to prephenate occurs 100 times faster in water than in methanol (Copley and Knowles, 1987; Grieco et al., 1989).

5.5.5.4 Organometallic Chemistry

The Barbier reaction is the reaction between a halogenated derivative and a ketone or an aldehyde in the presence of a metal. As an organometallic intermediate species is often postulated, this reaction is usually conducted after careful exclusion of water. Yet it has been shown that this reaction takes place not only in presence of some water, but even in water itself.

Transition metal complex catalyzed reactions exhibit different outcomes depending on whether they are conducted in water or not. Chao-Jim Li highlighted the greening of chemical reactions, focusing on the use of water as an alternative solvent for reactions involving metals, R = CH_2Ph (Li, 1996) (see fig. 6.8).

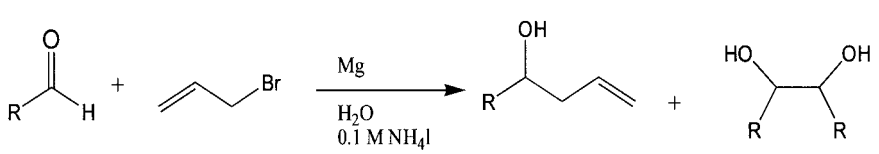


Figure 6.8

6.5.5.5 Nucleophilic Additions

The aldolization, a major synthetic tool involving a nucleophilic addition to the carbonyl double bond, is usually conducted under either acidic or basic conditions (Denmark and Lee, 1992). The yields of the aqueous aldolization logically follow the electrophilicity of the aldehyde, rising up to 82% using *p*-nitrobenzaldehyde. It has been shown that these aqueous aldolizations can be catalyzed by water-stable Lewis acids such as ytterbium or other lanthanide triflates (Kobayashi and Hachiya, 1992).

Quantitative studies of Michael-type additions in aqueous solutions are relatively scarce. Recently the rate-determining steps of the Michael reaction were investigated with substituted pyridines as nucleophiles (Heo and Bunting, 1992). The uncatalyzed Michael reaction proceeds nicely under neutral conditions when water is used as solvent, without any catalyst.

Other nucleophilic additions conducted in aqueous media can be found in the literature (Lubineau et al., 1994; Strauss, 1999). These reactions will include the benzoin condensation, the Prins reaction, and the Wittig-Horner reaction, and the Baeyer-Villiger oxidation.

6.5.5.6 Oxidations

Many classical oxidations are frequently performed in aqueous media, using oxidants such as potassium permanganate, sodium periodate, or sodium or calcium hypochlorite (Hudlicky, 1990). Cyclohexene can now be oxidized directly to colorless crystalline adipic acid with aqueous 30 percent hydrogen peroxide under organic solvent- and halide-free conditions, as discussed earlier (Sato et al., 1998) (see fig. 6.1).

6.5.5.7 Reductions

Apart from reactions with sodium borohydride, which is frequently used in water or water-alcohol mixtures to selectively reduce ketones or aldehydes, water is rarely used in reductions because of chemical incompatibility with most reducing agents. Nevertheless, water was shown to influence these types of reactions.

The reduction of imines can be performed with zinc powder in 5% aq. NaOH solution without any organic solvents under mild conditions (Tsukinoki et al., 1998). In comparison with other conventional methods, some advantages of this method are the fact that, since the reaction can be done in water at room temperature under atmospheric pressure, it is safe, and that hydrogen gas is not necessary because the proton source is water. Furthermore, Zn powder is cheap compared with metal hydrides, hydrogenation catalyst, and lanthanides, and is not sensitive to oxygen and water.

6.5.5.8 Artificial Enzymes That Act in Water Solution

Natural enzymes use the hydrophobic effect as a binding force in forming the enzyme–substrate complex. Artificial enzymes can be used to bind substrates and enhance reactivities in water (Breslow, 1995). Cyclodextrins, which are cyclic compounds composed of glucose units, can be used as the artificial enzymes (Bender and

Komiyama, 1978). Further references to this work and interesting discussions of the results may be found in a recent chapter by Breslow (Breslow, 1998).

6.5.5.9 Chemically Benign Synthesis at Organic-Water Interface

An organic-water interfacial synthesis technique has been developed which is based on the use of a surface-active catalyst complex in conjunction with an aqueous organic solvent mixture and an emulsifier to effect the desired reaction at the organic-water interface. By decoupling the various functions of the reaction medium and meeting them separately with a combination of aqueous and organic phases, instead of a single organic solvent, chances are improved for an environmentally benign synthesis. The technique also offers other significant advantages, including the ease of catalyst recovery and processing, a high reactivity, selectivity and reproducibility under mild reaction conditions, and a greater versatility compared to phase-transfer, micellar and other biphasic techniques (Lim and Zhong, 1996).

Some further examples of syntheses at organic-water interface are:

- coupling polymerization of 2,6-dimethylphenol (Dautenhahn and Lim, 1992; Zhong et al., 1995b)
- carbonylation of benzyl chloride (Zhong et al., 1995a; Zhong et al., 1996)
- carbonylation-induced cross coupling of diamino- and dihalo-aromatics (Lim and Zhong, 1996)
- autooxidation of tetralin (Ahn et al., 1997; Chung et al., 1998b; Chung et al., 1998a; Chung et al., 1999)

6.5.6 Subcritical Water

The solubility of compounds in water changes as the temperature/pressure are increased. The solubility of anthracene, pyrene, chrysene, perylene, and carbazole were determined at temperatures ranging from 298 K to 498 K and pressures from 30 bar to 60 bar in subcritical (superheated) water. Increasing temperature up to 498 K increased solubilities by 5 orders of magnitude. While large increases in pressure result in lower solubilities, over the narrow range of pressures studied, pressure had a minimal effect (Miller et al., 1998).

The ability of sub- and supercritical water to solubilize both functionalized aromatic compounds and molecular oxygen has been exploited for its use as a solvent to perform oxidative modification of a number of compounds. Alkyl aromatic compounds have been oxidized to aldehydes, ketones, and acids by molecular oxygen mediated by transition metal catalysts in subcritical water. A number of alkyl aromatics have been oxidized directly to their acids, including *p*-xylene, *o*-xylene, *m*-xylene, ethylbenzene, and toluene. Finally, conditions have been discovered which allow the oxidation reactions to stop at the aldehyde stage. Several aromatic methylenes could be oxidized to ketones, and anthracene could be oxidized to anthraquinone under the same conditions. The reactions were found to be very sensitive to the nature of the catalysts, with $MnBr_2$ and $CoBr_2$ providing the cleanest reactions and highest yields. Other metal salts led to severe charring or coupling reactions (Holliday et al., 1998).

The use of subcritical water to oxidize pollutants has been explored. Oxidation of aqueous solutions of a model azo dye pollutant (Orange II) was studied in a semibatch reactor operated at temperatures between 180 and 240°C and oxygen partial pressures from 10 to 30 bar. The dye concentrations were in a range (100 and 1000 mg L-1) that one may encounter in an industrial wastewater stream. Orange II oxidation undergoes a parallel-consecutive reaction pathway in which it first decomposes thermally and oxidatively to aromatic intermediates and then via organic acids to the final product—carbon dioxide. The thermal and oxidative disappearance rates of Orange II were found to be first-order reactions with respect to the mother compound, while the oxidation rate of intermediates was found to be second order when lumped by means of total organic carbon. The last activation energy suggests that some intermediates from the lump are oxidized directly to carbon dioxide. The results show the biodegradability of solutions increases with treatment time, but complete biodegradation with nonacclimated seed was not reached. Maximum biodegradability was reached in an experiment carried out at 200°C (Donlagic and Levec, 1997).

Conversion of polymers and biomass to chemical intermediates and monomers by using subcritical and supercritical water as the reaction solvent is probable. Reactions of cellulose in supercritical water are rapid (< 50 ms) and proceed to 100% conversion with no char formation. This shows a remarkable increase in hydrolysis products and lower pyrolysis products when compared with reactions in subcritical water. There is a jump in the reaction rate of cellulose at the critical temperature of water. If the methods used for cellulose are applied to synthetic polymers, such as PET, nylon or others, high liquid yields can be achieved although the reactions require about 10 min for complete conversion. The reason is the heterogeneous nature of the reaction system (Arai, 1998).

Destruction of 1,1,2-trichlorotrifluoroethane (CFC113) in supercritical and subcritical water has been performed over a wide range of pressure at 673 K. The hydrolysis reaction of CFC113 in the supercritical water could lead to complete destruction of CFC113, while the CFC113 destruction below the critical pressure of water was quite low (Park et al., 1996).

The use of subcritical water extends beyond destruction. A method for remediation of PCB-contaminated soil and sediments has been described that uses zerovalent iron as the dechlorination agent and subcritical water extraction (SWE) as the transporting medium. The initial findings indicate that this technique may be a viable method for remediation of PCB-contaminated soil and sediments (Yak et al., 1999).

6.5.7 Superheated and Supercritical Water

Superheated and supercritical water are used in several applications. Supercritical water is most often used in the destruction of organic wastes, including some chemical warfare agents, as an alternative to incineration (Katritzky et al., 1996; Sherman et al., 1998). Recent reports describe the use of both forms as a solvent and as a reactant in synthetic chemistry (Katritzky et al., 1996; An et al., 1997). Some of the reactions investigated include metal-mediated alkyne cyclizations, Pd-catalyzed alkene arylations, aldol reactions, the Fischer indole synthesis, and hydrolysis reactions. Waterborne coatings and the destruction of wastes in supercritical water are fully

commercialized. The separations, applications, and syntheses reported here are quite promising (Li and Chan, 1997; Tester et al., 2000).

Water near or above its critical point (374°C, 218 atm) is a potential medium for organic chemistry. Using near-critical or supercritical water (SCW) instead of organic solvents in chemical processes offers environmental advantages and may lead to pollution prevention (Tester et al., 1998). Interest in doing chemistry in SCW is not entirely new, however (Savage, 1999). Water near its critical point possesses properties very different from those of ambient liquid water. The dielectric constant is much lower, and the number and persistence of hydrogen bonds are both diminished (Hoffmann and Conradi, 1997). As a result, high-temperature water behaves like many organic solvents in that organic compounds have high solubilities in near-critical water and complete miscibility with SCW. Moreover, gases are also miscible in SCW so employing a SCW reaction environment provides an opportunity to conduct chemistry in a single fluid phase that would otherwise occur in a multiphase system under more conventional conditions.

Savage's excellent review provides information on hydrogenation or dehydrogenation, C-C bond formation, rearrangements, hydration/dehydration, elimination, hydrolysis, partial oxidation, and H-D exchange (Savage et al., 1995). Major areas are also devoted to chemical conversion, using decomposition and oxidation. Over half of the articles cited in this review dealt with supercritical water oxidation. At high temperatures and pressures, pure liquid water becomes a surprisingly effective medium for the reactions of organic compounds. It may function simultaneously as a convenient solvent, catalyst, and reagent for reactions, which are typically acid- or basecatalyzed (Kuhlmann et al., 1994).

The oxidation rate of methanol in SCW and the subsequent production and destruction of the primary intermediate, formaldehyde, has been investigated using Raman spectroscopy as an in situ analytical method. Effluent samples were also examined using gas chromatography. An elementary reaction mechanism, which reproduces accurately the quantitative features of methanol oxidation and formaldehyde production, is used to identify key rate controlling reactions during the induction period and the transition to the primary oxidation path (Rice et al., 1996).

Cellulose is rapidly hydrolyzed in supercritical water (SCW) to recover glucose, fructose, and oligomers (cellobiose, cellotriose, cellotetraose, etc.). Cellulose decomposition experiments were conducted with a flow-type reactor in the range of temperature from 290 to 400°C at 25 MPa. Hydrolysis product yields (around 75%) in supercritical water were much higher than those in subcritical water. At a low temperature region, the glucose or oligomer conversion rate was much faster than the hydrolysis rate of cellulose. Thus, even if the hydrolysis products, such as glucose or oligomers, are formed, their further decomposition rapidly takes place and thus high yields of hydrolysis products cannot be obtained. However, around the critical point, the hydrolysis rate jumps to more than an order of magnitude level higher and becomes faster than the glucose or oligomer decomposition rate. This is the reason why a high yield of hydrolysis products in supercritical water was obtained (Sasaki et al., 1998).

The decomposition of aqueous ammonium nitrate at elevated temperatures and pressures occurs and is a function of chloride, nitrate, and total acidity. Catalysis requiring both chloride and acid was observed in solutions containing 20% (w/w)

NH_4NO_3 at 180°C. Dinitrogen formation correlated with the production of additional acidity by the reaction

$$5NH_4NO_3 \rightarrow 4N_2 + 2HNO_3 + 9H_2O.$$

These results bear on the industrial preparation of NH_4NO_3 and suggest conditions under which nitrous oxide emissions might be important to the global N_2O budget (Macneil et al., 1997).

6.5.8 Ionic Liquids as Solvents

Seddon showed that 1-ethyl-3-methyl imidazolium chloride-aluminum(III) chlorides are ionic liquids at temperatures as low as −90°C (Seddon, 1996; Earle and Seddon, 2000). These nonvolatile ionic liquids can solvate a wide range of organic reactions including oligomerisations, polymerizations (Lynn et al., 2000), alkylations (Ross et al., 2001), and acylations (Seddon, 1997; Welton, 1999).

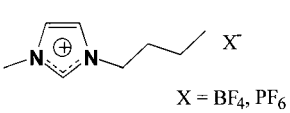
6.5.8.1 Introduction

Ionic systems consisting of salts that are liquid at ambient temperatures can act as solvents for a broad spectrum of chemical processes. These ionic liquids, which in some cases can serve as both catalyst and solvent, are attracting increasing attention from industry because they promise significant environmental benefits, according to American, British, and French researchers.

Probably the most important advantage is that they have no measurable vapor pressure. Unlike conventional solvents used in the industrial syntheses of organic chemicals, they are nonvolatile and therefore do not emit vapors. With ionic liquids, you do not have the same concerns as you have with volatile organic solvents, which can contribute to air pollution. Ionic liquid chemistry is a very new area that is not only extremely interesting from a fundamental chemistry point of view, but could also have a very large impact on industry (Freemantle, 2000).

Hélène Olivier at the French Petroleum Institute (IFP) at Rueil-Malmaison, near Paris, has developed a butene dimerization process that uses an ionic liquid as a catalyst support (Chauvin et al., 1996). The process offers economic benefits over an existing IFP butene dimerization process widely used in the petrochemical industry.

The group used 1-*n*-butyl-3-methylimidazolium salts, as nonaqueous solvents for Rh-catalyzed two-phase hydrogenation, isomerization, and hydroformylation of unsaturated substrates. They found that the catalyst can be "immobilized" either because of ionic character or by using polar modified ligands. The anions they used were BF_4^-, PF_6^-, SbF_6^-, and $CuCl_2^-$. Since the ionic liquids are easy to prepare and are stable in air and water they were of great chemical interest (see fig. 6.9). Interestingly, when



X = BF_4, PF_6

Figure 6.9

Table 6.6. Hydrogenations in BMI^+ salts.

Solvent	Conversion (%) pent-1-ene	Yield (%) pentane	Yield (%) pent-2-ene	TOF (min^{-1})
acetone	99	38	61	0.55
$BMI^+ SbF_6^-$	96	83	13	2.54
$BMI^+ PF_6^-$	97	56	41	1.72
$BMI^+ BF_4^-$	10	5	5	0.15
$BMI^+ CuCl_2^-$	18	0	18	0
$BMI^+ PF_6^-$	99	25	74	0.73

$BMI^+SbF_6^-$ was used in the catalytic hydrogenation of pent-1-ene the rates were nearly five times higher than for the comparable homogeneous reaction in acetone (see table 6.6).

6.5.8.2 Chemistry of Ionic Liquids

The ionic liquids of interest are low-melting-point molten salts that are liquid around room temperature. They typically have a liquid range of about 300°C, far in excess of the 100°C for water or 44°C for ammonia. The archetypal ionic liquid system is 1-ethyl-3-methylimidazolium chloride-aluminum chloride, known in abbreviated form as (emem)Cl-$AlCl_3$. It is liquid and thermally stable from almost −100°C to around 200°C, depending on the molar ratio of (emim)Cl and $AlCl_3$ added to the system. For example, when the molar proportions are equal, the system is a neutral stoichiometric compound, $(emim)^+$-$(AlCl_4)^-$, which melts at its congruent melting point of about 6°C. The lowest melting point, −96°C, is achieved when the molar percentages of the system are 35% (emim)Cl and 65% $AlCl_3$.

Low-melting-point ionic liquids typically exhibit mixed organic and inorganic character. The cation is usually a heterocyclic cation such as $(emim)^+$, 1-butyl-3-methylimidazolium-$(bmim)^+$-or N-butylpridinium. These organic cations, which are relatively large compared with simple inorganic cations, account for the low melting points of the salts (Hagiwara and Ito, 2000).

The anions, on the other hand, determine to a large extent the chemical properties of the system. For example, the main anions present in chloroaluminate ionic liquid systems such as (emim)Cl-$AlCl_3$ are Cl^-, which is a Lewis base; $(AlCl_4)^-$, which is neither acidic nor basic; and the Lewis acid $(Al_2Cl_7)^-$. The concentration of each anion, and therefore the Lewis acidity of the system, varies depending on the relative amounts of $AlCl_3$ and (emim)Cl added to the system.

Tetrafluoroborate$(BF_4)^-$ and hexafluorophosphate$(PF_6)^-$, are among other types of anions that are attracting the interest of ionic liquids research groups. These ions do not combine with their corresponding Lewis acids and are therefore not potentially acidic.

The spectrum of physical and chemical properties of ionic liquids is much larger than that of classical organic or inorganic solvents. As well as wide liquid ranges, they offer ranges of physical properties such as density and viscosity and also have high heat conductivities. In addition, the miscibilities of ionic liquids with organic

compounds can be varied extensively by altering the chain lengths of the alkyl substituents on the cations. A good quality ionic liquid in a stoppered flask or sealed tube looks exactly like water. Some of the more viscous ones look like glycerol, but generally they are free-flowing colorless liquids.

The chloroaluminate ionic liquids are water sensitive. When you expose them to air, they produce HCl. The tetrafluoroborates and hexafluorophosphates, on the other hand, are air and water stable. They can be worked with in an open beaker. Because they are nonvolatile, there is no smell, and they can be used in high-vacuum systems.

Ionic liquids with organic cations such as $(emim)^+$ or $(bmim)^+$ generally have high thermal and chemical stability are relatively easy to make. Mixing two white powders, 1-butyl-3-methylimidazolium chloride and aluminum chloride, together in a beaker, they just collapse into a liquid. Boiling commercially available 1-methylimidazole with 1-chloro-butane, followed by cooling, readily makes the imidazolium starting material.

More than 600 ionic liquid systems can, in principle, be generated from around 10 simple anions such as $(BF_4)^-$ and $(PF_6)^-$ and the 1-alkyl-3-methylimidazolium cation substituted with various alkyl groups in the 2-, 4-, or 5-position, or N-alkylpridinium substituted in the 3- or 4-position. When heteropolyanions and tetralkylammonium and tetraalkylphosphonium cations are added to the list, a grand total of more than a quarter of a million ionic liquid systems is possible.

With this vast variety, it is usually possible to tailor the solvents to specific chemical reactions. Ionic liquids have a range of physical chemical properties that can be tuned with a precision that is hard to imagine for a given reaction. Ionic liquids are good solvents for a wide range of inorganic, organic, and polymeric materials. There are ionic liquids that will dissolve covalent compounds. Ionic liquids can lead to process intensification.

A wide range of catalyzed organic reactions can be carried out in room-temperature ionic liquids. These include alkylations, acylations, reductions, oxidations, oligomerizations, and polymerizations. In some cases, the ionic liquid acts as both solvent and catalyst. A typical Friedel-Crafts reaction takes six seven hours to give you about 80% yield of a mixture of isomers. In a room-temperature ionic liquid, the reaction is complete in about 30 seconds with essentially 100% conversion (Green et al., 2000). The product isolation protocol for the reactions done in ionic liquids does require the use of organic solvent and distillation, both of which significantly reduce the overall "greenness" of the process. Even though it has been shown that many chemical reactions can be carried out in ionic liquids, methods to recover the reaction products remain a challenge. Eric J. Beckman, Joan Brennecke, and co-workers have reported the complete removal of a low-volatility organic solute from an ionic liquid with supercritical CO_2 (Blanchard et al., 1999).

In their test system, the researchers used the ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate $(bmim)(PF_6)$, which is stable in the presence of oxygen and water, with naphthalene as a low-volatility model solute. Spectroscopic analysis revealed quantitative recovery of the solute in the supercritical CO_2 extract with no contamination from the ionic liquid. They found that CO_2 is highly soluble in $(bmim)(PF_6)$ reaching a mole fraction of 0.6 at 8 MPa, yet the two phases are not completely miscible. The phase behavior of the ionic liquid-CO_2 system resembles that of a cross-linked polymer-solvent system (Moerkerke et al., 1998), even though

(bmim)(PF_6) is a low viscosity, low-molecular-weight liquid. Finally, the dissolution of CO_2 in the ionic liquid is completely reversible: pure ionic liquid remains after extraction of the naphthalene and depressurization.

6.5.8.3 Ionic Liquids as Ordered Ionic Solvents

A series of novel hexafluorophosphate salts, based on N,N′-dialkylimidazolium and substituted N-alkylpyridium cations, display liquid crystalline behavior at temperatures above their melting point (Gordon et al., 1998). The temperature range over which liquid crystalline behavior is observed increases markedly with increasing alkyl chain length. Alkyl substitution at the 3- and 4-positions on the pyridinium ring results in a decrease in the melting point compared with the equivalent unsubstituted salt, but also leads to a large decrease in the tendency toward liquid crystalline behavior (or mesogenicity). Such salts are potentially of great interest as ordered ionic solvents, combining the advantages of ionic liquids with those of liquid crystal solvents. The application of more "traditional" molecular liquid crystalline materials as ordered solvents for polymerization and stereochemically controlled organic reactions is an area of increasing interest.

6.5.8.4 Ionic Liquids as Molten Salts for Solar Cells

Molten salts are ionic liquids and as such can be utilized in a wide range of electrochemical applications where high conductivity and ionic mobility are required (Papageorgiou et al., 1996). Their ionic nature renders them negligibly volatile in the liquid state. These properties as well as relatively low viscosity, the large electrochemical window, thermal stability, miscibility with solvents or other salts and hydrophobicity are a few of the desirable qualities found in certain molten salts.

Room temperature molten salt systems based on methyl-hexyl-imidazolium iodide appear to afford particular advantages over organic liquids as solvents for solar cell electrolytes. Cell performance showed outstanding stability, with an estimated sensitizer turnover in excess of 50 million (Papageorgiou et al., 1996).

6.5.8.5 Chemistry in Ionic Liquids: Dimerization

Two-phase systems in which an insoluble organic substrate is reacted with a catalyst dissolved in an ionic liquid show promise for commercial use (Chauvin and Helene, 1995; Freemantle, 1998). One such system is a nickel-catalyzed olefin dimerization. The dimers are produced selectively and decanted from the ionic liquid. The catalyst/ionic liquid phase is recycled without loss of activity. Other reactions investigated include:

- Olefin metathesis (Chauvin et al., 1996);
- The synthesis of branched fatty acids (Freemantle, 1998);
- Oxidations (Chauvin et al., 1996); and
- Catalytic hydrogenation (Chauvin et al., 1996).

An ionic liquid was successfully used as a replacement for polar aprotic organic solvents in the chemoselective O-alkylation of naphthols (Freemantle, 1998).

6.5.8.6 Chemistry in Ionic Liquids: Catalytic Hydrogenation

The use of two-phase catalysis in water or high-polar organic solvents is one of best approaches to clean catalytic hydrogenation (Hermann and Kohlpainter, 1993). Ionic solvents with a wide range of liquid phase (down to −81°C) based on 1-*n*-butyl-3-methylimidazolium cations can be used in these reactions.

The reaction of 1-*n*-butyl-3-methylimidazolium chloride (BMIC) with sodium tetrafluoroborate or sodium hexafluorophosphate produced the room temperature-, air- and water-stable molten salts $(BMI^{+})(BF_4^{-})$ and $(BMI^{+})(PF_6^{-})$, respectively in almost quantitative yield. The rhodium complexes $RhCl(PPh_3)_3$ and $(Rh(cod)_2)(BF_4^{-})$ are completely soluble in these ionic liquids and they are able to catalyze the hydrogenation of cyclohexene at 10 atm and 25°C in a typical two-phase catalysis with turnovers up to 6000 (see fig. 6.10).

The ionic liquids acting as solvents in these hydrogenation systems do not show any noticeable difference in the turnover rate with the Wilkinson catalyst. It is important to note that at the end of the hydrogenation reaction the product is removed from the two-phase catalytic system by simple decantation and the rhodium catalysts are almost completely retained in the ionic liquid (Steines et al., 2000).

Much of the research is focusing on the development of ionic liquids that are immiscible with reactants and products but dissolve catalysts. Such systems, in which the products can be easily separated, offer immense potential industrial development. These two-phase or "biphasic" catalytic processes offer the benefits of both homogeneous and heterogeneous catalysis. They combine the mild conditions and high efficiency and selectivity of homogeneous catalysis with the easy separation of catalyst from reaction products and optimal use of catalyst that are possible with heterogeneous catalysis. It may be assumed that most of the known transition metal-catalyzed reactions could be carried out in organic-inorganic ionic liquids by fitting the liquid composition with the selected catalyst precursors.

6.5.8.7 Chemistry in Ionic Liquids: Friedel-Crafts

Friedel-Crafts reactions in the ionic liquid system 1-methyl-3-ethylimidazolium chloride-aluminium(III) chloride can be performed with excellent yields and selectivities, and in the case of anthracene, have been found to be reversible. This ionic liquid has been shown to demonstrate catalytic activity in reactions such as Friedel-Crafts acylations (Surette et al., 1996; Boon et al., 1986) alkylation reactions (Koch et al., 1976),

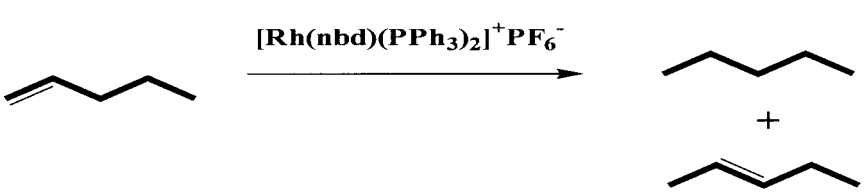


Figure 6.10

isomerisation of alkanes (Chauvin et al., 1990), and the alkylation of isobutane with butene (Chauvin et al., 1994).

The reactions work efficiently, giving the stereoelectronically favored product. In the acetylation reaction of naphthalene (1) the major product was the thermodynamically unfavored 1-isomer, with a 2% yield of the 2-isomer. This is in accordance with best literature yield and selectivity. It has been suggested that the position of attack on naphthalene is determined to a large extent by steric factors (Olah, 1973). In the ionic liquid, the acylation is thought to be the free acylium ion (Chevrier and Weiss, 1974). Since the acylium ion is much smaller than the adduct, attack at sterically more hindered positions can occur (Adams et al., 1998).

6.5.8.8 Chemistry in Ionic Liquids: Diels-Alder

The Diels-Alder reaction is an important and widely used reaction in organic synthesis (Sauer and Sustmann, 1980), and in the chemical industry (Griffiths and Previdoli, 1993). Rate enhancement of this reaction has been achieved by the use of solvents such as water, surfactants, very high pressure, lithium amides, alkylammonium nitrate salts, and macrocyclic hosts (Sherman et al., 1998). Diels-Alder reactions can be run in neutral ionic liquids (such as 1-butyl-3-methylimidazolium trifluoromethanesulfonate, 1-butyl-3-methylimidazolium hexafluorophophate, 1-butyl-3-methylimidazolium tetrafluoroborate, and 1-butyl-3-methylimidazolium lactate). Rate enhancements and selectivities are similar to those of reactions performed in lithium perchlorate-diethyl ether mixtures.

Ionic liquids offer a highly polar but noncoordinating environment for chemistry. It is difficult to dissolve catalysts in nonpolar, noncoordinating molecular solvents such as hexane. Polar solvents, such as acetonitrile, tend to coordinate metal complexes. Ionic liquids such as the tetrafluoroborates offer a straightforward replacement of a solvent with a polar solvent that is noncoordinating.

The Stille coupling reaction has been performed in 1-butyl-3-methylimidazolium tetrafluoroborate. Use of this solvent system allows for facile recycling of the solvent and catalyst system, which can be used at least five times with little loss in activity. An interesting preference in starting catalyst oxidation state for use with aryl bromides and aryl iodides was observed (Handy and Zhang, 2001).

Palladium-catalyzed arylation of the electron-rich olefin butyl vinyl ether has been accomplished in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate using as the arylating agents aryl iodides and bromides instead of the commonly used, but commercially unavailable and expensive, aryl triflates. The reaction proceeds with high efficiency and remarkable regioselectivity, leading almost exclusively to substitution by various aryl groups at the olefinic carbon α to the heteroatom of butyl vinyl ether (Xu et al., 2001).

6.5.8.9 Conclusions

The reactions that have been observed so far in ionic liquids represent the tip of the iceberg. In the future, research will involve efforts to optimize such phenomena as the relative solubilities of the reactants and products, the reaction kinetics, the liquid range of the solvent, the cost of the solvent, the intrinsic catalytic behavior of the

media, and the air stability of the system. It will be possible to design a solvent to optimize a reaction with control over both yield and selectivity, rather than to let the solvent dictate the course of the reaction. Industrial employment of ionic liquids is growing. The use of ionic liquids in industry is seen as being highly speculative.

Three important economic drivers can also bring significant potential benefits for the environmental impact of chemical processes:

- greater reaction selectivity;
- enhanced reaction rates with more active catalysts;
- the operation of processes with fewer processing steps and milder conditions.

In some ways ionic liquids can deliver some of these benefits, but there are still unanswered and critical questions to large-scale use of ionic liquids:

- cost;
- robustness in use;
- ease of product separation;
- heat- and mass-transfer questions;
- recyclability and reuse;
- ease of manipulation on industrial scale;
- materials compatibility;
- safety.

However, little has entered the public domain concerning the use of ionic liquids on an industrial scale, and nothing has been claimed, even in general terms, to suggest that room-temperature ionic liquids are being used in a viable chemical process being operated commercially. Recent emphases on ionic liquid research and applications could change this.

As an indication of things to come, a year ago IFP in Paris revealed that it had just launched a commercial process based on ionic liquids that are available for licensing. The Difasol process for dimerizing butenes to isooctenes was developed at Rueil-Malmaison, and pilot-scale trials were carried out at IFP's pilot facilities at the Industrial Research & Development Center at Solaize, near Lyon.

The new Difasol process for manufacturing isooctenes consumes less catalyst. The process dimerizes *n*-butene in a continuous two-phase operation that uses the industrial Dimersol nickel catalyst dissolved in a chloroaluminate ionic liquid. The *n*-butenes are introduced continuously into the reactor, and the products are only poorly miscible with ionic liquid, and separate in settler. The process shows 70–80% conversion with 90–95% selectivity (Freemantle, 1998).

The final tasks remain:

- performance
- cost
- recycling

6.5.8.10 Solvent Table for Organic Reactions

Table 6.7 provides references for solvents used in organic reactions.

Table 6.7. Organic reactions.

Solvent	Description	Reference
general	Hazardous Solvent Source Reduction	(Callahan and Green, 1995)
	Environmentally Benign Chemistry Aims for Processes that Don't Pollute	(Illman, 1994)
	Options For Reducing Greenhouse Gas Emissions in the Chinese Industrial Sector	(London et al., 1998)
	Pollution Prevention, Green Chemistry, and the Design of Safer Chemicals	(Garret, 1996)
	Solvent Replacement For Green Processing	(Sherman et al., 1998)
	Solvents—Molecular Trees For Green Chemistry	(Brennecke, 1997)
	Art in science: utility of solvents in green chemistry	(Nelson, 1998)
	Safe Solvent Resist Process For Sub-Quarter Micron T-Gates	(Via et al., 1997)
	Improving the environment through process changes and product substitutions	(Draths and Frost, 1998)
	Green chemistry: challenges and opportunities	(Clark, 1999)
water	A "Green" Route to Adipic Acid: Direct Oxidation of Cyclohexenes with 30 Percent Hydrogen Peroxide	(Sato et al., 1998)
	Organic Reactions in Micro-Organized Media—Why and How	(Ruasse et al., 1997)
	Water-Promoted Organic Reactions	(Lubineau et al., 1994)
	The design of green oxidants	(Collins et al., 1998)
	Water as a solvent for chemical reactions	(Breslow, 1998)
	Water as a benign solvent for chemical syntheses	(Li, 1998b)
	Chemically Benign Synthesis at Organic-Water Interface	(Lim and Zhong, 1996)
	Organic Chemistry in Unconventional Solvents	(Grieco, 1991)
	Classical Organic Reactions in Pure Superheated Water	(Kuhlmann et al., 1994)
	Recent progress in glycochemistry and green chemistry	(Zhang et al., 1999)
	Water in supercritical carbon dioxide microemulsions: spectroscopic investigation of a new environment for aqueous inorganic chemistry	(Clarke et al., 1997b)
	Aqueous and Enzymatic Processes for Edible Oil Extraction	(Rosenthal et al., 1996)
	Carbon Dioxide: A Greener Way to Process Biomolecules	(Gwynne, 1996)
	Concerning the Regiochemical Course of the Diels-Alder Reaction in Supercritical Carbon Dioxide	(Renslo et al., 1997)
	Homogeneous Organic Reactions as Mechanistic Probes in Supercritical Fluids	(Brennecke and Chateauneuf, 1999)

(*Continued*)

Table 6.7. Continued.

Solvent	Description	Reference
	Supercritical Carbon Dioxide as a Substitute Solvent for Chemical Synthesis and Catalysis	(Morgenstern et al., 1996)
	Supercritical carbon dioxide: the "greener" solvent	(Black, 1996)
	Reduction of Volatile Organic Compound Emissions During Spray Painting	(Donohue et al., 1996)
ionic liquids and co2	Green processing using ionic liquids and CO_2	(Blanchard et al., 1999)
ionic liquids	Diels-Alder reactions in ionic liquids	(Earle et al., 1999)
	Opportunities for ionic liquids in recovery of biofuels	(Fadeev and Meagher, 2001)
carbonates	Dimethylcarbonate as a methylating agent: A new perspective for safe and highly selective mono-N-and mono-C-alkylations	(Selva and Tundo, 1998)
	Selective Mono-Methylation of Arylacetonitriles and Methyl Arylacetates by Dimethylcarbonate	(Tundo et al., 1996)
	Selective monomethylation reactions of methylene-active compounds with dimethylcarbonate. An example of clean synthesis	(Tundo, 2000)
aerosol	Imine-Isocyanate Chemistry: New Technology for Environmentally Friendly High-solids Coatings	(Wicks and Yeske, 1996)
	A photochemical alternative to certain Friedel-Crafts reactions	(Kraus et al., 1998)
glycerol	The New Challenger—the Potential of Glycerol in Green Chemistry	(Moulouncui et al., 1995)
catalysts	Enhancing the efficiency of a synthetic reaction. Palladium-catalyzed allylic alkylation	(Trost, 1998)
catalysts	The Role of Catalysts in Environmentally Benign Synthesis of Chemicals	(Simmons, 1996)
perfluorocarbons	Organic reactions without an organic medium: utilization of perfluorotriethylamine as a reaction medium	(Nakano and Kitazume, 1999)
immobilized	Catalysis of Liquid Phase Organic Reactions Using Chemically Modified Mesoporous Inorganic Solids	(Clark and Macquarrie, 1998)
	Immobilized ionic liquids as Lewis acid catalysts for the alkylation of aromatic compounds with dodecene	(DeCastro et al., 2000)
cyclohexane	Catalysis of the Knoevenagel Reaction by Gamma-Aminopropylsilica	(Macquarrie et al., 1997)
SCF	Intermediates in Organometallic and Organic Chemistry—Spectroscopy, Polymers, Hydrogenation and Supercritical Fluids	(Poliakoff and George, 1998)
	Chemical Reactions in Supercritical Fluids	(Ikariya et al., 1995)

Table 6.7. Continued.

Solvent	Description	Reference
solventless	Biocatalytic Solvent-Free Polymerization to Produce High Molecular Weight Polyesters	(Chaudhary et al., 1997)
	Environmentally Benign Chemistry—Microwave-Induced Stereocontrolled Synthesis of Beta-Lactam Synthons	(Banik et al., 1997)
	A growing cadre of scientists is finding ways to reduce pollution, not by changing existing products, but by inventing cleaner ways to make them. Discusses some work in solvent-less chemistry.	(Chase, 1995)
	Solvent-free organic syntheses	(Varma, 1999)
Biphasic	Fluorous biphasic catalysis: A new paradigm for the separation of homogeneous catalysts from their reaction substrates and products	(Fish, 1999)

6.5.9 Other Green Solvents

6.5.9.1 Supercritical Hydrofluorocarbons

The dipolarity/polarizability parameter π^*, introduced by Kamlet and Taft, was measured for difluoromethane (HFC 32) and pentafluoroethane (HFC 125) and compared with those previously reported for 1,1,1,2-tetrafluoroethane (HFC 134a). This was carried out as a function of temperature and pressure, to cover the liquid and supercritical states over the range 30–130°C and 40–300 bar (Abbott and Eardley, 1999).

5.5.9.2 Oxygenated Solvents

Copper, silver, and gold colloids have been prepared by Chemical Liquid Deposition (CLD) with dimethoxymethane, 2-methoxyethyl ether, and ethylene glycol dimethyl ether. The metals are evaporated to yield atoms which are solvated at low temperatures and during the warm-up process colloidal sols with metal clusters are obtained. Evaporation of the solvent was carried out under vacuum-generating metal films. These films are showing very low carbon/hydrogen content and were characterized by elemental analyses and infrared spectroscopy (Cardenas et al., 1994).

Complex formation equilibria in binary mixtures of chloroform with dipropyl ether (PE), diisopropyl ether (IPE), methyl tert-butyl ether(MBE), tetrahydrofuran (THF), 1,4-dioxane (DOX), acetone (AC), and methyl acetate (MA) have been analyzed in detail. The complex formation equilibria in chloroform mixtures was compared to those previously examined for halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) mixed with the same oxygenated solvents. It was found that the H-bonds formed by halothane are stronger than those formed by chloroform (Dohnal and Costas, 1996).

Vapor-liquid equilibria (VLE) for binary mixtures of halothane with propyl ether (PE), isopropyl ether (IPE), 1,4-dioxane (DOX) and 2,5-dioxahexane (monoglyme)

(G1) have been measured at 293.15 K. Complex-formation equilibria for these four halothane-oxygenated solvent mixtures have been analyzed in detail using several association models (Dohnal et al., 1996).

Using ^{1}H NMR spectroscopy the complex-formation equilibria between halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) and methyl tert-butyl ether or tetrahydrofuran in various inert solvents (hexane, heptane, decane, cyclohexane) were measured as a function of temperature (Tkadlecova et al., 1995).

6.5.9.3 HFC and HCFC

The Montreal Protocol (1987) called for a phase-out of CFCs. It was determined that the new substances break down in the environment to give predominantly carbon dioxide, water, and inorganic salts of chlorine and fluorine. The only exception is that some substances also break down to yield trifluoroacetic acid (HTFA), a substance resistant to further degradation. Based on available data, one can conclude that environmental levels of TFA resulting from the breakdown of alternative fluorocarbons do not pose a threat to the environment (Boutonnet et al., 1999).

Hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) are used or developed as substitutes for fully halogenated chlorofluorocarbons. Based on the results of closed-bottle tests, the biodegradation of HFC-32, HCFC-123, HCFC-124, HFC-125, HFC-134a, HCFC-141b, HCFC-225ca, and HCFC-225cb was less than 60% after 28 days and therefore these compounds are considered not readily biodegradable. Standard acute toxicity tests with HCFC-123, HCFC-141b, and HCFC-225ca using algae, water fleas, and fish revealed EC50 values in the range of 17–126 mg/L. EC50 values of HFC-134a ranged between 450–980 mg/L. Fish studies with HCFC-141b and HCFC-225ca revealed bioaccumulation factors of < 3 and 15–64, respectively. A study with plants revealed no effect of HCFC-141b on seed germination and growth of wheat (Triticum aestivum), radish (Raphanus sativus), and cress (Lepidium sativum). In conclusion, HFCs and HCFCs are not very toxic to aquatic organisms and terrestrial plants. No evidence for any aerobic biodegradation for most of the HFCs and HCFCs was found (Berends et al., 1999).

Chlorofluorocarbons (CFCs) are stable in the atmosphere and may reach the stratosphere. They are cleaved by UV-radiation in the stratosphere to yield chlorine radicals, which are thought to interfere with the catalytic cycle of ozone formation and destruction and deplete stratospheric ozone concentrations. Due to potential adverse health effects of ozone depletion, chlorofluorocarbon replacements with much lower or absent ozone depleting potential are developed. The toxicology of these compounds that represent chlorofluorohydrocarbons (HCFCs) or fluorohydrocarbons (HFCs) has been intensively studied. All compounds investigated (1,1-dichloro-1-fluoroethane (HCFC-141b), 1,1,1,2-tetrafluoroethane (HFC-134a), pentafluoroethane (HFC-125), 1 chloro-1,2,2,2-tetrafluoroethane (HCFC-124), and 1,1-dichlor-2,2,2-trifluoroethane (HCFC-123)) show only a low potential for skin and eye irritation. Chronic adverse effects on the liver (HCFC-123) and the testes (HCFC-141b and HCFC-134a), including tumor formation, were observed in long-term inhalation studies in rodents using very high concentrations of these CFC replacements. All CFC replacements are, to varying extents, biotransformed in the organism. mainly by cytochrome P450-catalyzed oxidation of C-H bonds. The formed acyl halides are hydrolyzed to give excretable carbox-

ylic acids; halogenated aldehydes that are formed may be further oxidized to halogenated carboxylic acids or reduced to halogenated alcohols, which are excretory metabolites in urine from rodents exposed experimentally to CFC replacements. The chronic toxicity of the CFC replacements studied is unlikely to be of relevance for humans exposed during production and application of CFC replacements (Dekant, 1996).

6.5.9.4 Miscellaneous Benign Solvents

Based on the list given in chapter 5, there will be numerous possible replacements. The following examples illustrate this. High-yield, general, one-pot synthesis of substituted isoindolequinones, a group of important radiosensitizers, which sensitize hypoxic cells to the lethal effect of radiation in cancer radiotherapy. Primary amines react with 2,3-bis(2-(trimethylsilyl)ethynyl)-5,6-dimethylhydroquinone (2) in methanol at room temperature under an inert atmosphere to give substituted isoindole-quinones 2-alkyl-1,3,5,6-tetramethylisoindole-4,7-quinone (4) in almost quantitative yields. Moderate yields of 4 are also obtained using 2,3-diethynyl-5,6-dimethylhydroquinone (3) and amines as reactant and solvent under the similar conditions. Tris(2-aminoethyl) amine (TREN) reacts with 2 in MeOH/THF on reflux to produce the isoindolequinone derivative of TREN. Water with 2 on reflux in MeOH forms an isobenzofuranquinone. This indicates that the formation of similar heterocycles from small molecules (e.g., Group VA and VIA hydrides) and 2 is likely. Readily synthesizable starting materials, ease of chromatographic isolation of the product, reaction generality, use of no catalyst, and cost-effective environmentally benign solvents such as MeOH/EtOH make this novel reaction simple and convenient (Chakraborty et al., 1997).

Perfluorotriethylamine is a good alternative reaction medium for Lewis acid catalyzed reactions and it can be easily recycled by simple extractive workup. Recently, inert and less toxic fluorous (perfluorinated) fluids have been recognized and are attracting attention as new alternative solvents. However, it is still not clear what kinds of reactions to run in these solvents and how to run them. The scope and limitations of the utility of fluorous liquids as alternative reaction media for Lewis acid catalyzed reactions, which are of great current interest due to their unique reactivities and selectivities, were studied. Among fluorous amines, perfluorotriethylamine, which exhibits relatively high lipophilicity due to its short perfluoroalkyl chains and suitable boiling point, could be an ideal alternative solvent (Nakano and Kitazume, 1999).

Selection of the solvent is important in determining the chemical reactivity, selectivity, and yield of industrial synthesis operations. Most synthesis solvents except carbon tetrachloride are not Class I or Class II ozone-depleting substances, so in contrast to solvents used in cleaning and coating operations, their supply is not threatened. Many of them, however, are on the 33/50 list, and ways to reduce their use are being sought actively. Ideally, new techniques would allow reactions to occur in the absence of solvents; to this end, some progress has been made using microwaves. Most synthetic reactions are solvent based, however, and will continue to be so for the foreseeable future. This search is more complicated than in the case of cleaning and coating operations as not only should the solvating characteristics of the replacements match those of the original solvent as closely as possible, but the new synthesis

solvents must also be inert to the reactants and products, and the yield of the reaction should not be compromised.

6.6 Readily Available Drop-in Replacements

As with other applications, the approach requiring the fewest modifications to already existing synthetic processes is to find a drop-in replacement for the conventional solvent. For example, it is common to replace extremely flammable diethyl ether with methyl *tert*-butyl ether (Budavari et al., 1989) or carcinogenic benzene with toluene (Femec and McAffrey, 1994). Such facile substitutions are not always available, however, and experimentation is often required to find a suitable replacement. Some examples of effective solvent substitutions are given in tables A1–A3. In the synthesis of phosphonitrilic hydroquinone prepolymers, the carcinogenic and ozone-depleting solvent carbon tetrachloride was replaced with cyclohexane with a slight increase in yield (Femec and McAffrey, 1994). Chloroform was considered an explosive hazard in solvating Schmidt reactions involving azides, and it was replaced with dimethoxyethane (Galvez et al., 1996). Dichloromethane, or methylene chloride, is one of the most popular synthesis solvents, but it is a suspected carcinogen and is highly volatile (bp = 40°C). Ogawa and Curran (Ogawa and Curran, 1997) demonstrated that benzotrifluoride (low toxicity, bp = 102°C) can be an effective replacement for dichloromethane in many reactions, with similar yields. For example, benzotrifluoride is a replacement for dichloromethane (see fig. 6.11) (Sherman et al., 1998).

Tetrahydrofuran (THF) is another important process solvent often used to solvate reactions involving strong bases. The workup of strong base reactions often includes an aqueous extraction, creating the problem of contaminated aqueous waste because THF is completely water miscible. Typically, elaborate steps such as solvent exchange by distillation are taken to avoid THF contact with water. This is an energy-intensive process, and a more economical solution is desirable. Hatton's group (Molnar et al., 1996) has examined the use of THF derivatives that have similar solvating characteristics but are essentially nonvolatile and water insoluble as reaction solvents. A particularly effective solvent is *n*-octyl tetrahydrofurfuryl ether, which has been shown to be a satisfactory replacement for THF in a series of reactions in the synthesis of the human immuno-deficiency virus (HIV) protease inhibitor Crixivan. A number of solvent switches and off-line recovery operations can potentially be avoided using this approach. These solvents therefore satisfy the criteria for green processing in that they are less prone to enter the environment and that a number of energy-intensive separations and solvent exchanges can be avoided. Experiments have also shown that if THF is attached via an ether linkage onto a polystyrene-type polymer backbone, the solvent can be recovered efficiently through ultrafiltration (Molnar et al., 1996).

6.6.1 Water in Phase Transfer and Aqueous Surfactants

Water is an ideal candidate as a replacement solvent. It is nontoxic, nonflammable, readily available, inexpensive, and easy to handle. Unfortunately, switching from organic to aqueous solvents is not a simple task. As with coating applications, the high polarity of water offers many difficulties in its implementation as a reaction medium

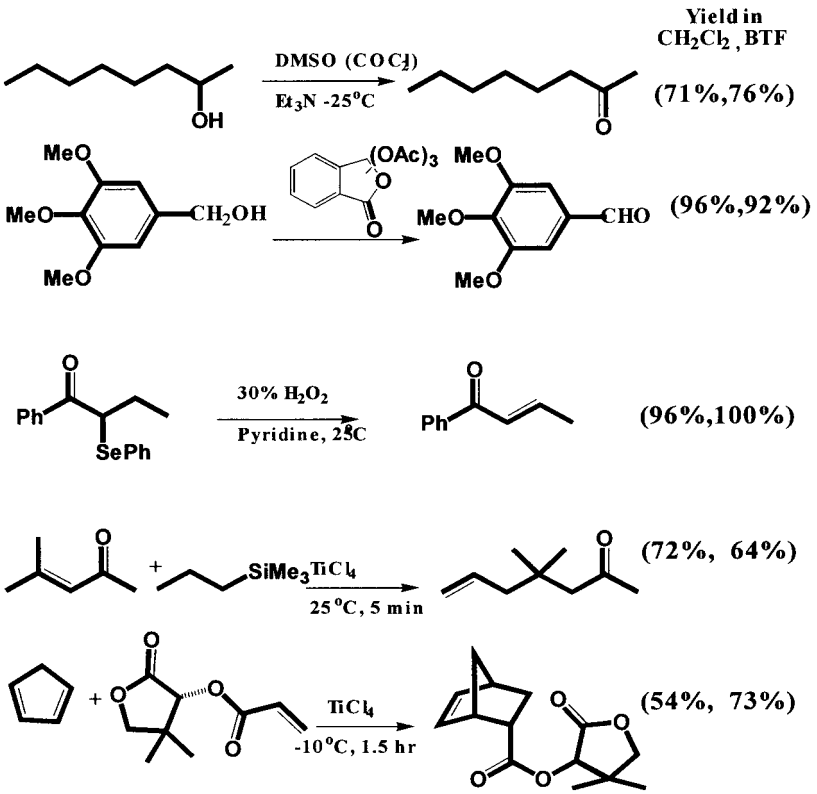


Figure 6.11

because many organic compounds do not exhibit good aqueous solubility. Nonetheless, significant progress has been made in developing reaction chemistries that take place in substantially aqueous environments.

Phase-transfer catalysis takes advantage of the solvating properties of biphasic systems. Rearrangements are solvated in the organic and aqueous phases and a phase transfer catalyst is used to bring them to react in the organic phase (Goldberg, 1989). Aqueous alkali hydroxides can be used to replace flammable bases of sodium metal, sodium hydride, sodamide, and other alkoxides, whereas expensive anhydrous or aprotic organic solvents such as dimethylsulfoxide, dimethylformamide, and hexamethylphosporamide can be replaced with dichloromethane, chloroform, hexane, and benzene. The reaction temperature is lowered while the reaction rate improves because the increased reactivity of anions in the nonpolar solvent. Reactions performed with phase-transfer catalysts have been reviewed in several books, as have asymmetric phase-transfer reactions. Reactions performed with phase-transfer catalysts have been reviewed in several books (Goldberg, 1989; Dehmlow and Dehmlow, 1993; Starks et al., 1994), as have asymmetric phase-transfer reactions (O'Donnell, 1993).

Another approach is to perform the reaction at the organic-aqueous interface. Reagents are moved from the organic to the aqueous phase but remain localized near the interface,

and thus the reagents need not be significantly water soluble. Catalysts are either solvated homogeneously in a supported thin aqueous film or at the interface by surface active ligands (Dartt and Davis, 1994; Lim and Zhong, 1996; Tenbrink et al., 1998).

The use of the bulk organic solvent can be avoided completely by exploiting the properties of aqueous surfactant solutions in which the surfactants aggregate to form micelles consisting of apolar cores comprised of the hydrophobic tail groups stabilized by coronae formed by the hydrophilic surfactant heads (Fendler and Fendler, 1975; Bunton, 1991). The apolar core plays the role of the organic solvent, whereas the palisade layer can provide a medium of intermediate polarity. Few studies specifically address the use of these aqueous micellar solutions as replacements for traditional organic solvents. For example, Monflier showed that solvent-free telomerization of butadiene with water to form octadienols could be carried out effectively in the presence of a nonionic surfactant; the conventional process is performed in the solvent sulfolane (Monflier et al., 1995). Replacement of the organic phase with surfactants to exploit micellar phase-transfer catalysis principles was reported recently by Battal et al. (Battal et al., 1997) for the alkylation of phenol and aniline. This group had previously demonstrated the synthesis of a surfactant by micellar autocatalysis, whereby the surfactant product itself catalyses the reaction (Kust and Rathman, 1995).

In some cases even the use of micellar solvent phases can be avoided and the reactions can be carried out in an entirely aqueous medium. For water-soluble reagents, catalytic reactions such as hydrogenations and hydroformylations may be carried out homogeneously in the aqueous phase with water-soluble ligands such as triphenylphosphinotrisulfonate (Sheldon et al., 1998).

Usually the generation of the organometallic reagent takes place in anhydrous organic solvents, but using softer metals allows this reaction to take place in water. Shu et al. (Shu et al., 1995) demonstrated epoxidation of cyclooctene using ozone in water where the products were easily recovered by phase separation. Brominations are performed readily in water instead of in carbon tetrachloride (Shaw et al., 1997). These examples indicate the potential minimization of solvent usage by the development of new water-based chemistries for green processing.

6.6.2 Supercritical Fluids

Water and carbon dioxide are the two most commonly used supercritical fluids for mediating reactions. These fluids are nontoxic, nonflammable, and inexpensive. However, the technology is expensive to implement, particularly for water because of the specialized equipment necessary to conduct reactions at high temperatures and pressures.

Supercritical water (647 K and 217 atm) is considerably less polar than water at ambient conditions and has the ability to solvate most organic molecules. In the presence of oxygen, organic compounds are quite reactive in supercritical water, with complete oxidation realized at short reactions times. Supercritical water oxidation (SCWO) processes are being developed for waste management as aqueous wastes containing 1 to 20% organics can be oxidized economically to CO_2 and water (Tester et al., 1998). For water with less than 1% organics, activated carbon is more economical for waste treatment and for water with greater than 20% organics, incineration is ideal. For in-depth discussions on SCWO, see Marrone et al. (1998) and Savage et al. (1995). More recently, research has been conducted to improve catalysts (Aki et al.,

1996) and reactors (Tester et al., 1998) that must withstand the corrosive conditions faced in SCWO operations.

$SCCO_2$, a nonpolar fluid, has been investigated as a solvent for many reactions in the areas of fuels processing, biomass conversion, biocatalysis, homogeneous and heterogeneous catalysis, environmental control, polymerization, materials synthesis and chemical synthesis, as reviewed by a number of authors (Weinstein et al., 1999; Black, 1996), (Eckert et al., 1996). DeSimone's group has investigated this medium for precipitation polymerization of acrylic acid (Romack et al., 1995b), synthesis of poly(1,6-dimethylphenylene oxide) (Kapellen et al., 1996), free radical telomerization of tetrafluoroethylene (Romack et al., 1995a), cationic polymerization of vinyl and cyclic ethers (Clark and DeSimone, 1995), and dispersion polymerization of styrene (Canelas et al., 1996). It has been found that fluorination and the formation of micelles with fluorinated surfactants enhance polymer solubility in $SCCO_2$ (Canelas et al., 1996; McClain et al., 1996). SCCO2 has been used as a solvent for homogeneous catalytic hydrogenations (Jessop et al., 1996), and Burk et al. (Burk et al., 1995) have shown it to be a good medium for asymmetric hydrogenations.

6.6.2.1 Additional References

1. Thermal studies of metal films prepared with oxygenated solvents (Cardenas et al., 1994)
2. Isomerism of Amides Coordinated to Platinum—X-Ray Crystal Structure of Dichloro-Bisacetamide-Platinum(II) (Cini et al., 1996)
3. Thermodynamics of Complex Formation in Chloroform-Oxygenated Solvent Mixtures (Dohnal and Costas, 1996)
4. Thermodynamic Study of Complex Formation by Hydrogen Bonding in Halogenoalkane-Oxygenated Solvent Mixtures—Halothane With Propyl Ether, Isopropyl Ether, 1,4-Dioxane, and 2,5-Dioxahexane (Dohnal et al., 1996)
5. Association Between Halothane and Oxygenated Solvents by H-1 NMR Spectroscopy (Tkadlecova et al., 1995)
6. Biodegradation and ecotoxicity of HFCs and HCFCs (Berends et al., 1999)
7. Environmental risk assessment of trifluoroacetic acid (Boutonnet et al., 1999)
8. Toxicology of Chlorofluorocarbon Replacements (Dekant, 1996)
9. Heat Transfer from Supercritical Carbon Dioxide in Tube Flow—a Critical Review (Pitla et al., 1998)
10. Effect of acid strength of co-precipitated chromic alumina catalyst on the conversion and selectivity in the fluorination of 2-chloro-1,1,1-trifluoroethane to 1,1,1,2-tetrafluoroethane (Rao et al., 1999)
11. A Novel High-Yield Synthesis of Substituted Isoindolequinones (Chakraborty et al., 1997)

6.6.3 Solvent-free Conditions

Historically, chemists have seemed to think along the lines of the Latin maxim, possibly derived from Aristotle, *corpora non agunt nisi fluida seu soluta* (compounds react only in the liquid state or if dissolved). This has made solvents commonplace in

chemical syntheses, but many compounds used as solvents can be deemed "environmentally unfriendly." Fortunately, many reactions can be performed without a solvent. This is done by grinding the reagents together in a mortar or ball mill, or by applying heat, microwaves, or ultrasound. Often an inorganic support, such as alumina, silica gel, or clay for neat reagents, proves beneficial for the reaction.

Here, the term "no-solvent" means the absence of a traditional solvent—the reactants are neat and may well be solids. Where one reactant is in sufficiently large excess to qualify as a solvent, for example in Friedel-Crafts alkylations or acylations with excess benzene or toluene, the reactions are not normally classified as "no-solvent." The phrase "solid-phase (solid-state) reaction" today often describes a reaction carried out on a solid phase, like a resin, to which the reaction intermediates are bound by adding reagents in solution. These reactions have become very important in combinatorial chemistry, but they do not meet the definition of "no-solvent." The "no-solvent" reactions refer only to the primary reactions themselves and not to workup conditions which may or may not involve solvents (Dittmer, 1997).

Production of polymers contributes to pollution during synthesis and after use. A polymer produced by microorganisms is already a commercial product (Biopol). Unfortunately, however, cellular synthesis remains limited by the cost of downstream processing and the fact that the synthesis is aqueous-based, and it is impossible to perform the synthesis in the absence of a solvent. Recent research describes an enzyme-catalyzed polymer synthesis in which there is no solvent. This bulk polymerization mirrors conventional synthesis but eliminates the needs for extremes of temperature and corrosive acid catalysts. This represents the first rapid and efficient synthesis of polyesters from bulk polymerization under ambient conditions with very low concentrations of a biocatalyst (Chaudhary et al., 1997).

Solid-phase microextraction (SPME), a new solvent-free sample preparation technique, was invented by C. Arthur and J. Pawliszyn in 1990. This method was mainly applied for the extraction of volatile and semivolatile organic pollutants in water samples. However, since 1995, SPME has been developed to various biological samples, such as whole blood, plasma, urine, hair, and breath, in order to extract drugs and poisons in forensic field. The main advantages of SPME are: high sensitivity, solventless, small sample volume, simplicity, and rapidity (Liu et al., 1998).

The solid state photochemical reaction of indole with 1,4-naphthoquinone yielded 5H-dinaphtho(2,3-a:2′,3′-c)carbazole-6,11,12,17-tetrone in addition to 2-(3-indolyl)-1,4-naphthoquinone which was also the only product in the solution photoreaction. Solventless thermochemical reactions of indole with phenanthrenequinone in the presence or absence of zinc chloride gave 10-(1H-indol-3-yl)-9-phenanthrenol and 9,10-dihydro-9-(1H-indol-3-yl)-10-(3H-indol-3-ylidene)-9-phenanthrenol or 10,10-di-1H-indol-3-yl-9(10H)-phenanthrenone, respectively. All of these products were only obtained in trace amounts in corresponding solution reactions, and are different from the adduct 10-hydroxy-10-(1H-indol-3-yl)-9(10H)-phenanthrenone obtained in the solution photoreaction (Wang et al., 1998).

6.6.2.1 Microwave-Guided Reactions

Recent developments in microwave-accelerated solventless organic syntheses have been summarized (Varma, 1999, 2000). This expeditious and solvent-free approach

involves the exposure of neat reactants to microwave irradiation in conjunction with the use of supported reagents or catalysts which are primarily of mineral origin. The salient features of these high-yield protocols are the enhanced reaction rates, greater selectivity and the experimental ease of manipulation. Among other reagents recently described in the literature on this eco-friendly green approach, the use of recyclable mineral oxides or supported reagents like $Fe(NO_3)_3$-clay (clayfen), $Cu(NO_3)_2$-clay (claycop), NH_4NO_3-clay (clayan), NH_2OH-clay, $PhI(OCAc)_2$-alumina, NIO_4-silica, CrO_3-alumina, MnO_2-silica, $NaBH_4$-clay, and so on, are highlighted in MW-promoted deprotection, condensation, cyclization, rearrangement, oxidation, and reduction reactions including the rapid one-pot assembly of heterocyclic compounds from in situ generated intermediates.

This solventless approach opens up numerous possibilities for conducting selective organic functional group transformations more efficiently and expeditiously using a variety of supported reagents on mineral oxides. There are distinct advantages of these solvent-free protocols since they provide reduction or elimination of solvents thereby preventing pollution in organic synthesis "at source." The chemo-, regio-, or stereoselective synthesis of high-value chemical entities may see the translation of these laboratory "curious" experiments to large-scale operations.

A range of technical difficulties indicated that specifically designed reactors were required. Hence, the CSIRO continuous microwave reactor (CMR) and microwave batch reactor (MBR) were developed for organic synthesis. On the laboratory scale, they operated at temperatures (pressures) up to 200°C (1400 kPa) and 260°C (10 MPa), respectively. Advantages and applications of the units must be considered, along with safety issues. Features include the capability for rapid, controlled heating and cooling of reaction mixtures, and elimination of wall effects. Concurrent heating and cooling, and differential heating were unique methodologies introduced to organic synthesis through the MBR. Applications of the microwave reactors for optimizing high-temperature preparations, for example, the Willgerodt reaction and the Fischer indole synthesis, were demonstrated. Water was a useful pseudo-organic solvent, applicable to environmentally benign synthetic chemistry (Strauss and Trainor, 1995).

In summary, enabling technologies and methodologies have been established and combined to afford various environmentally benign processes for laboratory-scale organic synthesis and for the production of fine chemicals, intermediates, and pharmaceuticals. The technologies comprised continuous and batch microwave reactors and catalytic membranes. The methodologies included solvent-free conditions, catalysed or uncatalyzed processes, the use of aqueous media at high temperature and nonextractive techniques for product isolation. Applications included Hofmann eliminations, Willgerodt and Jacobs-Gould reactions, indole transformations, aldol condensation, Rupe and Meyer-Schuster rearrangements, and C-C coupling reactions (including a tandem Heck coupling-dehydrogenation). New processes for catalytic etherification, uncatalyzed hydrogen transfer, and a one-step arylamidation were also developed (Strauss, 1999).

6.6.3.2 Noncovalent Derivatization

The technique of noncovalent derivatization employs the noncovalent intermolecular forces (hydrogen bonding, π-stacking, lipophilic-lipophilic interactions, and electrostatic interactions) to trap the molecular species in organized matrices.

The procedure of forming molecular assemblies in order to manipulate bulk physical properties allows for reduced usage of chemical resources. For example, instead of performing several time-consuming, solvent-based, chemical reactions in order to synthesize a series of candidate compounds for structure-activity studies, noncovalent derivatization allows for the addition of simple, inexpensive, readily available "complexing reagents." For this to be successful as pollution prevention, these assemblies must significantly reduce the number of synthetic reactions carried out. Often the formation of these assemblies involves no organic solvents since the supramolecular structures can often be constructed via solid state grinding or aqueous dispersing techniques (Warner, 1998).

By understanding the molecular topography of the simplest reactive species (the simplest derivative of the lead compound), bulk physical properties may be modified in an environmentally benign manner by noncovalent complexation with auxiliary reagents. Rather than derivatize a molecule by covalently attaching functional groups, one may be able to form a stoichiometric association with a simple conjugate molecule—thereby imparting the desired physical property.

6.6.3.3 Ultrasound

The acid catalyzed and ultrasound stimulated hydrolysis of solventless tetraethoxysilane-water mixtures was studied at 39°C as a function of HCl added to the mixtures ($\log(HCl)^{-1}$ ranged from 0.8 to 2.0). The exothermal hydrolysis reaction causes an increasing temperature (ΔT_t) as a function of the reaction time, t. The isothermal hydrolysis rate constant, k, has been evaluated from the experimental (ΔT_t) versus t data, after corrections for the increasing temperature effects (Donatti and Vollet, 1996).

5.6.3.3.1 Additional References Additional solvent-free references can be found in the following:

1. New Solvent Free Organic Synthesis Using Focused Microwaves (Loupy et al., 1998)
2. Tellurium in the "No-Solvent" Organic Synthesis of Allylic Alcohols (Xu et al., 1997)
3. Organic Solvent- and Halide-Free Oxidation of Alcohols with Aqueous Hydrogen Peroxide (Sato et al., 1997)
4. Solvent-Free Polymerizations and Processes: Minimization of Conventional Organic Solvents (Long and Hunt, 1998)
5. Solvent-free Organic Syntheses (Varma, 1999)
6. Invited Review. A Combinatorial Approach to the Development of Environmentally Benign Organic Chemical Preparations (Strauss, 1999)
7. Ecofriendly Fast Batch Synthesis of Dioxolanes, Dithiolanes, and Oxathiolanes Without Solvent Under Microwave Irradiation (Perio et al., 1998)
8. Efficient One Pot Synthesis of Nitriles from Aldehydes in Solid State Using Peroxymonosulfate on Alumina (Bose and Narsaiah, 1998)
9. Biocatalytic Solvent-Free Polymerization to Produce High Molecular Weight Polyesters (Chaudhary et al., 1997)

10. Solid-Phase Synthesis of Oximes (Hajipour et al., 1999)
11. Solid-Phase Microextraction (SPME) of drugs and poisons from biological samples (Liu et al., 1998)
12. Reduction of Solid Benzophenones with Sodium Borohydride (Epple and Ebbinghaus, 1998)
13. Research on Photochemical and Thermochemical Reactions Between Indole and Quinones in the Absence of Solvent (Wang et al., 1998)
14. Effects of HCl On the Ultrasound Catalyzed Teos Hydrolysis as Determined by a Calorimetric Study (Donatti and Vollet, 1996)
15. Selective and Solventless Etherification of Polyoxyalkylene Hydroxyl Functions (Abribat et al., 1996)
16. Invited Review—Developments in Microwave-Assisted Organic Chemistry (Strauss and Trainor, 1995)
17. Solvent-free organic syntheses (Varma, 1999)
18. No-Solvent Organic Synthesis (Dittmer, 1997)

6.7 Inorganic Chemistry

The problems being addressed by inorganic chemistry in the 1990s will continue to be challenges well into the twenty-first century. For example, coordination chemistry will continue to provide compounds with unusual properties and uses, and will become an increasingly important component in bioinorganic chemistry. Nuclear technology will continue to challenge the inorganic chemist in issues related to the treatment of nuclear wastes and the clean-up of environmental contamination. Organometallic chemistry will continue as one of the most active areas of catalysis research, especially in the chemical, energy, pharmaceuticals, and pollution control industries. Solid-state chemistry will advance with the growing requirements for better batteries, electronic components, photovoltaic devices, and so on, and the synthetic procedures being conducted at high pressures and temperatures will assist the needs of geochemists. Synthetic inorganic chemistry will tend to be more directed to meeting specific goals, such as new compounds as reagents in organic synthesis, compounds with superconducting properties and inorganic polymers with unusual mechanical and thermal properties. New methods to meet the needs of the production of inorganic chemicals will involve environmentally friendly synthesis. Thus inorganic chemistry will continue in importance to meet the needs for chemical, energy and materials production (Navratil, 1998). The use and development of green solvents here will also be important (Vantendeloo, 1998).

6.7.1 Additional References

In the following we present further references for green solvents in inorganic chemistry:

1. Oxo- and Hydroxo-Bridged Heme-Copper Assemblies Formed from Acid-Base or Metal-Dioxygen Chemistry (Kopf et al., 1999)
2. Cobalt Proteins (Kobayashi and Shimizu, 1999)

3. Bio-inorganic Chemistry: What Is it, and What's So Exciting? Overview (Valentine and O'Halloran, 1999)
4. Inorganic Chemistry of the Dissolution Phenomenon: The Dissolution Mechanism of Calcium Apatites at the Atomic (ionic) Level (Dorozhkin, 1999)
5. Solid solutions (Patzke and Binnewies, 1999)
6. Elemental Bioavailability in Nutrient Solutions in Relation to Precipitation Reactions (Derijck and Schrevens, 1998)
7. Metal Complexes in Medicine—Design and Mechanism of Action (Sadler and Guo, 1998)
8. Recent Publications in Solid-Phase Chemistry—Part 2 (James, 1998)
9. Polyol-Metal Complexes—26—a Three-Dimensional Triply-Connected Alkoxo-Metal Net in a Carbohydrate-Bismuth(Iii) Complex (Klufers and Mayer, 1998)
10. Growth and Characterization of Yba°$_2$Cu°$_3$O°$_7$-X High T-C Superconducting Crystals (Einarsrud et al., 1997)
11. Merlinoite Synthesis Studies With and Without Organocations (Quirin et al., 1997)
12. Use of Amido Grignard Reagents in Inorganic Chemistry—Synthesis and Crystal Structure of Anti (Ragaini et al., 1997)
13. Water in Supercritical Carbon Dioxide Microemulsions—Spectroscopic Investigation of a New Environment for Aqueous Inorganic Chemistry (Clarke et al., 1997a)
14. Binuclear Iron, Manganese and Copper Centers in Biology—Synthetic Analogue Approach (Mukherjee, 1997)
15. New Fluorinated Hydroxamic Acid Reagents for the Extraction of Metal Ions With Supercritical CO°$_2$ (Glennon et al., 1997)
16. Recent Publications in Solid-Phase Chemistry (James, 1997)
17. Thermodynamic Equilibrium, Kinetics, Activation Barriers, and Reaction Mechanisms for Chemical Reactions in Karst Terrains (White, 1997)
18. Solvent Effects On Isomerization Equilibria—an Energetic Analysis in the Framework of Density Functional Theory (Lelj and Adamo, 1995)
19. Use of High Pressure Techniques For Measuring Reaction Rates in Liquid Solutions (Hubbard and Vaneldik, 1995)

6.8 Nuclear and Photochemistry

6.8.1 Nuclear Chemistry

Almost everywhere the topic of radioactivity is taught in the physics or chemistry classes of secondary schools. The question has been raised whether the common approach of teaching this topic would contribute to a better understanding of the risks of ionizing radiation: and, if the answer is negative, how to explain and improve this situation? How to effectively teach this topic and relate how solvents are involved is important (Eijkelhof, 1996).

What constitutes a successful educational program in nuclear and radiochemistry for advanced undergraduate students? The instructional program consists of lectures

and laboratory exercises that cover the fundamentals of nuclear theory, radiochemistry, nuclear instrumentation, radiological safety, and applications in research, medicine, and industry. Guest lectures and field trips broaden the students' exposure to nuclear science (Peterson, 1997). There are ample opportunities to insert green solvents here.

The history of chemical engineering thermodynamics shows that its main concern has been development and extension of concepts and ideas that physicists and physical chemists have proposed in only general terms. For example, van der Waals proposed his theory of fluids in 1873 but its use for chemical engineering came only later, starting in the 1920s, when MIT's Warren K. Lewis (and others) developed the generalized charts that we find today in Ferry's handbook and in undergraduate chemical engineering textbooks. A variety of recent concepts from physics and physical chemistry is now under active development by chemical engineering researchers. Examples include the integral theory of fluids, polymer equilibria, molecular simulation with computers, density functional theory, the theory of electrolytes, fluctuation theory, and the properties of fluids under unusual conditions such as the critical region and the metastable state which contains supercooled fluids at negative pressures. In every case, remarkable progress has been made toward achieving a better understanding of the properties of matter. That understanding, in turn, is useful not only for better design of chemical processes, but also for discovering novel techniques for making new chemical products. The first area concerns phase equilibria in mixtures of polymers with solvents or with other polymers; the main focus is directed at liquid–liquid equilibria which are more difficult to describe than vapor–liquid equilibria. The second area concerns the properties of polyelectrolyte hydrogels in contact with aqueous solutions. Here emphasis is on experimental studies of swelling properties with semiquantitative description based on polymer-network elasticity and Donnan equilibria. The third area concerns selective precipitation of globular proteins from aqueous solution using a salt as the precipitating agent. A theoretical description, similar to that used for colloidal solutions, requires fundamental experimental data (e.g., osmotic virial coefficients) obtained by light-scattering and osmometry (Prausnitz, 1995).

The applications of plasma chemistry to environmental problems and to green chemistry are emerging fields that offer unique opportunities for advancement. There has been substantial progress in the application of plasmas to analytical diagnostics and to waste reduction and waste management. A recent review discussed the chemistry and physics necessary to a basic understanding of plasmas, something that has been missing from recent technical reviews. The current status of plasmas in environmental chemistry was summarized and emerging areas of application for plasmas were delineated. Plasmas are useful for environmental chemistry (analysis, materials modifications, and hazardous waste treatments) (Mollah et al., 2000).

6.8.2 Photochemistry

New solvents should be examined for compatibility with photochemistry. Laser light scattering is used with a variable-volume view cell in an almost fully automated setup for accurately determining the phase behavior of pure or mixed fluids. The automated light-scattering technique yields good data, is relatively quick, and is non–labor inten-

sive. Another advantage of the system is that it is comparatively inexpensive (Sun, 1993).

The free-radical propagation rate coefficients for methyl methacrylate (MMA) in liquid and supercritical carbon dioxide have been successfully determined using pulsed-laser polymerization (PLP) method. The effect of carbon dioxide solvency on the propagation rate coefficient, k(p), is examined at 180 bar for a temperature range of 20–80°C. The resulting activation energy is (25.4 +/– 1.2 kJ.mol^{-1}, and the preexponential factor is (5.2 +/– 3.0×10^6 L/mol.s. These results are compared to the bulk activation parameters for the propagation rate coefficient of MMA as set forth by the IUPAC working party on "Modeling of Kinetics and Processes of Polymerization." The discrepancy in the propagation rate coefficients at the lower temperature regime is attributed to a solvent effect of CO_2. This is consistent with the results from a recent PLP study of this monomer (Quadir et al., 1998).

The photodimerization reaction of anthracene in supercritical CO_2 was studied systematically at different CO_2 densities. Unlike in normal liquid solvents, the reaction in supercritical CO_2 is significant even at anthracene concentrations as low as a few micromolar. At comparable anthracene concentrations, the photodimerization reaction is one order of magnitude more efficient in CO_2 than in normal liquid solvents. The results also show that the efficient photodimerization reaction of anthracene is hardly affected by the local density augmentation (or solute–solvent clustering) in supercritical CO_2 (Bunker et al., 1997).

Fluorescence spectra and quantum yields of pyrene in supercritical CO_2 have been determined systematically as functions of temperature, CO_2 density, and pyrene concentration. Under near-critical conditions, contributions of the pyrene excimer emission in observed fluorescence spectra are abnormally large. The results cannot be explained in the context of the classical photophysical mechanism well established for pyrene in normal liquid solvents. The photophysical behavior of pyrene in a supercritical fluid is indeed unusual. The experimental results can be rationalized with a proposal that the local concentration of pyrene monomer in the vicinity of an excited pyrene molecule is higher than the bulk in a supercritical solvent environment. It is shown that the calculated ratios between the local and bulk concentrations deviate from unity more significantly under near-critical conditions (Sun and Bunker, 1995).

The exponential series method of analysis is applied to single photon counting measurements of phenanthrene fluorescence decay in $SCCO_2$ at 32 and 35°C and at pressures ranging from 76 to 207 bar for chromophore concentrations between 5×10^{-5} and 5×10^{-6} M. The analysis revealed trimodal fluorescence lifetime distributions near the critical temperature that can be explained by the presence of solvent–solute and solute–solute clustering. This local aggregation causes an increase in nonradiative relaxations and, therefore, a decrease in the observed fluorescence lifetimes. Furthermore, the pressure has little or no effect on the clustering over the pressure range studied along an isotherm (Rhodes and Fox, 1996).

The mole fraction solubilities of ten copper(II) and five chromium(III) β-diketonates were measured in $SCCO_2$ with a spectroscopic technique and found to vary over four orders of magnitude. Observed trends indicate that the solubility in supercritical carbon dioxide is strongly dictated by the character of the hydrocarbon or fluorocarbon shell surrounding the central metal atom. A regular solutions approach was used for Cr(acac)°3 to quantitatively attempt to predict the solubility in $SCCO_2$. Solubility

data, solubility parameter trends, and limitations of regular solutions theory applied to supercritical fluids are discussed (Bunker, 1995).

Some further solvent uses in photochemistry can been gleaned from the following references:

1. Complex Formation Between 2-Propanone and Chloroform-D. A Review of Published Work (Fell and Shurvell, 1996)
2. Some EPR Spin Probe and Spin Label Studies of Polymer Systems (Wasserman et al., 1996)
3. Microemulsions as a New Working Medium in Physical Chemistry—An Integrated Practical Approach (Casado et al., 1994)

6.9 Analytical Chemistry

6.9.1 Background

Analytical chemistry has played a critical role in chemistry for centuries. Sixteen new elements were discovered in the eighteenth century, 51 in the nineteenth century and 26 in the twentieth century. The influence of some chemical schools, the incidence of conjunctural circumstances, the difficulties implied by some discoveries, serendipitous and fictitious discoveries, and so on, are considered to focus on specially remarkable cases of historic interest (Perezbustamante, 1997).

The development of new areas of chromatography continues. Chromatographers have used packed columns containing chiral stationary phases with subcritical or $SCCO_2$ mobile phases to separate enantiomers from many compound classes with very good results. Researchers have reported both analytical and preparative separations. Several types of chiral stationary phases have been used in the sub- and supercritical fluid chromatography modes. The current level of understanding of selector-analyte interactions that are involved in the enantio-discrimination processes is critical today. These chromatographic methods have several advantages in comparison to conventional liquid chromatography. The effects of temperature and the nature of polar modifiers added to carbon dioxide, when used as the mobile phase are important.

Compared with chiroptical methods and nuclear magnetic resonance spectroscopy (NMR), only chiral chromatography by direct and indirect methods is suitable for the accurate determination of enantiomeric impurities of less than 1% and for quantitative stereochemical analyses of small sample amounts (for example, in vivo studies of the metabolic pathway or pharmacokinetic effects of chiral pharmaceuticals.)

Super critical fluids (SCF) are an attractive method for the separation of enantiomers, including those of thermally labile and nonvolatile compounds that cannot be investigated by enantioselective chromatography. The use of sub- and supercritical fluids such as modified carbon dioxide as a mobile phase combines high solvating power with good diffusion coefficients and low viscosity. The main advantages SFC has over LC are higher efficiency, shorter analysis time, faster method development, and reduced usage of organic solvents, especially in preparative SFC. Additionally, a wide range of detectors developed for GC and LC applications are compatible with SFC.

Packed-column SFC also is suitable for preparative-scale enatioseparations. Compared with preparative LC, sub- or supercritical fluid chromatography results in easier product and solvent recovery, reduced solvent waste and cost, and higher output per unit time. Because of its reduced sample capacity, SFC usually allows the separation of 10–100 mg samples per run. Chromatographers can compensate for these sample amounts by using shorter analysis times and repetitive injections (Wolf and Pirkle, 1997).

6.9.2 Alternative Solvents for Separation Processes

The application of organic solvents and organic solutions with carrier compounds for the separation of organic substances and metal ions from different sources is well known. These separations are usually performed by extracting the target compound into the organic phase for purification, enrichment, and pollution remediation. As with cleaning, coating, and synthetic applications, it is advantageous to replace the organic solvents used in liquid extractions with solvents that are environmentally friendly. In some cases it is beneficial to implement new separation techniques that reduce the need for large volumes of organic solvents. Liquid extraction techniques employing supercritical fluids and aqueous formulations containing surfactants or soluble polymers are most frequently considered because of their environmentally friendly characteristics and because they often afford increased extracting strength.

Room temperature ionic liquids have potential as extractants in recovery of butyl alcohol from fermentation broth; water solubility in ionic liquid and ionic liquid solubility in water are important factors affecting selectivity of butyl alcohol extraction from aqueous solutions (Fadeev and Meagher, 2001).

6.9.2.1 Supercritical Fluid Extraction

The characteristics of supercritical fluids make them ideal for the recovery of natural products (Ferreira et al., 1999). As a result, the food industry was among the first to implement supercritical fluid extraction (SFE) widely using CO_2. Not only is this process environmentally benign, it is also nontoxic, a primary concern when manufacturing edible products. Applications in the food industry include coffee decaffeination, and processes involving hops, vanilla, paprika, celery seed, and chili peppers (Krukonis et al., 1994). In one example, the extraction of grape seed oil using SFE yielded a final product of better quality than that obtained using conventional extraction.

SFE has also replaced many regulated solvents in analytical chemistry applications in recent years, primarily because it provides a more reliable measure of the concentrations of environmental contaminants and can play an important role in pollution assessment, abatement, and control Dolezal and co-workers have shown the advantages of using SFE compared to the conventional Soxhlet extraction with toluene for determining the presence of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans in ashes from a municipal incinerator (Dolezal et al., 1995). Analysis of agrochemical samples from soils after extraction by Soxhlet methods are now replaced by analysis following supercritical extractions (Kilbane, 1998). Alzaga et al. (1995) extracted Pirimicarb (a pesticide present in sediments of rivers) using supercritical CO_2 modified with triethylamine and compared the results to those obtained with the

conventional Soxhlet method. The supercritical fluid method offered increased precision, shorter analysis time, and a 10-fold reduction in solvent usage. Other efforts yielded similar results; for example, Reighard used CO_2 enhanced by the addition of methanol (cosolvent) to extract nitroaromatic and phenolics, environmental pollutants (Reighard and Olesik, 1997). Some cosolvents may be regulated. An attractive interim option from an environmental standpoint is the use of HFCs or HCFCs. At supercritical conditions these solvents effectively extract relatively polar compounds such as polychlorinated biphenyls, dibenzo-*p*-dioxins, and dibenzofurans without the use of a cosolvent (Roth, 1996).

6.9.2.2 Aqueous Surfactant and Macromolecular Solutions

Removal of organic or heavy metal ion contaminants from aqueous streams can be achieved using a variety of different separation strategies, one of which is solvent extraction. Potential counter-contamination of the streams being treated with the extracting solvent can be avoided by eliminating the organic solvent altogether in favor of aqueous-based solvent systems that rely for their effectiveness on the presence of dissolved surfactant micelles or polymers. These aggregates or polymers can solubilize organic solutes with the aqueous phase or form complexes with the metal ions to be removed. Recent advances allow surfactants and polymers to be used for the remediation of contaminated groundwater sources (Mosler and Hatton, 1996), whereas Haulbrook et al. (Haulbrook et al., 1993) reported the partitioning behavior of several aromatic hydrocarbons between N-vinylpyrrolidone/styrene (NVPS) and water.

A particularly important class of surfactants for the solubilization of organic compounds in aqueous solution is the polyethylene oxide-polypropylene oxide-polyethene oxide family of block copolymers (Alexandridis et al., 1994). These polymers form polymeric micelles that have a high capacity for the solubilization of organic compounds. Surfactants and polymers can be used for the remediation of contaminated groundwater sources by mobilizing contaminants trapped in the soil matrix through reduction in interfacial tension or solubilization within micellar cores (for organics), by binding of metal ions with the charged surfaces of ionic micelles and polyelectrolytes, and by metal ion complexation with ligands solubilized within the micelles or attached to polymer backbones (Mosler and Hatton, 1996). The high capacity of block copolymer micelles for trace contaminants offers the possibility of tailored design of block copolymers for future separations. An advantage of these polymeric micellar systems is that the micelles form only above a certain temperature, called the critical micelle temperature (CMT). When the loaded micellar solution is cooled below the CMT, the micelles dissolve and the PAH precipitates out of solution, thus enabling the simple and efficient regeneration of the micellar solution.

Water-based solvent systems originally developed for the separation and purification of proteins and other biomaterials (Walter et al., 1985) have been suggested for the treatment of contaminated aqueous waste-streams. Certain pairs of water-soluble polymers are incompatible in solution together, and this can lead to phase separation in which two phases are formed. Both phases are predominantly water, and each contains only one of the two polymers. Similar phase behavior results with some polymers and high concentrations of organic salts. The properties of the two phases ensure that the environment-afforded targeted species is different in the two phases.

This provides the driving force for separation of different species. A commonly used phase-forming polymer is polyethylene glycol (PEG), which may or may not be derivatized to impart added selectivity to the separation. Rogers' group has investigated the potential for using such systems for the separation and recovery of environmentally toxic heavy metals (Rogers et al., 1996) and of pertechnetate from simulated Hanford tank wastes (Bond et al., 1999). The removal of color from textile wastes has also been addressed using such systems, which have the advantage that they are not organic solvent based and are primarily water, and the PEG polymers used for phase separation are virtually nontoxic and nonflammable, are inexpensive and available in bulk, and have reasonable phase separation characteristics. As solvent replacements, then, PEG-based aqueous biphasic polymer systems are an environmentally favorable alternative to traditional organic solvent phases (Huddleston et al., 1999).

Another class of solvents that appears to have significant appeal for green processing of metal waste solutions relies on solvent-coated magnetic particles dispersed within the feed phase to be treated (Nunez et al., 1996). Once the desired solutes have been removed by extraction, these particles can be recovered conveniently using magnetic filtration.

For further references to solvent use in analytical chemistry the following should prove helpful:

1. Precipitation of Proteins in Supercritical Carbon Dioxide (Winters et al., 1996)
2. Photochemistry in Modified Supercritical Carbon Dioxide—Effect of Modifier Concentration on Diffusion Probed by Triplet-Triplet Energy Transfer (Worrall and Wilkinson, 1996)
3. High-Pressure NMR of Polymers Dissolved in Supercritical Carbon Dioxide (Dardin et al., 1997)
4. A Steady-State and Time-Resolved Fluorescence Study of Quenching Reactions of Anthracene and 1,2-Benzanthracene by Carbon Tetrabromide and Bromoethane in Supercritical Carbon Dioxide (Zhang et al., 1997)
5. Thermodynamic Studies of Chemical Equilibrium in Supercritical Carbon Dioxide-cosolvent Solutions Using UV-Vis Spectroscopy (Lu et al., 1999)
6. Determination of Atractylon in Atractylodes Rhizome Using Supercritical Fluid Chromatography On-Line Coupled With Supercritical Fluid Extraction by the Direct Induction Method (Suto et al., 1998)
7. Determination of Pesticides and polychlorinated biphenyls in water: a low-solvent method (Ong and A., 1995)
8. Analysis of Volatile Compounds From Supercritical Extracted Soybeans by Headspace Gas Chromatography and Thermal Desorption of a Polymer Adsorbent (Snyder and King, 1994)

6.10 Biochemistry

To a great extent the influence of green solvents in biochemistry will come via changes made in organic and analytical chemistries. For example, a typical application

would be studies of ligand binding to myoglobin in aqueous solution. Measurements of the corresponding solvent structural relaxation rates by frequency resolved calorimetry allows the discrimination between solvent composition and viscosity-related effects. At low temperatures, the nature of the cosolvent and temperature at low cosolvent concentrations will affect the results (Kleinert et al., 1998).

Further, synthesis of models and modeling of biochemical processes necessarily involve choice of solvents. For example, a 34-residue peptide corresponding to the 64–97 sequence of the rat bradykinin receptor, was selected as a model of hydrophobic transmembrane peptide segment for systematic study of synthesis and purification strategies. Application of conventional Boc/Bzl chemistry resulted in very low yield of the synthesis (around 4%) when DMF was used as the solvent for coupling reactions. As shorter resin-bound fragments of TM-34 showed improved swelling in 80% NMP/DMSO, the synthesis was repeated in this mixed solvent and the yield increased to 12%. Purification could be achieved by loading the crude materials dissolved in 90% AcOH onto a C-4 HPLC column and eluting with a TFA/MeCN linear gradient (Oliveira et al., 1997).

A novel application of ionic liquids in biochemistry involved duplex DNA as the anion and polyether-decorated transition metal complexes. When the undiluted liquid DNA-or molten salt-is interrogated electrochemically by a microelectrode, the molten salts exhibit cyclic voltammograms due to the physical diffusion (D-PHYS) of the polyether-transition metal complex. These DNA molten salts constitute a new class of materials whose properties can be controlled by nucleic acid sequence and that can be interrogated in undiluted form on microelectrode arrays (Leone et al., 2001).

Finally, the biocatalyzed hydrolytic kinetic resolution of 2-, 3-, and 4-pyridyloxirane by the *Aspergillus niger epoxide hydrolase* (EH) has been explored. This was used to perform a gram scale preparation of these epoxides of (S) absolute configuration using a process performed at a concentration as high as 10 g/L (82 mM). All three epoxides have been obtained in a nearly enantiopure form (ee > 98%). Interestingly, it was shown that this biotransformation could be achieved using plain water instead of buffer solution, an important improvement as far as downstream processing of an eventual industrial process is concerned (Genzel et al., 2001).

6.11 Medicinal

6.11.1 Background

Pharmacy practice demands that pharmacists draw upon competencies and outcomes that enable them to perform the functions that support the delivery of pharmaceutical care. Many pharmacy schools have established specific outcome objectives for their students based on published pharmaceutical care functions, practice skills, and revised accreditation standards. To meet these objectives, students must examine clinical situations rationally and logically, then gather, organize, interpret, and analyze data pertinent to the patient in question. Students must be competent to make judgments and therapeutic decisions based on available data, learn from past problem-solving successes and failures, and integrate knowledge to improve the quality of life for patients. This instructional approach to medicinal chemistry is one way to help faculty bring

practical relevance to the scientific classroom, and encourage students to meet practice-based outcomes with an understanding of the scientific rationale behind the decisions they will make as professionals (Alsharif et al., 1999).

The micronization of various drugs is beset with serious problems due to the insufficient brittleness of crystals when using a jet mill. A new study was reported involving the investigation of an alternative micronization technique using the aerosol solvent extraction system (ASES). Several steroids, some for systemic and some for administration by inhalation, were dissolved in an organic solvent and sprayed into supercritical carbon dioxide. The resulting particles were characterized with regard to chemical and physical properties. The following steroids were investigated: beclomethasone-17,21-dipropionate, betamethasone-17-valerate, budesonide, dexamethasone-21-acetate, flunisolide, fluticasone-17-propionate, prednisolone, and triamcinolone acetonide. The spraying solution contained 1% (w/w) of drug; the solvents were dichloromethane, methanol, or a mixture of both. The median particle size of the steroid particles was in most cases lower than 5 μ m and consequently within the respirable range. If a surface active ingredient was added to the spraying solution the particle size increased and the contact angle decreased. Most of the steroids used could be micronized by means of the ASES-process with a residual dichloromethane content lower than 350 ppm in all cases (Steckel et al., 1997).

The commonly used propellants and inhalants from the chlorofluorocarbon (CFC) type are known to deplete the ozone layer so that replacement by alternative propellants is required. A new study attempted to show the feasibility to reformulate fluticasone-17-propionate, a very promising anti-inflammatory drug, using the propellant heptafluoropropane (HFA-227). The glucocorticoid was micronized by a new technique using supercritical carbon dioxide (aerosol solvent extraction system, ASES) resulting in very fine particles. Metered-dose inhaler formulations were performed using a pressure filling technique. ASES products showed a very narrow particle size distribution with slightly different crystal properties. These products were compared to metered-dose inhaler formulations with jet-milled drug. The fine particle fractions, determined with a twin stage impinger, of CFC-free formulations with one ASES product were equivalent to the CFC-formulation Flutide(TM) both having a fine particle fraction of roughly 60%. The processing of steroids using supercritical carbon dioxide proved to be a useful technique for the micronization and surface coating with a surfactant in one process step (Steckel and Muller, 1998).

Supercritical carbon dioxide was used for bone delipidation. It appeared that this technology is very efficient since supercritical CO_2 is able to diffuse into microporous solids much better than liquids and that it has a good solvent capacity for lipids. Moreover, it is safe since it involves no toxic chemical and is potentially usable with allografts as well as xenografts (Fages et al., 1994).

6.12 Teaching Laboratories

Conventional chemistry textbooks used in universities and high schools cover traditional chemistry plus thermo-, photo-, and electrochemistry The effect of sound on chemical systems has completely been ignored. Although the mechanisms of many sonochemical reactions remain unresolved, the rapid expansion of knowledge in sono-

chemistry has already justified its inclusion in present chemistry curricula. Furthermore, exploring and equipping students with a new tool for investigating chemistry is also important based on educational principles. It is hoped that these sonochemical applications will facilitate the learning of chemistry in terms of cognitive, psychomotor, and affective domains (Goh et al., 1996).

7

Green Solvents for Industrial Chemistry

7.1 Environmentally Friendly Processes

Environmental concerns have raised public awareness of environmental issues and are driving forces for regulation; the impact of regulation on the cost of production is expected to become important in determining the international competitiveness of the U.S. chemical industry (Pereira, 1999). In response to cost pressures, industry has launched a number of initiatives aimed at improving efficiency and reducing environmental impact. Some of these environmental success stories are receiving increased national attention due to programs such as the Presidential Green Chemistry Challenge Awards program. In addition to traditional metrics for evaluating process performance, such as productivity, environmental considerations increasingly are important in process development.

Environmental process objectives would include the following:

- higher product selectivity
- high conversion
- improved energy efficiency
- use of benign solvents
- raw materials substitution
- conversion of hazardous products to less hazardous products prior to shipment
- on-site production of hazardous materials
- conversion of byproducts to products
- lower secondary emissions
- low aqueous waste

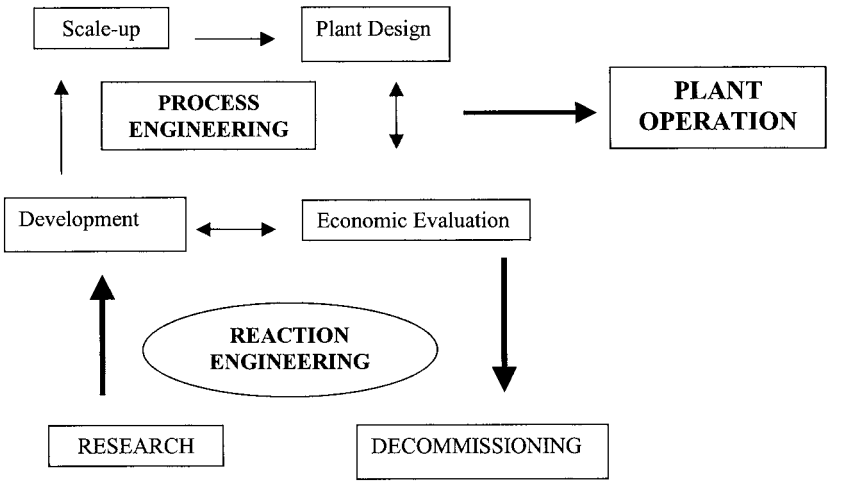


Figure 7.1 Schematic of life cycle phases of a typical chemical process.

Chemical processes evolve through life-cycle phases, beginning with research, and then moving to process engineering, plant operation, and eventually, decommissioning (see fig. 7.1). The number of technology options available for reducing environmental impact are highest early on in the life cycle and then decrease drastically. In contrast, costs associated with resolving an environmental problem typically increase exponentially as the process matures and the scale of equipment gets larger. There is, therefore, a considerable incentive to address and resolve environmental issues early in the life cycle (Bollinger et al., 1996).

Chemical reactions responsible for producing high value-added products are, in most cases, also responsible for generating byproducts and pollutants. New chemical and biochemical approaches are providing new reaction concepts. As in the development of traditional chemical and petrochemical processes, reaction engineering, broadly defined as the field that quantifies the engineering aspects of chemically reactive systems, is providing enabling tools that accelerate the development of environmentally friendly processes. Meanwhile, the research frontiers are providing new reaction engineering tools, from computational chemistry to probe the nature of catalytic active sites to computational fluid dynamics modeling for designing the internals of reaction-separation systems.

The long-term goal is to develop processes having 100% raw materials utilization, or zero waste. The near-term strategy for controlling emissions is to institute pollution prevention programs and install cost-effective end-of-pipe technologies. These technologies typically control generic classes of air pollutant emissions such as carbon monoxide, volatile organic compounds (VOCs), nitrogen oxides (NO_x) and sulfur oxides (SO_x). Technologies for treating wastewater are also available. Over time, a shift in focus is expected, from mere compliance to a point where environmentalism, like safety, is fully integrated into the corporate culture.

7.2 Industry's Response to Global Environment

7.2.1 Responsible Care Initiative

As the chemical industry strives to restore its image and build credibility in the eyes of the public, companies have come to realize that they no longer can afford to surrender responsibility for their products at the close of a sales transaction. As a result, chemical makers are taking a broader role in the marketplace as responsible stewards of their products. These practices aim to make "health, safety, and environmental protection an integral part of designing, manufacturing, marketing, distributing, using, recycling, and disposing of products" (Ainsworth, 1994).

This should only be the beginning. Eventually, the stewardship process is expected to reach all parts of an organization, not only from product or business perspectives but also in terms of company operations and functions. The Responsible Care's Product Stewardship Code of management practice covers all stages of a product's life. As manufacturers get a grip on the most immediate links in the product stewardship chain—marketing, distribution, and end use—they are beginning to extend their reach, looking back to design and improvement of products as well as forward. Many companies have approached the "green" issue by reevaluating existing products and processes (including solvents).

7.2.2 Sustainable Development

Sustainable development is a fuzzy concept. As a concept, however, it meets the needs of the present without compromising the needs of future generations (Morse, 1998). From a business perspective, sustainable development is often separated into three interdependent areas: economic, environmental, and social.

Sustainability in economic terms means the efficient management of scarce resources as well as a prospering industry and economy. In the environmental sense it means not placing an intolerable load on the ecosphere and maintaining the natural basis for life. In social terms it means that human beings are the center of concern (Morse, 1998).

The chemical industry must rethink the next set of standards and not simply push Responsible Care to the next incremental step. Sustainable development means economic growth that does not deplete irreplaceable resources, does not destroy ecological systems, and helps reduce some of the world's gross social inequalities.

The current reality is that most chemical companies are looking at Responsible Care, ecoefficiency, and waste reduction as their response to sustainability. The key to sustainable development is in balancing the economic concerns with the environmental and social issues.

The chemical industry views sustainable development as a challenge put before all parts of society. In the advances made in its own operations, its improved performance and in the improvements to the human condition made through its products, the chemical industry sees cause for optimism and believes that sustainable development can be the intellectual framework around which the chemical industry, other industries and other sectors of society can reach consensus on how to improve living standards and the environment.

The main challenges facing the world include:

- optimizing the benefits obtained from depleting resources;
- assuring against excessive strains placed on the ecosystem;
- recognizing the dynamic growth of the world population;
- remedying social and economic inequalities.

7.2.3 Contributions of the Chemical Industry to Sustainable Development

The chemical industry is a key industry. Its products and services are instrumental in meeting the needs of society. It is present in all areas of life, from food and clothing, housing, communications, transport—right through to leisure activities. In addition, it helps to solve the problems of other sectors of industry, such as the energy sector, information technologies, environmental industries and the waste disposal sector, as examples.

Due to its size, the chemical industry is an important supplier to a broad range of downstream industries and is, as well, a customer of a broad range of products and services from other industries. It follows, therefore, that the chemical industry plays a major role in providing/supporting performance improvements, research and development progress and, last but not least, employment in other industries.

7.2.4 The Chemical Industry's Leadership in Innovation

The chemical industry's contribution is to continue innovation of new products that meet customer needs and manufacturing processes that reduce risks to health and the environment. This contribution is based upon the knowledge and experience the industry has acquired from applying innovation not only to making, handling, and using chemical compounds, but also to reprocessing, recycling, and solving environmental problems. The challenge facing the chemical industry is to maximize innovation, which can contribute to society meeting its goals for sustainable development.

The chemical industry is firmly convinced that leadership in innovation represents the best way of attaining sustainable development. For the individual company, this means

- a consistent orientation toward products, technologies, and solutions which offer the greatest promise for the future;
- development of new integrated environmental technologies;
- a close cooperation with the customers of the chemical industry;
- adaptation to the conditions of global competition;
- bringing the most promising products quickly on the market;
- strengthening the R&D effort which requires resources which can only be financed from profitable earnings;
- actively contributing ideas and suggestions to the policy debates taking place in society;
- improving process yield (efficiency).

7.2.5 Approach to the Environmental Goal of Sustainable Development

In order to take environmental protection further, environmental standards need to be set to serve as parameters—established within the framework of a market economy. It is then up to each industry to determine how these standards are to be attained within its sector. For the chemical industry, the following parameters are relevant:

- Scientific environmental monitoring systems are of particular importance. The aim must be to integrate environmental protection considerations into products and processes as early as possible in the development phase.
- Energy costs are crucial to the chemical industry.
- Competitive access to energy is necessary to the chemical industry. The chemical industry is contributing to this goal by continuously reducing the environmental impact of its activities.

7.3 Occupational Toxicology

7.3.1 Threshold Limit Values and Biological Exposure Indices

Industrial workers make up the segment of the population that is most vulnerable to chemical injury. To protect them from occupation-related harm, the American Conference of Governmental and Industrial Hygienists publishes annually revised threshold limit values (TLVs), guidelines for permissible chemical exposure at the workplace. http://www.acgih.org/Resources/press/HAL.htm

TLV refers to concentrations of substances in parts per million or milligrams per cubic meter in the air to which most workers can be exposed on a daily basis without harm. These values apply to the workplace only. They are not intended as guidelines for ambient air quality standards for the population at large. TLVs should be treated as guidelines only and not as fixed standards. The recommended goal is to minimize chemical exposure in the workplace as much as possible.

TLVs are expressed in three ways:

- Time-weighted average (TLV-TWA) designates the average concentration of a chemical to which workers may safely be exposed for 8 h per day and 5 days per week.
- Short-term exposure limit (TLV-STEL) designates permissible exposure for no more than 15 min, and no more than four times per day, with at least 60-min intervals between exposures.
- Ceiling concentrations (TLV-C) are concentrations that should not be exceeded at any time.

Biological exposure indices (BEI) provide another way of looking at exposure to chemicals. This method supplements air monitoring for compliance with TLV standards. BEI are standards of permissible quantities of chemicals in blood, urine, or exhaled air of exposed workers.

7.3.1.1 Respiratory Toxicity

Toxins (gases, vapors, or aerosols) may injure respiratory tissue, or they may cause systemic toxicity by penetrating the tissue and entering the circulation. Injuries to the respiratory system vary in severity (depending on the agent and the degree of intoxication) from irritation to edema, fibrosis, or neoplasia. The site of toxicity depends on the water solubility of a gas or on the size of aerosol particles or droplets.

The upper respiratory system is susceptible to attack by water-soluble gases such as ammonia, chlorine, sulfur dioxide, and hydrogen fluoride. Before a gas can gain access to the tissue, it has to penetrate the mucus lining. This barrier imparts some protection against very small quantities of toxic gases, but it does not protect the tissue against large doses.

Aerosols of particles larger than 2 μm also cause damage to the upper respiratory system. Arsenic oxides, sulfides, and chlorides are used in a variety of industries, such as manufacturing of colored glass, ceramics, semiconductors, and fireworks and in hide processing. However, upper respiratory exposure to these compounds is most likely to occur in ore smelting industries and in pesticide manufacturing.

7.3.2 Allergic Responses

Allergies are a result of dysfunction of the immune system. The immune system, which is designed to inactivate and eliminate foreign bodies, reacts abnormally in some individuals when challenged with specific substances. The most frequently encountered occupational allergies are asthma and contact dermatitis.

7.3.2.1 Common Agents

The agents that induce an allergic response vary greatly and can involve such things as organic chemicals, metals, dusts, and bacteria. Examples of some chemicals frequently responsible for occupation-related allergies are toluene diisocyanate (TDI), used in plastic and resin manufacturing; formaldehyde, widely used in manufacturing phenolic resins, in textile finishes, in the processing of hides, and in numerous other industrial processes; and hexachlorophene, use in manufacturing germicidal soaps and cosmetics.

7.3.2.2 Allergies of Food Industries

A number of allergies affect workers employed in agricultural and food industries.

7.3.3 Liver Damage

Chemical injuries to the liver depend on the type of toxic agent, the severity of intoxication, and the type of exposure, whether acute or chronic. The six basic types of liver damage are fatty liver, necrois, hepatobiliary dysfuntions, viral-like hepatitis, and (on chronic exposure) cirrhosis and neoplasia. A number of organic chemicals and drugs induce fatty liver and liver necrosis.

Occupationally, liver injury is most likely to occur following exposure to vapors of volatile halogenated hydrocarbons (such as chloroform, carbon tetrachloride, and bromobenzene), which may enter the bloodstream via the pulmonary route. However, hepatotoxins may enter the gastrointestinal tract, and hence the liver, in the form of fine particles. They are inhaled, then expelled from the bronchi or trachea into the oral cavity, and swallowed with saliva.

7.3.4 Other Toxic Responses

The hematopoietic and nervous systems are frequently severely affected by industrial toxins.

7.3.4.1 Hematopoietic Toxins

Benzene, a component of motor fuel that is also widely used as an industrial solvent and as a starting material in organic synthesis, is a hematopoietic toxin. Chronic exposure to benzene vapors leads to pancytopenia, that is, decreased production of all types of blood cells (erythrocytes, leukocytes, and platelets). The long-term effect of benzene exposure is acute leukemia.

7.3.4.2 Neurotoxins

Nonmetallic neurotoxins are frequently used in industry in manufacturing of chemicals and resins or as solvents. Some examples are hydrogen sulfide (which paralyzes specifically the nervous centers that control respiratory movement), carbon disulfide, *n*-hexane, methyl *n*-butyl ketone, and acrylamide. Exposure to all of these substances may occur through inhalation of vapors. In addition, carbondisufide and acrylamide may enter the system by dermal absorption. *n*-Hexane and methyl *n*-butyl ketone are not toxic by themselves but are activated by cytochrome P-450 to the neurotoxic hexanedione ($CH_3COCH_2CH_2COCH_3$).

7.3.5 Toxicity and Population

Concerns about chemicals in the environment have focused major attention on the possible consequence for humans, animals, and whole ecosystems. However, we still lack back basic knowledge and procedures for evaluating the potential impacts of chemicals, compound mixtures, or artificial concentrations of natural substances that have an adverse effect on human health and the environment. Such knowledge will be essential for developing products with adequate safeguards against unwanted side effects.

Reasonably good methods are available for testing the potential carcinogenic effects of chemicals on surrogate species for humans, particularly rodents. The correlation between these surrogates and humans is far from proved and is hotly debated. However, on the basis of experience buttressed by significant testing, use of surrogate species seems to have been most helpful in reducing exposure to many suspect carcinogens.

There is a need for better tests to assess ecological damage potentially caused by single-compound chemicals, the byproducts of various waste-treatment processes, and the degradation products of intentional products or unintentional process emissions that find their way into the environment. Better understanding of the basic biochemical processes occurring in the environment is necessary to decide where to look, what to look for, and what to measure and how to measure it (Division, 1996).

A searchable model that links air emissions from an individual plant to the toxicity of each chemical emitted as well as exposure to residents living near the plant was released by the Environmental Protection Agency. The Risk-Screening Environmental Indicators model is based on EPA's Toxics Release Inventory (TRI), which lists some 600 chemicals, the emissions of which have been reported annually by 38,000 facilities in the past 10 years. However, the new model adds data on chemical toxicity and human exposure to produce an indicator of relative risk.

The chemical industry has historically been the top TRI emitter, but by figuring in toxicity and exposure, the baton has been passed to a new leader—the primary metals industrial sector. The model does not provide chemical-specific quantitative risk assessments. Instead, EPA developed toxicity weights for each chemical. Those are combined with exposure, fate, and transport information to generate an "indicator value" for the health impact of emissions from a particular factory (Johnson, 1999).

7.3.6 Industry and Environmental Problems

The last 50 years have seen the introduction of many new chemicals. For some, important adverse environmental effects emerged. The search to replace those without further environmental effects has become a strong driving force in industry, in the scientific community, and in the general public. The focus has been mostly on testing for acute human toxicity with surrogates and on estimating long-term chronic effects in humans, primarily emphasizing cancer, again with surrogates. Researchers should strive to include effects on entire ecosystems, and long-term, multigenerational effects on fertility, reproductive quality, and hormonal functions. Of major interest will be chemicals with the potential to be persistent, toxic, and bioaccumulative. However, chemicals that are persistent but not toxic or bioaccumulative, such as CFCs, have also led to environmental problems, as have chemicals that are persistent and toxic but not bioaccumulative. Evaluations of such chemicals are also needed.

Following are some examples of products or processes that created unforeseen environmental problems after their introduction.

1. Products
    a. pesticides, such as DDT, endrin, dieldrin, and benzene hexachloride (BHC)
    b. alkylbenzene sulfonate (ABS) synthetic detergents
    c. polychlorinated biphenyls (PCBs)
    d. chlorofluorocarbons (CFCs)
    e. lead used in gasoline and paint
    f. some chlorinated solvents
    g. wood preservatives

2. Processes
    a. chlorination for disinfection (in some situations)
    b. mercury release from chlor-alkali cells
    c. older coal gasification (now replaced with modern, but expensive, technologies)
    d. dioxin release from incineration and some chemical reactions

If we just look at how solvents play roles in two of these, we begin to see the necessity for green solvents. Major environmental problems resulted from lead in gasoline and paint, and its use in these products has been eliminated. That required the development of new formulations for gasoline, new designs for engines, and substitutes for paint pigments. For gasoline, the altered formulations are now being shown to be the source of problems in their own right.

An Environmental Protection Agency advisory panel called for a substantial reduction in the use of methyl *tert*-butyl ether (MTBE) as a gasoline additive. The group also recommended that Congress remove the current requirement that 2% of reformulated gasoline by weight consists of oxygen—a mandate of the 1990 Clean Air Act Amendments. MTBE is by far the most common oxygenate employed to meet that mandate. This action is to address the growing problem of MTBE from leaking gasoline tanks and from spills contaminating water supplies (Grisham, 1999a).

Oxygenates used as additives in reformulated gasoline do little to reduce ozone pollution, according to a report by a committee of the National Research Council (NRC). The study looked at the performance of ethanol and methyl *tert*-butyl ether and found that although gas reformulated with MTBE is slightly more effective at reducing ozone, the impact of both oxygenates is very small (Grisham, 1999b).

Substitutes for the CFCs that cause depletion of stratospheric ozone are being developed. Those which will be used in the near future (hydrochlorofluorocarbons (HCFCs) are of concern because a decomposition product, trifluoroacetic acid, might be very persistent and, under extreme conditions, have the potential to cause an undesirable environmental impact.

The degradation chemistry of the alternative chlorofluoro- and fluorohydrocarbons HCFC-22, HCFC-123, HCFC-124, HFC-134a, HCFC-141b, and HCFC-142b and the main removal processes from the troposphere of these halogenated hydrocarbons and their oxidation products are becoming clear. Lifetimes of the parent hydrochlorofluorocarbons (HCFCs) and HFC-134a range from 1.3 to 20 years, with oxidation by the OH radical being the dominant removal process. Based on recent kinetic information, it is calculated that none of the relatively stable intermediate oxidation products such as COF_2, COFCl, CF_3COF, and CF_3COCl will substantially build up in the atmosphere, the global abundances of these compounds being generally less than 1% those of the parent compounds. Maximum deposition occurs in tropical regions, associated with high oxidation rates of the parent compounds, and high rainfall. These predicted concentrations and deposition fluxes are orders of magnitude smaller than what is thought to be toxic for humans, for the fauna, and for the flora (Kanakidou et al., 1995).

The above are only a few examples of the numerous major environmental problems that were created by the introduction of new products and processes. They should serve as reminders, as societies develop new products and processes to satisfy their

needs and desires. The potential of any chemical for environmental damage must be assessed before its commercialization, and our capability for doing so should be expanded, although we recognize the possibility that new chemicals might replace other substances, natural or manmade, already in use that could be even more damaging. Those cases demonstrate the need for continuous review of costs and benefits, which might not be the same for all countries and communities.

7.4 What Are Green Industrial Solvents?

In order to reduce the adverse impacts of chemicals the National Research Council provided a number of recommendations that would assist in linking science and technology to society's environmental goals (Division, 1996). Let us use these as a measuring stick to begin a discussion of green industrial solvents.

1. Better test methods should be developed to evaluate, model, and monitor the potential long-term environmental impacts of single compounds emitted as a result of new products or processes.
2. Better test methods should be developed to define and ultimately to model and predict the byproducts and degradation products associated with production and use of materials. Basic studies of biochemical effects and of the impact of various chemicals and other adverse effects on the biochemistry of sensitive plant and animal species should be strongly supported.
3. Strong support should be given to innovative ideas for modeling and tests on lower-order surrogate species that help to reduce the cost of tests for potential adverse environmental health effects on humans or shorten the response time needed to obtain that information.
4. International standardization of testing and international sharing of testing responsibilities should be promoted to reduce costs and speed the availability of reliable and reproducible assessments.
5. The emerging concept of developing experimental "mini-ecosystems"—focused on controlled-exposure environments for testing and for developing mathematical simulations of ecosystem impact based on limited, specific tests—should be supported.

The implementation of the Montreal Protocol, the Clean Air Act, and the Pollution Prevention Act of 1990 has resulted in increased awareness of organic solvent use in chemical processing. The advances made in the search to find "green" replacements for traditional solvents have been tremendous. With reference to solvent alternatives for cleaning, coatings, and chemical reaction and separation processes, the development of solvent databases and computational methods that aid in the selection and/or design of feasible or optimal environmentally benign solvent alternatives for specific applications have been discussed (Sherman et al., 1998).

Solvents, defined as substances able to dissolve or solvate other substances, are commonly used in manufacturing and laboratory processes and are often indispensable for many applications such as cleaning, fire fighting, pesticide delivery, coatings, synthetic chemistry, and separations (Grayson, 1985). Billions of pounds of solvent waste are emitted to the environment annually, either as volatile emissions or with aqueous

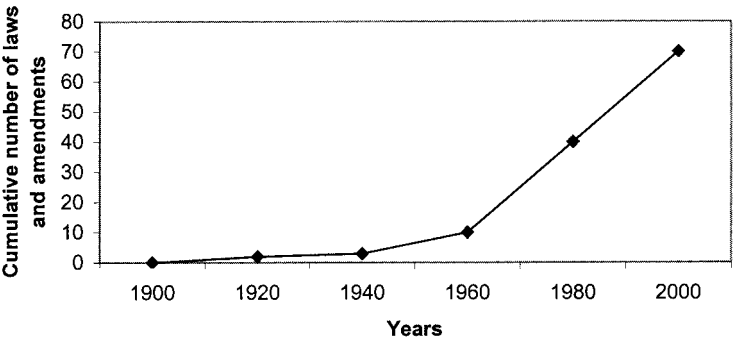


Figure 7.2 Cumulative federal regulations.

discharge streams (Anastas, 1994). Many of these solvents are known to upset our ecosystems by depleting the ozone layer and participating in the reactions that form tropospheric smog. In addition, some solvents may cause cancer, are neurotoxins, or may cause sterility in those individuals frequently exposed to them. While contained use of these solvents would be acceptable from both an environmental and a health perspective, such operations are difficult to achieve, and alternative solvents are currently being sought to minimize the problems inherent in solvent release to the environment.

As our awareness and understanding of how solvents affect the environment and human health grow, so do the regulations that govern use of these chemicals (fig. 7.2) (Gendron, 1994; Sherman et al., 1998). Government agencies such as the Occupational Safety and Health Administration (OSHA) have been installed to protect workers from solvent exposure (see table 7.1). Indeed, OSHA has implemented strict regulations, called permissible exposure limits (PEL), for chemical concentrations to which one may be exposed without detrimental health effects. Examples of the PEL values, as well as health effects for a variety of solvents are listed in table 7.2.

Solvents restricted under the Montreal Protocol are categorized as Class 1 or Class II compounds, many of which are listed in table 7.3. Class I compounds have already undergone a major phase-out, whereas Class II compounds will be completely phased out of use by 2030.

Table 7.1. Major United States environmental laws.

Law	Year
Clean Air Act (CAA)	1955
Occupational Safety and Health Administration (OSHA)	1975
Superfund Amendments and Reauthorization Act of 1986 (SARA)	1986
Clean Air Act Amendments (CAAA)	1989
Pollution Prevention Act of 1990 (PPA)	1990

Table 7.2. Compounds on the U.S. EPA 33/50 list.

Compound	Solvent Use	Toxicity	OSHA PEL (8-hr TWA), ppm	LD_{50}, Orally in Rats
Benzene	Synthesis, feedstock, waxes, oils, resins	Carcinogen	10	3/8 mL/kg
Chloroform	Degreasers, rubbers, resins, waxes	Anticipated carcinogen	50	0.9 mL/kg
Carbon tetrachloride	Degreasers, rubbers, resins, waxes, feedstock	Poison, anticipated carcinogen	9528	
Methyl ethyl ketone	Coatings, resins	Headaches, dizziness, nausea	200	6.86 mL/kg
Methyl isobutyl ketone	Similar to MEK	Similar to MEK	100	Similar to MEK
Methylene chloride	Polymers, synthesis, cleaning and degreasing	Narcotic in high concentrations	25	1.6 mL/kg
Perchloroethylene	Dry cleaning, degreasing	Narcotic in high concentrations	100	8.85 g/kg
Toluene	Feedstock, paints, resins, extractants, gasoline additive	Narcotic in high concentrations	200	7.53 g/kg
1,1,1-trichloroethane	Adhesives, coatings, inks, degreasers, waxes, alkaloids	Narcotic in high concentrations	350	0.58 mL/kg
Trichloroethylene	Cleaning, degreasers, waxes, resins, rubbers, paints, extractants, feedstock	Inebriation at moderate exposure Heavy exposure can cause ventricular fibrillation, death	100	4.92 mL/kg
xylenes	General solvent, feedstock	Narcotic in high concentrations		7.71 mL/kg

Table 7.3. Ozone-depleting solvents restricted under the Montreal Protocol.

Class	Ozone-Depleting Substances
Class I	CFCs (chlorofluorocarbons) Halon 1211 (bromochlorodifluoromethane) Halon 1301 (bromotrifluoromethane) Halon 2402 (dibromotetrafluoroethane) CCl_4 (carbon tetrachloride) Methyl chloroform (1,1,1-trichloroethane) CH_3Br (methyl bromide) $C_lH_jBr_kF_l$ (hydrobromofluorocarbons)
Class II	HCFCs (hydrochlorofluorocarbons)

Hazardous air pollutants such as hexane and methanol are regulated under the Clean Air Act (CAA) (U.S. EPA, 1990a). Volatile organics, defined by the U.S. Environmental Protection Agency (U.S. EPA) as compounds that evaporate at the temperature of use and react with oxygen to form tropospheric ozone, are also restricted under the CAA. Further, the Toxic Release Inventory Bill requires solvent users to record their releases and waste carefully. A summary of many of the federal, state, and local regulations is found in a review by Breen and Dellarco (Breen and Dellarco, 1992).

The new paradigm—pollution prevention—should serve as the keystone of federal, state, and local environmental policy. Support for the new approach is broad based and includes environmentalists, industrialists, lawmakers, academicians, government regulators and policy-makers, and the general public. It will require a cooperation among environmental, industrial, and regulatory interests. The roles and contributions of the chemical engineer, synthetic organic and inorganic chemist, and the process analytical chemist will be integral to the full articulation and implementation of the new vision (Breen and Dellarco, 1992).

The Pollution Prevention Act of 1990 propelled these regulatory issues to the forefront of process design by suggesting, "the use of materials processes or practices that reduce or eliminate the creation of pollutants or waste at the source. It includes practices that reduce the use of hazardous materials, energy, water or other resources and practices that protect natural resources through conservation or more efficient use" (U.S. EPA, 1990b).

The U.S. EPA followed the Act by compiling a list of 17 priority pollutants, including some solvents, whose use was to be voluntarily reduced by 50% in 1995. This list, known as the U.S. EPA 33/50 list, was based on the criteria that the chemicals are used in large volume, they are detrimental either to the environment or to human health, and there are available methods to reduce their use (U.S. EPA, 1992). The 33/50 list in conjunction with the previously mentioned global and federal regulations has provided a solid starting point for scientists and engineers to reevaluate traditional methods and to discover ways to limit or eliminate the use of hazardous solvents.

As a result, many methods for solvent pollution prevention have been developed (Englehardt, 1993; Venkataramani et al., 1992). New synthetic pathways that do not demand the use of deleterious solvents or are inherently more selective for the compound of interest have been investigated (Haggin, 1995; Sheldon, 1994). Adjustments can be made to process equipment to protect against fugitive emissions (Lipton, 1992). Process integration techniques have been effective in minimizing waste generation and optimizing solvent recovery and recycling (Ahmad, 1997; Dienemann and Bacher, 1994; Manousiouthakis and Allen, 1995; El-Halwagi, 1992; Sheldon, 1994). Solvent replacement techniques have also come to the forefront as many solvents are banned or discouraged from industrial use. In this case the only option is to find an alternative solvent.

The impact these regulations and methods have had on solvent use is seen clearly in figs. 7.2 and 7.3 (Kirschner, 1994). Over the past 15 years the use of both hydrocarbon and chlorinated solvents has declined with only a minor increase in consumption of oxygenated solvents. In addition, while process solvents, consumer products and various miscellaneous applications have exhibited fairly constant solvent consumption, the cleaning and coatings industries have markedly decreased solvent use over

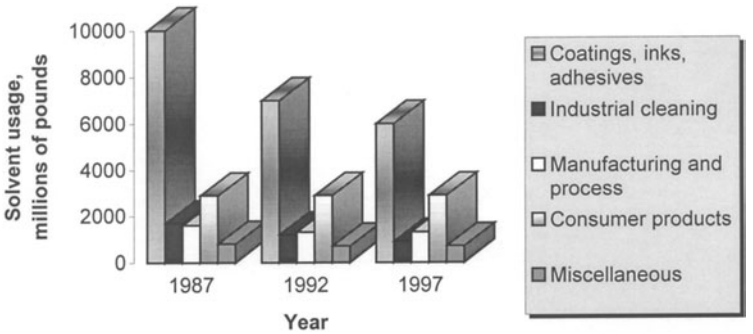


Figure 7.3 Solvent use by application. Adapted from Kirschner (1994).

the last decade. A more detailed breakdown of U.S. solvent consumption can be found in an editorial by D'Amico (D'Amico, 1995).

The purpose of this section of the book is to bring together research efforts in the quest to find "green" replacements for traditional solvents used in chemical processing and industries. The chapter will present industrial sectors, where solvent use is important. New solvents and processing alternatives will be presented. Readers are directed to a monograph by Miziolek and Tsang for a comprehensive review of the challenges and progress in finding halon replacements (Miziolek and Tsang, 1995).

7.5 Solvents by Industrial Reaction Process

Solvents are used widely in the chemical processing industry, as they are necessary for the solvation of the reactants and products in reaction processes. Selection of the solvent is important in determining the chemical reactivity, selectivity, and yield of industrial synthesis operations. Most synthesis solvents except carbon tetrachloride are not Class I or Class II ozone-depleting substances, so in contrast to solvents used in cleaning and coating operations their supply is not threatened. Many of them, however, are on the 33/50 list, and ways to reduce their use are being sought actively. One route is to find or develop replacement solvents, which are attractive for reasons of safety, toxicity, emissions, and other aspects covered increasingly by the many government regulations. Ideally, new techniques would allow reactions to occur in the absence of solvents; to this end, some progress has been made using microwaves (Chaddick, 1995; Varma, 2000). Most synthetic reactions are solvent based, however, and will continue to be so for the foreseeable future. There is clearly a need, then, to search for alternative solvents for synthesis operations more environmentally friendly than the existing solvents. This search is more complicated than in the case of cleaning and coating operations as not only should the solvating characteristics of the replacements match those of the original solvent as closely as possible, but the new synthesis

solvents must also be inert to the reactants and products, and the yield of the reaction should not be compromised.

A clear example of the process of solvent evaluation is found in the cleaning industry. Solvents are widely used to remove contaminants from a variety of substrate materials. Common contaminants include solid particulates, waxes, greases, cutting and lubrication fluids, buffing compounds, flushing oils, quenching oils, heat-treating salts, rosin fluxes, protective coatings, and finishes. Selection of a particular solvent and cleaning process is based on the type of substrate(s) to be cleaned, the type of soil(s) to be removed, the degree of cleanliness required, the desired method of application, and many other operating conditions and constraints. Solvent usage in maintenance and general production activities, precision cleaning, semiconductor production, printed-circuit-board (PCB) fabrication, and paint stripping are further examples.

7.5.1 Solvents for the Health Field

Some new work has been done here which shows the effects of solvents exposure. A new study illustrates a simple method of detoxification using heat chamber depuration (sauna), and raises awareness in the practice of medicine of the importance of taking an environmentally oriented historical approach. The connection between symptoms of chronic degenerative diseases and environmental and/or nutritional factors is missed in many cases due to lack of obtaining an environmentally oriented medical history. Taking such a history and dealing with the cause of illness using avoidance and/or appropriate therapy is preventive and cost-effective for both the patient and society (Krop, 1998).

Green chemistry has developed rapidly since its introduction in the early 1990s. The concept of designing chemical products and processes, such that hazardous substances are not used or generated, has resulted in both environmental and economical benefits without compromising creativity and innovation. Companies in the chemical, pharmaceutical, agricultural, and many other industrial sectors have researched, developed, implemented, and commercialized green chemistry technologies that have resulted in increased profits while ensuring environmental sustainability (see table 7.4). The key to the success of this approach lies in the quality of the fundamental science and basic research that is being conducted in this area by top scientists (Anastas and Williamson, 1998).

Supercritical CO_2 can be used in the health care industry. The promise of using supercritical technology in solving environmental problems, in the food, petroleum, and gas industry, as well as in chromatography, pharmaceutics, and so on, has been demonstrated (Beckman et al., 1995).

Reversed micelles can be used to concentrate water-soluble materials in the water pool of $SCCO_2$. The extraction of water-soluble vitamins into reversed micelles has been examined. The efficiency of extraction was strongly affected by the extraction temperature and the concentration of reversed micelles, and the selectivity depended on the size of micelles. Water-soluble vitamins could be efficiently and rapidly extracted. The selective extraction of a model mixture of vitamins from pharmaceutical preparations was also demonstrated. Moreover, the usefulness of the proposed method for the determination of vitamins in various commercial tablets was also demonstrated. Using this method, the surfactant remains mixed with the extracted com-

Table 7.4. Green solvents applicable to pharmaceutical field. (Ash and Ash, 1996).

Acetic acid
Acetophenone
Benzyl benzoate
Diethylene glycol dibutyl ether
Diethylene glycol dimethyl ether
Dimethyl sulfoxide
Ethyl acetate
Ethylene glycol dimethyl ether
Glycerol
Hexane
Methanol
Polyglycol E 200
Propylene glycol
t-Butanol
Tetrahydrofuran
Supercritical carbon dioxide

pounds. Supercritical carbon dioxide containing 7.5% ethanol as entrainer was found to be the most efficient solvent for removing residual surfactant from the extract (Ihara et al., 1995).

Previously mentioned was a method for operators with limited training have designed rapidly screening pharmaceuticals by thin-layer chromatography for use in areas with limited resources. Personnel can be trained in a short time to perform screening analysis of drugs (Kenyon et al., 1995).

Supercritical fluid extraction is a potential technique for the purification of pharmaceutical products containing residual solvents. The solubilities of three inhibitors of inflammatory activity, Ketoprofen, Piroxicam, and Nimesulide, in supercritical CO_2, measured using a dynamic saturation technique, were reported at pressures between 100 bar and 220 bar and at two temperatures: 312.5 K and 331.5 K. The solubilities exhibit a clear dependence on the solvent density, and this has been used to provide a simple and precise correlation of the data (Macnaughton et al., 1996).

The problems addressed by inorganic chemistry continue to be challenges well into the twenty-first century. For example, coordination chemistry will continue to provide compounds with unusual properties and uses, and will become an increasingly important component in bioinorganic chemistry. Organometallic chemistry will continue as one of the most active areas of catalysis research, especially in the chemical, energy, pharmaceuticals, and pollution control industries. New methods to meet the needs of the production of inorganic chemicals will involve environmental friendly synthesis (Navratil, 1998).

Significant improvements in the isolation of pharmaceutical compounds from plasma, serum and urine, have been achieved using ultra low mass sorbent bed and thin disk solid-phase extraction (SPE) material. The use of low sorbent masses or disk SPE material has allowed a significant reduction in solvent usage and extraction times. Several SPE RP-HPLC methods have been developed using these materials, including

LC-MS methods. When the chromatographic conditions allow the eluent to be injected directly or injected after dilution with distilled water (Plumb et al., 1997).

The commonly used propellants from the chlorofluorocarbon (CFC) type are known to deplete the ozone layer so that replacement by alternative propellants is required. It was shown that $SCCO_2$ was useful in a new system. The glucocorticoid was micronized by a new technique using supercritical carbon dioxide (aerosol solvent extraction system, ASES) resulting in very fine particles. Metered-dose inhaler formulations were performed using a pressure filling technique. ASES products showed a very narrow particle size distribution with slightly different crystal properties. The fine particle fractions, determined with a twin stage impinger, of CFC-free formulations with one ASES product were equivalent to the CFC-formulation Flutide (TM), both having a fine particle fraction of roughly 60%. The study proved the feasibility of reformulating fluticasone propionate with the alternative propellant HFA-227. The processing of steroids using supercritical carbon dioxide proved to be a useful technique for the micronization and surface coating with a surfactant in one process step (Steckel and Muller, 1998).

Chlorofluorocarbon (CFC) replacements have recently been used for their lower stability and because they have carbon-hydrogen bonds, which means that their atmospheric lifetime is expected to be much shorter than those of CFCs. The adsorption properties of 1,1,2-trichloro-1,2,2-trifluoroethane (CFC113) and its replacement compounds, 1,1-dichloro-2,2,2-trifluoroethane (HCFC123), 1,1-dichloro-1-fluoroethane (HCFC141b), and 1,1-dichloro-1,2,2,3,3-pentafluoropropane (HCFC225ca) on four kinds of activated carbons were investigated. The adsorption isotherms of inhalational anesthetics (halothane, chloroform, enflurane, isoflurane, and methoxyflurane) on the activated carbon were measured to evaluate the action mechanism of inhalational anesthesia. The anesthesia of CFC replacements can be estimated by the Freundlich constant N of the adsorption isotherms (Tanada et al., 1997).

Lysozyme was encapsulated in biodegradable polymer microspheres which were precipitated from an organic solution by spraying the solution into carbon dioxide. The polymer, either poly(l-lactide) (I-PLA) or poly(DL-lactide-co-glycolide) (PGLA), in dichloromethane solution with suspended lysozyme was sprayed into a CO_2 vapor phase through a capillary nozzle to form droplets which solidified after falling into a CO_2 liquid phase. By delaying precipitation in the vapor phase, the primary particles became sufficiently large, from 5 to 70 μm, such that they could encapsulate the lysozyme. At an optimal temperature of −20°C, the polymer solution mixed rapidly with CO_2, and the precipitated primary particles were sufficiently hard such that agglomeration was markedly reduced compared with higher temperatures. More uniform particles were formed by flowing CO_2 at high velocity in a coaxial nozzle to mix the droplets at the CO_2 vapor–liquid interface. This process offers a means to produce encapsulated proteins in poly(DL-lactide-co-glycolide) microspheres without earlier limitations of massive polymer agglomeration and limited protein solubility in organic solvents (Young et al., 1999).

7.5.2 Industrial Solvents by Applications

Ash and Ash have provided an invaluable reference to the many solvents employed across multiple industries (Ash and Ash, 1996). This reference work describes more

than 1700 trade name products and chemicals that are used as solvents in the chemical industry and in research. Solvents are used a wide range of industries and applications including: metal cleaning and degreasing, dry-cleaning operations, automotive and aviation fuel additives, paints, varnishes, lacquers, paint removers, plastics and rubber products, adhesives, textiles, printing inks, pharmaceuticals, and food processing. As a sample of the possible green solvents useful in industry, we would like to cross reference the possible solvents in some areas with the green solvents described in chapter 5. Shown below are the possible areas covered in Ash; table 7.5 shows a sampling of the overlap (Ash and Ash, 1996).

adhesives
agriculture
antifreeze
brake fluids
ceramics
chemical processing
construction and building materials
cosmetic and personal care products
dry-cleaning chemicals
electronics manufacturing
food processing
foods
fuel additives
gas scrubbing
industrial, institutional, and household cleaning
inks
leather treatment
metal treating and processing
mineral processing
mining
paints and coatings
paper and pulp processing
petroleum and oil processing
pharmaceuticals
plastics and resins
rubber compounding and processing
textiles and fibers
waxes and polishes

In the following sections we would like to provide in greater depth information in the above listed application areas. The section headings will follow the order given in table 7.5: adhesives; agriculture; fuel additives; chemical processing; cosmetic and personal care products; industrial, institutional, and household cleaning; metal treating and processing; food processing; paints and coatings.

7.5.2.1 Adhesives

There is an increased need to develop environmentally benign (no pollution or release of hazardous materials into the air, water, or soil from a coating or adhesive either during their manufacture, use and disposal, or recycle lifetimes), coatings and adhesives that have equivalent or superior properties to their conventional (nonenvironmentally benign) counterparts. A paper by McGinniss (1996) discussed some of the new concepts or technologies associated with environmentally benign barrier coatings for packaging, abrasion resistant coatings for plastic substrates, new developments in wood finishes, antifouling coatings, and new chemistry associated with the design of advanced coating systems. This paper also discussed how Battelle is helping the U.S. Air Force to eliminate hazardous waste associated with structural adhesive technology through the identification of equivalent adhesive systems reducing the number of adhesives used to repair current aircraft and missile equipment. Also discussed were

Table 7.5. Sampling of green solvents for some industrial applications.

Solvent	Ref #	I	II	III	IV	VI	VII	VIII	IX	X
3-Pentanol	***5870***				x					
Acetamide	***2900***					x				
Acetone	***690***	x								x
Acetonitrile	***2990***				x					
Acetophenone	***3810***									x
Actrel 116OL cleaner	***590***						x			
Actrel 3338L cleaner	***600***						x			
Actrel 3349L cleaner	***610***						x			
Actrel 3360L cleaner	***620***						x			
Actrel 4493L cleaner	***630***						x			
Benzene	***720***									x
Benzonitrile	***3870***									x
Benzyl alcohol	***3880***									x
Benzyl benzoate	***5120***					x				
Butoxyethanol	***770***									x
Butyl acetate	***780***					x				x
Cumene	***3800***				x					
Cyclohexane	***880***				x					x
Cyclohexanol	***890***									x
Cyclohexanone	***900***						x			x
Cyclopentane	***910***				x					
Decahydronaphthalene	***3480***									x
Diacetone alcoho	***940***									x
Dibutyl ether	***960***				x					x
Dibutyl phthalate	***980***					x				x
Diethylene glycol diethyl ether	***1050***									x
Diethylene glycol dimethyl ether	***1060***				x					
Dipropylene glycol monomethyl ether	***1220***						x			
d-Limonene	***2820***						x			
Ethyl acetate	***1510***	x								x
Ethyl formate	***1540***		x							
Ethylene glycol diethyl ether	***1590***						x			x
Ethylene glycol dimethyl Ether	***4800***									x
Formic acid	***1770***					x				x
Heptane	***1810***			x	x					
Hexane	***1840***					x			x	
Isoamyl acetate	***5240***									x
Isopropyl alcohol	***1920***		x	x						x
Kerosene	***1930***						x			
Methanol	***2120***								x	
Methyl acetoacetate	***4020***				x					
Methyl ethyl ketone	***2150***	x			x				x	x
Methyl oleate	***5030***		x							
Mineral spirits	***2220***	x	x	x			x			x
m-Xylene	***2840***			x						
n-Decane	***5290***			x						
Nitroethane	***3340***	x								x
Nitromethane	***3130***			x	x					
Octane	***4940***			x						
p-Chlorotoluene	***4130***	x						x		
Propyl acetate	***2500***									x
Propylene glycol	***2520***									x

Table 7.5. Continued.

Solvent	Ref #	I	II	III	IV	VI	VII	VIII	IX	X
Propylene glycol monophenyl ether	***2530***						x			x
Stoddard Solvent	***2590***									x
Sulfolane	***2600***									x
t-Butanol	***3150***		x							
Tetrahydrofuran	***2650***	x			x					
Tetrahydrofurfuryl alcohol	***2660***									x
Toluene	***2680***	x								x
Turpentine (Steam Distilled)	***2770***						x			x
Xylene (mixed)	***2800***	x					x			x

I. Adhesives
II. Agriculture
III. Fuel Additives
IV. Chemical Processing
VI. Cosmetic and Personal Care Products
VII. Industrial, Institutional, and Household Cleaning
VIII. Metal Treating and Processing
IX. Food Processing
X. Paints and Coatings

advances in the area of repulpable/recyclable pressure sensitive adhesives and silicone release coatings used in a variety of commercial applications (McGinniss, 1996).

Market research firm Frost & Sullivan predicts that the solvent market will move toward increased use of reduced-impact solvents such as esters, alcohols, and specialty solvents such as glycol ethers. These solvents will replace the chlorinated and cyclic hydrocarbons and the other volatile organic compounds that are currently contributing to smog problems. Frost & Sullivan also expects continued efforts to reformulate products to contain higher solids and less solvents, with water-based paints, inks, and adhesives leading the way. Various process aids and additives designed to replace environmentally regulated or hazardous compounds are briefly described, along with other products such as surfactants, defoamers, solvents, cleaners, paper production chemicals, and safe reagents for oxidation and pH adjustment (Chemical Week Assoc., 1995).

Methods in common use for the determination of PCBs in fish are time consuming, expose workers to toxic solvents, and generate significant volumes of hazardous wastes. Supercritical fluid extraction (SFE), with CO_2 and solid-phase cryogenic trapping, was applied to the analysis of PCBs in lyophilized fish tissues. Method evaluations were conducted using standard amended tissues and by comparison of SFE results to those obtained from conventional extraction procedures performed intra- and extramurally on fish with field-incurred PCBs. Good results for a range of PCBs were obtained after optimization of SFE conditions. Addition of alumina to the extraction vessel eliminated the need for off-line extract purification, despite the high lipid content of the tissues. Organic solvent usage was limited to 2 mL, in contrast to conventional procedures which require several orders of magnitude more solvent (Hale and Gaylor, 1995).

Plasma spray coatings have been evaluated as surface treatments for aluminum, titanium and steel substrates prior to adhesive bonding. These treatments are environ-

mentally benign in that they involve no chromates and emit no liquid or gaseous wastes. The coatings can be engineered for specific applications and are better suited for localized repair than chemical processes. For aluminum adherends, a 60Al-Si/40 polyester coating gives a performance equivalent to that of the best chemical treatment (phosphoric acid anodization) for some epoxy adhesives. With stronger, tougher adhesives, a Ti_6Al_4V coating provides improved performance to match that of phosphoric acid anodization. A Ti_6Al_4V coating on titanium substrates exhibits identical initial strength and durability to the best chemical controls under moderate temperature conditions. At high temperatures, the plasma spray coating continues to exhibit excellent durability while oxide-based treatments readily fail due to oxygen dissolution into the metal. For steel adherends, an Ni-Cr-Zn coating provides enhanced corrosion resistance and bendability even after exposure to aggressive environments or ambient conditions over long periods of time. Additionally, rubber bonds with the plasma spray coating are more tolerant to surface contamination than those with grit-blasted surfaces. These investigations indicate that the plasma spray process is more robust than conventional processes and can give equivalent or (in some cases) superior performance (Davis et al., 1997; Mollah et al., 2000).

Government regulations restricting VOC emissions have prompted the development of alternate compliant heat-activated adhesives with performance equivalent to solvent systems. Although varying degrees of success have met the many approaches taken, a hot-melt adhesive designed for lidding application with extrusion coating equipment shows improvement. In other applications, the improved technology of this system could provide VOC-free adhesive systems matching the performance of materials previously available only as high VOC-containing solvent systems (Wigdorski and Batorski, 1997).

7.5.2.2 Agriculture

Most innovations are based on a concept called cascade chemistry, in which all ingredients are combined at the outset and each reaction triggers the next. Environmentally safe solvents and catalysts are used wherever possible, and others, such as heavy metals, are recovered and used again. In addition to being clean and efficient, cascade chemistry is well suited to the synthesis of ring molecules and other precisely shaped compounds that are valuable in medicine, industry, and agriculture (Byrnes, 1995).

Managing land to produce food, fiber, or timber must have some environmental impact, the magnitude of which will depend on the cropping system and the intensity of management. Nitrogen is an indispensable input for modern agricultural systems, which not only aim to feed people but seek to sustain rural communities dependent on agriculture. Nitrate invariably appears in drainage from agricultural land in the absence of any significant input of nitrogen as a result of the breakdown of soil humus or from aerial deposition of combined nitrogen in various forms. Where only inorganic nitrogen fertilizers are applied in amounts and at times to satisfy crop demand, they are apparently used efficiently. Most of the nitrate which appears in soil in autumn comes from the microbial mineralization of soil organic matter. The soil microbial population breaking down organic matter does not differentiate between soil humus or organic matter added to soil by plowing in grass leys, forage legumes, or large quantities of organic manures. Adding such organic materials to soil can lead to the

release of much nitrate. Such microbial processes would be impossible to control in environmentally benign ways (Johnston, 1994).

The Less-Intensive Farming and Environment (LIFE) project is an interdisciplinary research study at IACR-Long Ashton designed to address, exploit, and integrate interactions of farming system components, holistically, and to provide the technology for economically viable, ecologically acceptable and environmentally benign production systems. Over a five-year period, adoption of less-intensive strategies based on integrated technology, reduced overall yields of wheat and oilseed grape by up to 18%, and yields of barley and oats by 11%. Nevertheless, production costs were also reduced by 32% and overall profitability was maintained. Within this period, substantial reductions in applied nitrogen (36%), herbicides (26%), fungicides (79%), and pesticides (78%) have been obtained over standard farm practices designed to reflect current arable crop production strategies (Jordan et al., 1997).

The set of partial differential equations developed for the simultaneous transfer of moisture, hear, and reactive chemicals under saturated/unsaturated soil conditions has been solved by the Galerkin finite element method. The chemical transport equations are formulated in terms of the total analytical concentration of each component species, and can be solved sequentially (Wu and Chieng, 1995).

Agricultural processing will still incorporate solvents. As an example, soybean flakes were extracted with supercritical carbon dioxide to produce a solvent-free, good-quality soybean oil. During the SFE process, volatile compounds were trapped on a porous polymer trap attached at the exhaust port of the SFE apparatus. The volatile profile obtained from the sorbent trap was found to be similar to the headspace profile from the SFE/soybean oil removed during the same extraction. In addition, crude soybean oil was heated in a stirred reactor and the volatiles, which were stripped by supercritical carbon dioxide in an attempt to improve oil properties, were collected on sorbent traps and analyzed by the above method for comparison. The described methodology permits the characterization of volatiles and semivolatiles in SFE soybean oil and can be used to monitor the extraction and quality of the resultant oil (Snyder and King, 1994).

7.5.2.3 Antifreeze, Brake Fluids, Petroleum and Oil Processing, Fuel Additives

An antidote has been found for ethylene glycol poisonings, but it is too costly for most hospitals. Ethylene glycol is a main ingredient in automotive antifreeze and other products. Every year, at least 6,000 people fall victim to ethylene glycol poisoning, which can lead to permanent disability or death unless it is treated immediately. Traditional treatment is complicated and tricky, but the new drug fomepizole (Antizol; Orphan Medical, Inc.) has been found to be a proven antidote (Leary, 1999).

Three engineers at NASA's Ames Research Center have developed a new nontoxic, biodegradable deicing fluid. The Ames Environmentally Friendly Anti-Icing Fluid, which works by clinging to surfaces to form a barrier against ice, contains no ethylene glycol—a poison found in other deicing agents—and no caustic ingredients, such as salt, which can corrode metal over time (Parmet, 1998).

"End-of-pipe" approach to the problems of solvents with respect to hydrocarbons present's a problem. A field study on the treatment of volatile petroleum hydrocarbons

(PHC) by biofiltration was conducted by the Petroleum Environmental Research Forum (PERF). Its objective was to assess the technical, regulatory, and economic feasibility of biofiltration for off-gases from petroleum processing and soil remediation equipment. It involved three small-scale biofilters provided by U.S. vendors, treating off-gas from two soil vapor extraction sites and a source of refinery wastewater. Comprehensive monitoring of biofilter operating parameters and performance was conducted. The results suggest that biofilters remove major petroleum hydrocarbon classes to strongly varying degrees. Typically more than 95% of aromatic compounds such as benzene, and odorous reduced sulfur compounds can be removed at residence times of one minute or less, while removal of more than 70% of light aliphatics will require residence times of several minutes, and will thus require correspondingly large filter volumes and higher capital expenditure. The high percentage removal of aromatic hazardous air pollutants (HAP) and odors can generally be accomplished at comparatively short residence times (one minute or less) while the need for high-percentage removal, particularly of light aliphatics (< C-5) will generally render biofiltration noncompetitive. A preliminary economic comparison of biofilters and established control technologies suggested that biofiltration may, for a representative design case involving off-gas from a refinery wastewater treatment operation, offer considerable savings in total cost of air pollution control for petroleum hydrocarbon streams if regulations require the control of aromatic HAP or odors (Leson and Smith, 1997).

7.5.2.4 Chemical Processing, Paper and Pulp Processing, Plastics and Resins, Rubber Compounding and Processing, Textiles and Fibers

Establishing the safety of the final end use compounds has become an integral part of the process of developing new products for quite some time. On the other hand, developing the chemical processes by which the end-use products are made has not been a generally recognized part. Making chemical manufacturing more environmentally benign by design must now become an integral part of the product development process. There are many dimensions to this issue. The use of building blocks, reagents, and solvents that pose less hazard to mankind and his environment is one aspect. The use of building blocks, reagents, and solvents that pose less hazard to mankind and his environment is one aspect. Using raw materials more efficiently and generating less waste is another. In this regard, the utilization of reactions that are simple additions wherein the product is the simple sum of the reactants with anything else needed only catalytically becomes a goal. To realize such a goal, the repertoire of synthetically useful reactions that are additions must be greatly increased.

The recognition of the environmental impact of much of the current chemical processing has spawned initiatives to address these issues. Drawing broader attention to the issues is a requirement if the goals of less hazardous and environmentally benign synthesis are to be achieved. The issues cannot simply be addressed by minor tinkering with current processes to improve their performance, although that is one of many of the strategies that creates new paradigms for synthesis is also required as well as everything in between (Trost, 1998).

Chemical engineers (and, increasingly, chemists) have been examining the use of carbon dioxide (both liquid and supercritical) in environmentally friendly chemical

processing. Carbon dioxide can perhaps be considered the organic solvent analog to water, because there is no penalty if it is removed from the environment, used in a chemical process, and returned to the environment in a clean state (Lipkin, 1996).

The aim of some work was to synthesize transparent and superinsulating monolithic carbogels in order to use them as transparent double-window insulation spacers at the laboratory scale. The monolithic silica carbogels were made by sol-gel technique using mixtures of a new family of precursors noted PEDS-Px (or polyethoxydisiloxanes) which are prepolymers of silica differing by their substoichiometric hydrolysis degrees with organic solvents in the presence of hydrofluoric acid with no excess of water added, and subsequent drying in the supercritical conditions with respect to CO_2. The research was focused at finding the best conditions of preparation of the monolithic silica carbogels in terms of optical and thermal insulation properties. A new solvent ethylacetoacetate (etac) was found to be much more soluble in liquid CO_2 than common alcohols and acetone, and the so obtained carbogels, with etac, present very interesting optical visible transmission and thermal properties, respectively. The best samples presented very good transparency close to the one shown by a flat glass pane together with a very small thermal conductivity (Begag et al., 1999).

The use of computational chemistry to address issues relative to process design was discussed in an article. The need for efficient software for massively parallel architectures was described. Methods to predict the electronic structure of molecules are described for the molecular orbital and density functional theory approaches. Two examples of electronic structure calculations are given. The first shows that one can now make extremely accurate predictions of the thermochemistry of small molecules if one carefully considers all of the details such as zero-point energies, core-valence corrections, and relativistic corrections. The second example shows how more approximate computational methods, still based on high level electronic structure calculations, can be used to address a complex waste processing problem at a nuclear production facility (Dixon and Feller, 1999).

A combination of fundamental and applied process research at Pacific Northwest National Laboratory resulted in the development of several new processing concepts. These concepts have in common the use of high-temperature pressurized water as a unique reaction medium for carrying out chemical reactions. Typical operating conditions of these processes range from 300 to 360°C and have pressures to above 200 bar. Investigation of the process chemistry and engineering for these new processing concepts required the development and scale-up of several high-pressure reactor systems. These processes, which are at various stages of development, address a broad mix of energy and environmentally related problems. Chemical processing in a high-temperature liquid water environment remains a relatively untapped area for commercial application (Sealock et al., 1996).

7.5.2.5 Construction and Building Materials

The construction industry and the industries which supply it have a vital role to play in the evolution of a culture of clean technology. Buildings have a crucial impact on the physical and economic health and well-being of the individuals, communities, and organizations which they are intended to support. The global impact of the architectural environment is increasingly evident. It is necessary for everyone involved to

recognize the role of buildings in the quality of our lives and the extent of our responsibilities in creating a sustainable habitat. Buildings and their components are basic needs that should be socially responsible products able to contribute to our physical, psychological, cultural and economic well-being; yet they frequently contribute to ill health and create significant financial liability. Modern planning, construction activity, building management, and demolition processes are innately unclean and environmentally exploitative. We need to identify the consequences of our actions and to process these to show how we might create a healthy built environment within the ecological limits. The existing culture of control of the environment must give way to a culture of appreciation and participation. A critical appraisal of the new generation of self-declared, environmentally benign buildings could assist in determining appropriate directions for evolution of the built environment (Halliday, 1997).

Electricity is a fundamental requirement for economic growth, and hydro-electric power is often thought to be environmentally benign. However, the construction and operation of many hydro-power dams have had significant negative impacts on the environment and rural economies. Reduced downstream flooding has destroyed fisheries and starved the floodplain soils of moisture and nutrients (Acreman, 1996).

While not chemistry per se, the "greening" of buildings will have an effect on solvent/chemical use. Evaporative cooling is used extensively for cooling in climates with medium-to-low humidity. In residential buildings the conventional mechanical systems tend to be both noisy and unsightly protuberances on buildings, whilst traditional cooling systems incorporated into the building structure which employ chimneys and the like tend to be designed for the specific building and so may not have wide application. A passive evaporative cooling system that can make use of natural ventilation at the building facade. The system makes use of the evaporative effect from water falling vertically along guides to produce a reduction in the temperature of the air entering the building. It can also be used as a design element in the building facade. Such a system provides an inexpensive, energy efficient, environmentally benign (not requiring ozone-damaging gas as in active systems) and potentially attractive cooling system. Further work is being undertaken to explore the integration of such a system into the building fabric (Giabaklou and Ballinger, 1996).

Plastic media blasting (PMB) as an alternative means of stripping has been described. PMB is a process for the fast, economic, and safe removal of coatings from practically any product. The process uses plastic particles that are pneumatically applied at low pressures of 20–40 psi. PMB can efficiently remove primers and top coats without damaging sensitive substrates, such as aluminum, brass, copper, magnesium, thin steel, and titanium, because the plastic granules are harder than coatings, but softer than underlying substrates. The process can be used on surfaces where chemical strippers cannot be used or must be applied with caution, such as panels of honeycomb construction, engineered plastic, fiberglass, and advanced composites. The process has developed into a distinct technology with the increase in environmental awareness and stricter environmental regulations (Mahoney, 1998; Mollah et al., 2000).

The state of refrigeration science and technology is changing rapidly due to the internationally coordinated program to phase out ozone depleting substances and greenhouse gases. The competitive position among the new systems is extremely complex, partly due to the willingness of some governments to legislate. Recent work

reports an investigation into the competitive position of systems for heating and cooling which make use of ambient air as the working fluid (Fleming et al., 1998).

The paradigm of sustainable construction has substituted in recent years the paradigm of industrialized housing construction that was basically based on prefabrication techniques. But, parallel to the generalized (globalize) objective of sustainable construction, the materials and building technical processes are modified through the innovations from other branches of the scientific-technologic knowledge like materials science, biotechnology, solid states physics, organic and inorganic chemistry, process engineering, production engineering and management, and other interdisciplinary areas. The tendency is toward an approach they call technological syncretism in housing production (Cilento, 1996a). The importance of building products life-cycle analysis, the idea of technological, economical, social, and ecological sustainability of construction, and the tendencies in new materials and processes that affects the professionals, promoters, contractors, and users (Cilentosarli, 1998).

The field measurement of dry deposition still represents a difficult task. In a new approach, a 1- to 2-cm thick layer of water in a petri dish with a diameter of 22 cm, serves as a surrogate surface. The atmospheric constituents taken up by the water can be analyzed chemically by the same procedure as for the wet deposition samples. In contrast to solid surrogate surfaces, water exhibits the following advantageous properties: low and constant surface resistance, high sticking coefficient for aerosols, and predictable sorption behavior for gases. The soluble fraction of Zn, Cd, Cu, Pb, and Fe in the dry deposition varied with the pH of the water phase corresponding to the adsorption tendency of these metals to oxide surfaces. The sampling method also allows tracing of regionally and locally emitted atmospheric pollutants. A study of the local pollution sources included road salting, construction work, and a refuse incinerator. Finally, evaluating the data can identify chemical reactions occurring in the atmosphere, such as the conversion of Cl- to HCl by HNO_3 or the oxidation of SO_2. The method proposed is relevant to measure reproducibly the dry deposition of a variety of compounds to water bodies and moist vegetation (Zobrist et al., 1993).

Liquid hydrocarbons and hydrofluorocarbons (HFCs) are the leading zero ozone depletion potential (ODP) blowing agents being considered for rigid polyurethane foam insulation used in the construction industry. Different isomers of pentane, namely normal-, iso- and cyclopentane, are the major hydrocarbons under consideration. The leading HFCs being evaluated are HFC-245fa (CF_3-CH_2-CF_2H) and HFC-365mfc (CF_3-CH_2-CF_2-CH_3). The solubility of such blowing agents in many of the typical polyols and isocyanates used by the construction industry is limited. Additives have been used to improve the solubility of blowing agents in the past. For example, ethoxylated nonylphenol was added to many polyols in order to enhance CFC-11 (CCl_3F) compatibility. A great many additives are being proposed today for use with hydrocarbons and HFCs. The solubility of the various pentane isomers in many polyols and isocyanates used to produce insulation boardstock in a continuous lamination process. The effects of blowing agent solubility on the processing characteristics of foam properties are also examined. Many nonreactive or monofunctional additives that improve solubility are found to affect the structural, thermal, or flammability performance of resulting foams (Singh et al., 1997).

The study of several hydrofluorocarbons (HFC) and fluorocarbons (FC) and their binary mixtures that have no ozone-depleting ability is being carried out in the frame-

work of Belarus National Program. The fluids include HFCs R134a, R152a, R125, and R32, and FC R218 (Grebenkov et al., 1996).

7.5.2.6 Cleaning Chemicals

Cleaning is a common practice in many diverse sectors of industry. Cleaning may range from simple maintenance activities such as wiping grease off a part with a solvent soaked rag to critical cleaning requiring the removal of microscopic particulates and oxides. Commonly used halogenated solvents include perchloroethylene (PERC), trichloroethylene (TCE), methylene chloride (METH), 1,1,1-trichloroethane (TCA), and trichlorotrifluoroethane (CFC-113). Many nonhalogenated solvents are in use. Table 7.6 provides a listing of commonly used solvents. Many commercial cleaners are

Table 7.6. Organic solvents commonly used in cleaning (Callahan and Green, 1995).

Solvent Type	Flashpoint °F TCC[+]	Boiling Point, °F	K_b Value	Evaporation Rate
Aliphatics				
Kerosene	141	356	32	N/A
Mineral spirits	105	315	31	N/A
Naphtha	30	206	39	14
Refined distillate	125	174	28	N/A
Stoddard solvent	100	310	32	23
Alcohols				
Butanol	47	241	N/A	5
Ethanol	40	167	N/A	14
Isopropanol (IPA)	56	177	N/A	13
Methanol	52	147	N/A	19
Aromatics				
Benzene	2	174	112	36
Toluene	45	230	105	22
Xylene	82	278	98	17
Chlorinated hydrocarbons				
Carbon tetrachloride	None	167	104	38
Chlorobenzene	85	266	N/A	12
1,1,1-Trichloromethane	None	162	124	53
Methyylene chloride	None	102	125	56
Perchloroethylene	None	249	90	15
Trichloroethylene	None	184	130	32
Esters and ethers				
Ethyl acetate	29	167	N/A	20
Diethylene glycol ethers (carbitols)	205	365	N/A	<1
Ethylene glycol ethers (cellosolves)	145	331	N/A	<5
Fluorinated hydrocarbons				
Trichloromonofluoromethane (CFC-11)	None	75	60	86
Trichlorotrifluoroethane (CFC-113)	None	118	31	65
Ketones				
Acetone	2	133	N/A	53
Methyl ethyl ketone (MEK)	28	172	N/A	37
Methyl isobutyl ketone (MIBK)	64	237	N/A	18

blends of one or more solvents. Additives to the formulation may include alkaline cleaners, detergents, surfactants, diluents, or stabilizers. The specific formulation is heavily dependent on the cleaning application and target effectiveness of the cleaner.

Given the large volume of solvents currently in use, and the regulatory pressures forcing some solvents out of the marketplace, industry is faced with a difficult task. Industrial sectors dependent on these materials must seek out replacements while maintaining productivity. Many companies presently using hazardous solvents are quickly moving to find viable alternatives. Most of the are companies making these moves have the capital and resources to assess and evaluate their ongoing needs. For larger solvent consumers, the stakes in finding and implementing viable substitutes are high.

For many small and medium-sized companies, the stakes are even higher. This is especially true for those unaware of current regulatory events and/or those who believe that they will be exempted. The availability of CFC-113 and TCA is actively declining and purchase costs are skyrocketing. Lead times to procure replacement equipment are increasing. At the same time, more and more manufacturing business will be given to competitors able to promote their changeover to "clean" process technology (see table 7.7).

7.5.2.6.1 Solvent Usage Solvents are widely used to remove contaminants from a variety of substrate materials. Common contaminants include solid particulates, waxes, greases, cutting and lubrication fluids, buffing compounds, slushing oils, quenching oils, heat-treating salts, rosin fluxes, protective coatings, and finishes. Selection of a particular solvent and cleaning process is based on the type of substrate(s) to be cleaned, the type of soils(s) to be removed, the degree of cleanliness required, the desired method of application, and many other operating conditions and constraints.

7.5.2.6.2 Maintenance and Production Activities Parts cleaning is a common component of maintenance and production activities. These activities often involve the removal of bulk or gross contamination. In the past, maintenance activities were conducted mainly with petroleum solvents such as mineral spirits while production activities employed the use of alkaline cleaners. The use of halogenated solvents became popular because they exhibited good solvency for organic contaminants; evaporated

Table 7.7. Main industrial sectors that use solvent cleaning (Sherman et al., 1998).

Industrial Sector	Type of Cleaning	Type of Soil Cleaned
Electronic cleaning	Defluxing of printed circuit boards	Soldering rosin
Precision cleaning	Cleaning of sensitive parts such as optical devices and gyroscopes that have ultra-high cleanliness standards	Organic residues, particulates
Metal cleaning	Surface preparation for machining or coatings	Oil, grease, particulates, inorganic salts
Dry cleaning	Cleaning of textiles that are not stable in aqueous solutions	Oil, organic residues.

readily, leaving the cleaned part dry; were less toxic than the solvents commonly in use; were nonflammable; and were less costly to operate and maintain than alkaline cleaners.

The most common method of using a solvent for cleaning is referred to as *cold-cleaning*. Cold-cleaning techniques include wiping or swabbing surfaces with a solvent soaked rag or shop towel, dipping and immersing the part into a small tank or container of solvent, or spraying with an aerosol solvent product. Most methods involve relatively simple and inexpensive equipment. The small amount of emissions per source and the diverse nature of these operations make emission control hard to apply.

With aerosol cleaning products, a quick spray and a blow-dry with compressed air, or a wipe with a dry rag or towel is all that is required to remove the unwanted soil. Another benefit of spraying is the motive force of the spray, which assists in soil removal. Because of the tendency for aerosol products to finely atomize the cleaning solvent and increase air emissions, some air-quality agencies are mandating the use of low-vapor-pressure solvents in hand-pump dispensers. This action reduces solvent loss to the atmosphere and increases the amount of waste solvent, which must be collected and stored for subsequent recycling or disposal.

While aerosol products provide a high degree of mobility as to where the cleaning will take place, they offer little in the way of control or cost-effectiveness. Aerosol products are very expensive in terms of unit cost per item cleaned. Unless workloads are very small or highly specialized, most maintenance facilities will operate one or more cold-cleaning tanks. Compared to aerosol products or vapor degreasing, cold-cleaners emit the least amount of solvent to atmosphere on a per unit basis. The large number of cold-cleaners in use, however, makes cold-cleaning a major source of emissions.

Spray cleaning of parts with solvent, using an airless gun similar to a paint sprayer, is also practiced. Spray cleaning is typically performed in a ventilated fume hood so as to protect the worker from solvent fumes. In addition to the fume hood, an emissions control system is often required. Many local air quality agencies prohibit the spray cleaning of parts with solvent or require an appropriate emission control system to be in place.

Vapor degreasing differs from cold-cleaning in that cleaning is performed by condensation of hot-solvent vapor onto the part as opposed to immersion of the part into cold solvent. Vapor degreasing offers a faster rate of cleaning because dissolution of dirt takes place at elevated temperatures and because the wetted part surface is always in contact with clean solvent. In addition to metals, vapor degreasing has been used for cleaning materials such as glass, ceramics, plastics, elastomers, coated items, or combinations thereof.

A *vapor degreaser* is a steel tank with a steam or electric heating coil below the liquid level to effect vapor generation. A water-jacketed vapor cooling and condensing zone above the vapor level is used to recondense solvent and control vapor loss. An additional level of emissions control may be achieved through the use of refrigerated freeboard condensers and/or carbon units. Compared to cold-cleaning, vapor degreasing equipment requires more energy and is more expensive to purchase and operate, but provides a greater degree of cleanliness.

Unlike cold-cleaners, vapor degreasers lose relatively small amounts of solvent as solid waste or liquid drag-out. Most emissions are due to vapor loss and the loss level is highly dependent on operator and operating conditions. Solvent losses for a poorly operated open-top vapor degreaser may be eight or more times greater than for a well-operated unit (Branson Ultrasonics Corporation, 1988).

7.5.2.6.3 Precision Cleaning Precision cleaning involves both cold-cleaning and vapor degreasing processes. The halogenated solvent CFC-113 has traditionally been the cleaning solvent of choice because of its chemical inertness and ability to penetrate extremely small gaps and spaces. Major applications include gyroscope and hydraulic system flushing, medical component cleaning, nuclear equipment decontamination, and liquid oxygen system flushing.

Medical and surgical equipment, orthopedic prostheses such as hip and knee joints, as well as many other biomedical products recleaned with CFC-113. In the production of plastic moldings such as syringes, spoons, bottles, and sample phials, CFC-113 may be used as a release agent. CFC-113 is also used as a carrier for ethylene oxide (ETO) in the sterilization of biologically contaminated equipment and supplies.

7.5.2.6.4 Semiconductor Production Integrated circuits (ICs) are the major product of the semiconductor industry, and their production involves the use of hundreds of materials, products, and processes. Many different machines are used in the wafer fabrication step and these machines need to be cleaned periodically. Most machine cleaning is performed with CFC-113.

During the component fabrication process, CFC-113 and TCA are widely used for cleaning surfaces and for stripping negative photoresist. Nonhalogenated solvents are often used for stripping positive resist. Following fabrication, the chips are tested for defects and the wafers cut into individual chips.

7.5.2.6.5 Solvents Except for the direct use of CH_2Cl_2 in equipment cleanup, most paint strippers sold are formulated products. Solvent-based strippers commonly employ a number of components that each accomplish a given task or function. The first component is a primary solvent that serves to penetrate the paint film and promote swelling. Cosolvents may also be used to increase the rate of penetration and to keep the various components from separating.

Other paint stripper ingredients include surface-active agents (surfactants), emulsifiers, thickeners, sealants, and corrosion inhibitors. Thickeners such as methyl cellulose derivatives are used to thicken the stripper so that it can be brushed onto vertical surfaces. Sealants such as crude or refined paraffin act to retard evaporation of the CH_2Cl_2 so that the stripper remains effective over a long period of time.

Home consumers generate a significant portion of paint stripping waste. Stripped items include doors, door frames, porches, and decks, as well as pieces of furniture. Most of the paint stripper employed by home consumers is for the refinishing of furniture. Stripper is generally applied with a brush and removed with a scraper. The furniture may then be rinsed off with water or cleaned with a solvent-soaked rag. Use of water on wood would be followed by drying and sanding, since the use of water

on wood often results in the raising of the grain. Most consumers dispose of the stripped paint in the trash.

7.5.2.7 Green Cleaning

The Green Clean Project is a voluntary pollution prevention initiative to explore water-based cleaning as an alternative to nonaqueous solvents, particularly perchloroethylene (PERC), used in the dry-cleaning industry (Green Clean Partnership, 1995). The water-based alternative being explored is Green Cleaning (a trade mark of Environment Canada), which uses water and detergent in technologically advanced washers and dryers to clean clothes normally dry-cleaned.

In order to replace the solvent used in dry-cleaning, the Green Cleaning Project used a combination of different technologies (e.g., new front-loading gentle wet clean machines) and different chemical products. The new chemicals are detergents which are fabric-friendly and pH neutral, and require no hot water usage.

The choice of solvent and cleaning method depends heavily on the material of which the part to be cleaned is composed, chemical nature of the contaminant (often a grease or oil), geometry constraints of the item (i.e., small holes or bends and twists), and cleanliness criteria (Million et al., 1993). Because there are so many considerations in choosing a cleaning solution, a universal "drop-in" replacement usually does not exist (D'Amico, 1995; Hairston, 1995). As a result, a vast number of specialized alternatives are available in the form of hydrochlorofluorocarbons (HCFCs), hydrofluorocarbons (HFCs), hydrocarbon solvents, oxygenated solvents, aqueous solvents, and supercritical fluid solvents. Stone and Springer (1995) have reviewed these alternatives for cleaning applications in the aerospace industry. Many of these alternatives are available in industrial quantities from well-known manufacturers. Although there are computational methods available that can be used in the selection of the most effective and economical cleaning solvent for a given application, much of the work reported to date in the solvent-cleaning literature involves solvent screening and not rational solvent selection.

7.5.2.8 Fluorocarbons

HFCs and HCFCs are alternative solvents that have been implemented in all industrial sectors except dry cleaning (Basu and Zyhowski, 1991). These solvents exhibit many of the desirable solvent properties of chlorofluorocarbon (CFC) compounds such as high density, high dielectric strength, thermal stability, chemical stability, and nonflammability. Thus, they are as close as possible to a drop-in replacement for CFCs because their use requires minimal retrofitting. Because these compounds are not fully halogenated, they have lower ozone depletion potentials than CFCs (Koelsch, 1993). They have been shown to be as effective as CFC-113 in removing solder flux from electronic assemblies when used in an azeotropic mixture with methanol (Bonner, 1989). These compounds have also been investigated in their "neat" form for the same purpose (Hey, 1990). Although they are effective cleaning solvents, HCFC and HFC compounds are considerably more expensive than CFC compounds, ranging from 2 to 5 times the cost because they require up to five synthetic steps to make versus one for many CFC compounds (Manzer, 1996). Furthermore, HCFCs

will be phased out by 2030, requiring those who use them to turn to other alternatives (Anderson, 1995).

Perfluorocarbons are non–ozone-depleting but have long atmospheric lifetimes. They are suitable for some precision cleaning processes, as they effectively remove particles and aid in drying (Kanegsberg, 1996). Newly introduced fluoroiodocarbons, which are nonflammable, noncorrosive, and appear to be nonozone depleting, are also emerging as possible replacements for CFCs (Higgin and Thorn, 1994). Some advocate using methylene chloride, PERC, and trichloroethylene as replacements for TCA and CFC compounds (Rupp and Hickman, 1995). Although methylene chloride and PERC are nonozone-depleting substances, they are on the U.S. EPA 33/50 list and are suspected carcinogens.

7.5.2.9 Hydrocarbon and Oxygenated Solvents

Volatile organic compounds (VOCs) such as xylene and methyl ethyl ketone have also been used as cleaning solvents, but now their use is being discouraged by inclusion in the U.S. EPA 33/50 list. Some users have returned to using aliphatic hydrocarbons (petroleum distillates) as alternative solvents (a common cleaning solvent before implementation of chlorinated compounds) because they are now available in high purity. They work best for solvating heavy grease and oil because of their chemical similarity but are not applicable to vapor degreasing because of their flammability. In addition, although they are not ozone-depleting substances, many hydrocarbons are regulated as VOCs (Koelsch, 1993). Reynolds (1991) recommends the Exxon line of high-purity hydrocarbon solvent as a replacement in chlorinated solvents for cleaning plastic substrates. In this case, the alternative solvent is able to solvate contaminants and the low surface tension results in desirable wettability.

For applications that require an oxygenated organic solvent to solvate contaminants such as grease, oil, wax, resins, and polymers, there are many available alternatives. A range of fluorinated organics is becoming available and these present attractive solvent substitutes. For example, pentafluoropropanol is a nonflammable, nonozone-depleting alcohol that can be used in situations in which alcohol is necessary for removing the contaminants (Lea, 1991). Similarly, hydrofluorethers provide a safe alternative for processes in which ethers are needed (Hairston, 1996a). Dow Corning's line of volatile methyl siloxane (VMS) compounds may be used to remove simple oils, grease, and silicone elastomers in the same way as hydrocarbon solvents (Williams, 2000). VMS compounds have the advantage that they are neither hazardous air pollutants nor ozone depleters (Hairston, 1996a). N-methyl pyrolidone is a high-boiling solvent suggested for use in degreasing operations (McGill, 1994). It has an advantage over other solvents in that it is biodegradable, but because it is nonvolatile, a rinsing cycle is required to eliminate residues. VOC-exempt *p*-chlorobenzotrifluoride (PCBTF) is another attractive solvent replacement option. PCBTF is being marketed for cleaning metal, plastics, electronic components, and glass while reducing volatile emissions (Oxychem, 1992).

Sometimes a two-step process is necessary to match the performance of chlorinated solvents. Marino suggests that using an ester-based propriety solvent in combination with a perfluorohexane rinse in a retrofitted vapor degreaser to replace TCA is a cost-competitive option (Marino, 1993).

7.5.2.10 Aqueous Blends

Another approach to solvent replacement is to switch from neat solvent to aqueous blends. These semiaqueous solutions contain organic additives such as terpenes, alcohols, and aliphatic hydrocarbons. Terpenes are very effective in dilute aqueous solutions for removing grease, resin, and adhesives. They are naturally derived from plants and can be disposed of fairly easily (Hairston, 1996a). Although these compounds are not ozone depleters, caution must be used, as the toxicity of terpene compounds has not been well characterized (Wolf, 1994). Brown et al. (1992) demonstrated that dilute aqueous terpene solutions could effectively replace TCA and methanol in cleaning metal parts for hip and knee replacements. Through a series of tensile tests, they demonstrated that the alternative cleaner worked up to 10% more effectively than the original solvents. In addition, they found that it was more economical to implement semiaqueous cleaning than to use the conventional methods. Others have reported similar results but often note that use of semiaqueous solutions requires some initial process modifications such as agitation and extra wash cycles (Wolf, 1994; Kennedy, 1994; Goeders et al., 1994; Copeland, 1990; Snyder, 1990; Thompson et al., 1990; Karrs S and M., 1993; Hayes, 1990). Another alternative solvent formulation uses aliphatic hydrocarbons diluted by water in the form of highly dispersed droplets stabilized by surfactants. These microemulsions, such as INVERT (supplied by the Dow Chemical Company, Midland, Mich.) have been found to be effective solvents for cold cleaning (Hairston, 1995).

Aqueous solvents have also found a niche in replacing chlorinated cleaning solvents in applications such as printed circuit boards, turbine blades, advanced composites, and automotive motor housings (Quintmeyer, 1991). Table 7.8 compares the physical properties of assorted aqueous cleaning formulation with those of common chlorinated solvents. These solvents contain additives such as rust inhibitors, surfactants, or chelating agents and work best if they are slightly alkaline (Quintmeyer, 1995). They clean with similar effectiveness and have the advantage of being easier to recycle and reuse than conventional solvents. In an aqueous environment the "soil" will float to the top and may be skimmed off, as opposed to conventional solvents where the soil and solvent remain homogeneous and require energy for separation (Nicholls, 1990). Augias, Inc. has gone a step further by adding special nutrients to their aqueous replacement solvent (Hairston, 1996a). As with the semiaqueous solution mentioned above, aqueous replacement solvents often require process adjustments

Table 7.8. Physical properties of assorted aqueous cleaners.

Physical Property	CH_2Cl_2	TCA	Aqueous A	Aqueous C
Boiling point, °C	39.8	74.1	100	100
Specific gravity	1.316	1.322	1.02	1.07
Flash point, °C	None	None	None	23.8
Vapor pressure, mmHg	340	90	—	—
VOC, lb/gal	10.98	10.32	<0.35	0.92
Surface tension, dynes	28	28	29	33

Note: Data from Quitmeyer (1995).

such as addition of agitation or ultrasonic (Lowell and Sterritt, 1990). Further, the high latent heat of evaporation for water makes drying more difficult, and often extra equipment for proper and efficient drying is required (Koelsch, 1993).

7.5.2.11 Supercritical Carbon Dioxide

Carbon dioxide (CO_2) is the most commonly used compound at supercritical conditions due to its accessible critical point ($T_c = 304.2K$, $P_c = 78$ atm). Supercritical CO_2 ($SCCO_2$) is a nonpolar solvent and thus is capable of effectively solvating nonpolar oils. Supercritical cleaning requires the parts to be placed in a high-pressure chamber that is heated until the CO_2 is beyond its critical point. The supercritical solvent is swept over the parts to be cleaned and sent to a recovery unit. When the chamber is decompressed, any residual solvent evaporates because CO_2 is a gas at atmospheric pressure. This method has been shown to work more efficiently for contaminated plastic than cleaning with CFC-113 (Salerno, 1990). The primary application of $SCCO_2$ cleaning is in the cleaning of precision instruments where the highest cleanliness standards are required (Weber, 1995; McGovern et al., 1994; 1995c; Hjeresen et al., 1994; Michardy et al., 1993; Gallagher and Krukonis, 1990; Purtrell et al., 1993). $SCCO_2$ is also being investigated as a dry-cleaning solvent to replace PERC (1995b), (Iliff et al., 1995).

7.5.2.12 Solvent-Free Cleaning

Clearly, the most effective way to avoid problems with solvent contamination of the environment is to eliminate the use of the solvent entirely. Even though this clearly is not possible for most applications, there are some innovative solvent-free cleaning processes that deserve mention.

- A pulsed KrF laser used to clean metal, magnetic material, plastic, and glass surfaces works very efficiently. It is a high-speed, area selective, low-noise process. However, because of its area selectivity, it is suitable only for cleaning small areas, making it best for printed circuit board cleaning (Lu and Aoyagi, 1994).
- Blasting with CO_2 snow or pellets is another way that coatings and contamination can be removed.
- Finally, steps can also be taken to prevent the contaminant from ever entering the process. For example, the development of low-solids "no clean" rosin fluxes for soldering printed circuit boards completely eliminates the need for a cleaning process (Sapre, 1990).

7.5.3 Electronics Manufacturing, Metal Treating and Processing

Alcan has been able to significantly cut costs at its Franklin Park plant by converting to a chrome-free, dried-in-place pretreatment. Its process has eliminated 7,500 lb of a chrome-bearing waste stream that previously had to be hauled away. In addition, by switching to the dried-in-place treatment, the plant was able to cut water usage from

25,000 gallons per day to 6,800. The chrome-free process further reduced water needs to 500 to 600 gallons a day. http//www.modernmetals.com/index.html

Further review of toxic metal emissions are the subject of another paper. The objective of sorbent-injection methods is to effectively capture the metal species (preferably transform it to an environmentally benign form) and to suppress the fraction in the submicrometer mode. The design of an effective sorbent-injection methodology thus requires an understanding of the fate of the metallic species and its transformation pathways (transfer to the gas phase, subsequent chemistry at high temperatures, and aerosol formation and growth dynamics) in the combustor. Given benign solvents, this will prolong their life (Biswas and Wu, 1998).

Numerical simulations were carried out using a multicomponent reactive solute transport model to study the migration of four heavy metals (Cd^{2+}, Pb^{2+}, Cu^{2+}, and Zn^{2+}) in a sand/bentonite mixture. The leachate pH has a significant effect on the migration of Cd^{2+} and Pb^{2+}, but has only limited effect on the mobility of Cu^{2+} and Zn^{2+} (Wu and Li, 1998).

Tons of spent abrasives result each year from the removal of old paint from bridges. Because the spent abrasives contain metals from the paint, some spent abrasives may be considered hazardous by the Toxicity Characteristic (TC) criteria. Incorporation of the spent blasting abrasives in nonstructural concrete offers an opportunity to recycle the spent abrasives while immobilizing potentially leachable metals. Solvents that are less aggressive will mean that abrasives will be necessary in some applications. Study results indicated that considerable quantities of these spent abrasives can be solidified/stabilized while reducing the leachability of cadmium, chromium, and lead and producing compressive strengths over 6895 kN/m2 (1000 psi) (Brabrand and Loehr, 1993).

As was reviewed earlier, copper, silver, and gold colloids have been prepared by Chemical Liquid Deposition (CLD) with dimethoxymethane, 2-methoxyethyl ether and ethylenglycol dimethyl ether. The metals are evaporated to yield atoms which are solvated at low temperatures and during the warm-up process colloidal sols with metal clusters are obtained (Cardenas et al., 1994).

Fire-retardant coatings currently in use contain a number of ingredients that are either considered to be "toxic" heavy metals or on the hazardous air pollutants (HAPs) list. In addition, there is concern that the use of halogenated chemicals in these coatings and other products will be banned in the future. A recent paper contains the details of two reformulations programs. The first is a reformulation of a low VOC chlorinated alkyd coating and the second is a reformulation of a chlorinated emulsion system. Both programs successfully reduced the heavy metals and lowered the HAPs to an acceptable level (Dahm, 1996).

The preparation, characterization, and mechanisms of formation of uniform simple and composite metal particles of different modal diameters and shapes are important. Such dispersions can be obtained by reduction of metal ions, in uncomplexed or complexed state, with suitable reducing agents and appropriate additives. There is an effect of the redox potential in a given oxidation/reduction system on the nature of the final particles. Monodispersed particles of metal compounds are prepared first and then reduced to pure metals either in a liquid or a gaseous medium. In doing so, one can produce powders of a given morphology by selecting the precursor particles of the desired shape (Goia and Matijevic, 1998).

New products are being developed to replace heavy metals in water-treatment and protective-coatings applications. The products have become available from suppliers of protective coatings under pressure from the U.S. EPA to remake paints and primers minus the solvents that contain volatile organic compounds. Manufacturers have come up with a variety of formulations that do not pose the environmental and health risks associated with chromium. These formulations are more expensive than chromium-based solutions, however, and are likely to remain so for the immediate future (Hairston, 1996b).

Water-based paints contain organic solvents and many additives, such as biocides, surfactants, pigments, binders, amines, and monomers. The chemical complexity may introduce new potential health hazards to house painters, in particular irritative and allergic disorders. Hygiene measurements were performed during normal working days when only water-based paints and no solvent-based paints were used. The painters were exposed to low concentrations of dust, metals, ammonia, formaldehyde, and volatile organic compounds. The work environment was considered better when working with water-based paints than with solvent-based paints. Taste or olfactory disturbances were less common. General, as well as work-related, eye and skin irritation was more common among the exposed workers. For other symptoms no significant differences were found. The study indicates that the introduction of water-based paints has improved the work environment for house painters (Wieslander et al., 1994).

7.5.4 Foods and Food Processing

Ochratoxin A (OA) is a natural contaminant of a large variety of foods of plant and animal origin. A capillary electrophoresis (CE) method for the quantification of OA in three very different commodities—roasted coffee, corn, and sorghum—has been developed. The extraction and isolation procedures combine a silica column and an immunoaffinity clean-up column analogous to other chromatographic methods. Each instrumental analysis, after extraction and purification, required 13 min, equivalent to HPLC analysis. CE-LIF can be applied to the quantitation of OA in roasted coffee, corn, and sorghum, reducing organic solvent usage relative to HPLC (Corneli and Maragos, 1998).

The following is an example of less toxic solvents in classical techniques. Lipid extraction preceding fatty acid methyl esters (FAME) preparation for gas chromatography is time-consuming and cumbersome. Lipid extraction can be omitted and performed in situ transesterification (ISTE) by heating lipid-containing foods at 90°C for 10 min after adding 0.5N NaOH in methanol for methanolysis and continued heating another 10 min for further methylation after adding 14% BF_3 in methanol. FAME prepared by ISTE showed fatty acid composition virtually identical to FAME prepared after lipid extraction from powder, liquid, phospholipid-rich, and tissue products. Due to its simplicity, speed, and reduced organic solvent usage, ISTE should be useful to determine overall fatty acid composition of foods (Park and Goins, 1994).

Pressurized hot water can be used to extract two fungicides, thiabendazole (TBZ), and carbendazim (MBC), from agricultural commodities including banana pulp, whole lemons, orange pulp, mushrooms, and rice at extraction temperatures below 100°C and an extraction pressure of 50 atm. The extraction parameters that were studied include temperature, equilibration time, flow rate, pH, and collection volume. Liquid–

liquid partitioning using ethyl acetate was then used to partition MBC and TBZ from the aqueous extractant and concentrate the analytes for final analysis and the determination of recovery. Reversed-phase ion-pairing HPLC with UV absorbance and fluorescence detection was used to determine the recoveries of TBZ and MBC from fortified homogenates. Using an extraction temperature of 75°C, the average recoveries of MBC and TBZ ranged 80.9–100.5% at fortification levels ranging from 0.14 ppm in fresh mushrooms to 10 ppm in whole lemon homogenates (Pawlowski and Poole, 1998).

Dynamic extractions of the organic flavour and fragrance compounds from dried lavender flowers and rosemary leaves using $SCCO_2$ were carried out. The data from the lavender and rosemary extractions were fitted to a model to produce the characteristic extraction curve. Using data obtained from rosemary extractions, an extrapolation method derived from the model was used with data from shorter extractions to show that the model provided quantitative analytical information (Walker et al., 1994).

An automated supercritical fluid extraction and in-line cleanup system has been developed for organochlorine and organophosphate pesticide residues contained in fats. This procedure utilizes $SCCO_2$ modified with 3% acetonitrile at 27.58 MPa and 60°C to extract and separate the pesticide residues from the fat on a C-1 bonded phase preparative column at 95°C. The automated C-1 system recovers 86 of 117 nonpolar to moderately polar organochlorine and organophosphate pesticides from fats. Pesticide residues can be separated from 0.68 g of butter fat and 0.67 g corn oil, resulting in 2.9 mg of butterfat and 2.1 mg corn oil residue coeluting into the pesticide fraction. Also, this integrated method can extract and clean a 5 g sample of fatty foods containing <18% fat and 70% moisture. Current methodology uses organic solvent extraction and gel permeation chromatography, along with a final Florisil column cleanup step. This automated C-1 system simplifies the extraction and cleanup step while reducing solvent usage and hazardous waste (Hopper, 1999).

Solubility of milk fat in supercritical (SC) ethylene and liquid propane was compared to previous results in $SCCO_2$. At the same operating conditions (temperature and pressure), solubility of milk fat was higher in SC ethylene than in CO_2, although levels generally remained below 5% (w/w), This resulted in significantly higher solubility in SC ethylene when compared at equivalent solvent density. Very little fractionation of milkfat occurred in liquid propane over the range of pressures (3.45 to 5.52 MPa) and temperatures (30 to 90°C) studied (Wang et al., 1995).

7.4.1 Inks, Paints and Coatings, Waxes, and Polishes

The function of a coating is to protect a surface from damaging environments such as extreme weather or corrosive chemicals. Coating technology spans a wide range of applications such as architectural, industrial, and antifouling coatings, and printing inks (Oil and Colour Chemists' Association, 1984). Coatings are typically classified according to the binder or resin that acts as the film-forming agent and not according to the applications in which they are used. Table 7.9 lists typical binders and their primary applications. Additives (pigments, catalysts, antifoam agents, and hardeners) play a large role in determining the effectiveness and properties of the coating. The final component of a coating formulation is the solvent necessary to give the formulation a manageable viscosity for application. Table 7.9 also lists traditional formulation

Table 7.9. Summary of resin types and applications (Sherman et al., 1998).

Resin	Cure Type	Formulation Solvent	Application
Vegetable oil	C	Hydrocarbons, toluene, xylene	Clear varnish, industrial enamels, printing inks, paint primer
Alkyd	C		Paint
Polyester	C	Esters, diacetone	Heat-sensitive plastics, vehicles, home appliances, wood
Amino	C		Paint, lacquer
Phenolic	C		Metal primer, marine enamels, tank and drum lining
Epoxy	C	Ketone, ethers, esters, toluene, xylene	Marine coatings, enamels, containers
Silicone	C	Xylene hydrocarbons, chlorinated hydrocarbons, ketones	Electrical insulating resins, paint additive, brick sealant
Acrylic	C/NC		Paint
Cellulose	NC	Ketones, esters	Wood finishing
Vinyl lacquers	NC	Ketones	Metal substrates
Chlorinated rubber	NC	Aromatic hydrocarbons, chlorinated hydrocarbons, esters, ketones	Alkaline substrates, marine coating
Urethane	C		Automotive coatings, wood sealer and finish, concrete sealer

Note: Abbreviations: C, convertible coating (reacts during cure); NC, nonconvertible coating.

solvents used for each resin type. Many of the common formulation solvents such as xylene, toluene, MEK, MIBK, and methanol are classified as VOCs or appear on the U.S. EPA 33/50 list (Morgan, 1996).

Not only are VOCs typically used in the coating industry, they are used in large quantities, and the nature of industry is such that solvent containment is much more difficult than in other areas of solvent usage. Consequently, solvent releases into the environment can be substantial. The large quantity of and long-term exposure to solvents that many painters face may cause chronic central nervous systems effects, cancer, and hematological disorders (Burgess, 1995). Fortunately, many advances have been made in coatings technology that allow the industry to substantially decrease the amount of solvent needed in the formulation of effective coatings—in some cases, to less than 3.5 lb VOCs/gal.

As an example, a new process, plaforization, is an organic phosphating process with several advantages over traditional treatment processes when used in the right applications. It both cleans and phosphates the parts in a single step. It operates at room temperature. There are no effluents to dispose of, either waterborne or solid sludges. Plaforization works by taking process oils into solution into a fluid containing a polymeric resin and phosphating agents. The oil is then encapsulated into the resin. The phosphate layer is laid down on the metal surface and the resin polymerizes with the encapsulated oil to provide further corrosion protection and impact resistance. The process chemicals are nonaqueous. The resin and phosphates are dissolved in a mixture of high-solvency oxygenated organic fluids which are blended to ensure that, in the cleaning/phosphating process, they bring the manufacturing lubricating oils into solution in the fluids (Carpenter, 1999).

7.5.5.1 High Solids Formulations

Paint is used on a huge range of surfaces for applications such as decoration, corrosion prevention, and abrasion or chemical resistance. The binder resin is the most important component in the paint system because it provides a hard surface film with the required attributes of adhesion, flexibility, and toughness. The important function of the pigment is to provide color and opacity for the paint film. Environmental and safety regulations have had a profound effect on the paint industry, forcing a change in the preferred organic solvents, with the aromatic and aliphatic hydrocarbons being replaced by more environmentally friendly versions such as the oxygenated solvents typified by the glycol ethers and ketones (Howard, 1996).

A coating is considered to be a high solids formulation when the binder and additive content is over 80% (w/w), although formulations having solids content between 60 and 80% are often included in this category (Holmberg, 1987). In high solid formulations, the approach is not to replace the conventional solvent with a less benign one such as is done in cleaning operations or to develop tailored solvents as is done in synthetic applications but merely to use less solvent. The advantages and disadvantages of high solids coating are summarized in table 7.10.

One of the main challenges in reducing the amount of solvent in a formulation is maintaining a manageable viscosity. Paint formulations with solids compositions up to 70% may still be thin enough to spray or roll, especially if application is done at a high temperature. Coatings that use natural oils such as linseed, tung, and soybean oil are often classified as high solids coating (Elvers et al., 1985). In this case an oil is dispersed in a small amount of hydrocarbon solvent and as the solvent evaporates, the oil polymerizes on exposure to oxygen. Now there is development of synthetic resins for high solids applications.

Many of the classes of resins listed in table 7.9 may be used in high solids coating formulations. However, to attain coatings that contain less than 30% solvent, modifications must be made to the binders used in conventional formulations. This is accomplished by using lower-molecular-weight resins that undergo cross-linking reactions as the paint cures or by using resin polymers that have narrow molecular weight distributions. Some difficulties such as slow physical drying and film shrinkage are encountered when adjusting the polymer in this manner. However, optimizing the formulation and cure conditions can minimize these difficulties. For example, Bittner and Epple (Bittner and Epple, 1996) demonstrated that polyurethane paint prepared in a high solids formulation using resin of low molecular weight and narrow-size distri-

Table 7.10. Advantages and disadvantages to high solids coating formulations (Varerkar, 1996).

Advantages	Disadvantages
Applicable to many resin types	Pigment flocculation
Equipment can be retrofit	Rheology difficult to control during application
Cost effective	May have inferior surface appearance
Excellent performance for protective maintenance and automotive coatings	

bution dries with similar hardness and homogeneity if dried at 80°C rather than at ambient temperatures.

Modifying the molecular structure of the resin, for example, by using branched resins (Elvers et al., 1985), results in polymers with lower intrinsic viscosities. In turn, the coating formulation requires less solvent to reach a certain viscosity. In addition, it can be advantageous to pay close attention to the different monomer types used in a copolymer resin. For example, Sullivan (Sullivan, 1994) outlines using 2-methyl-1,3-propanediol to improve the flexibility of high solids polyester coatings, while reducing solvent usage. Another example of viscosity reduction is the use of silicon-based monomers for the synthesis of polyester resins (Thames and Panjnani, 1995).

A related approach to high solids coatings is to incorporate a reactive chemical as the solvent. This allows control of the coating viscosity during application but minimizes the VOCs released because the solvent is cross-linked into the coating (Johnson, 1995; Robinson et al., 1994; Adams, 1996; Rupa Vani et al., 1993; Kuo et al., 1994; Hoffman, 1995). Reactive diluents take many forms, sometimes even as a natural oil as in the case discussed by Dirlikov et al. (1992) and Banov (1994).

Of course, benign solvent use is encouraged in addition to quantity reduction. For example, volatile methyl siloxanes (VMS) similar to those described for cleaning have been used in three different high solids silicone paints, resulting in a VOC reduction without compromising film quality (Finzel, 1996; Williams, 2000). Finally, the need for polymers with specifically tailored low molecular weights and distributions for effective high solids coatings has resulted in a variety of new polymerization initiators, synthetic techniques, and cross-linking additives (Kamath and Sargent, 1996; Nakano and Morimoto, 1990; Gould et al., 1996; Wicks and Yeske, 1996).

7.5.5.2 Aqueous Formulations

Waterborne coatings offer another set of options as they provide a safe, nontoxic, and environmentally benign method to dramatically reduce or eliminate volatile organic solvents. In addition, they are usually inexpensive and come in liquid form. Waterborne coatings, primarily in the form of latex paints, have been prevalent since the 1950s but were deficient in many areas such as flow behavior, drying properties, glossiness, corrosion, and foaming (Bieleman, 1996). However, strict environmental regulations and concern for worker exposure have focused attention on these types of coatings and research is targeted at improving the durability and application of water-based coatings (Karsa and Davies, 1995; Provdder et al., 1996). Waterborne paints are applied by spraying, rolling, and so on, but as with cleaning operations, the process usually requires some extra time and equipment to allow the coating to dry properly because of the high latent heat of water vaporization. The advantages and drawbacks of aqueous formulations are summarized in table 7.11.

Waterborne paints fall into two general classes: water-reducible coatings and emulsions. Water-reducible coatings consist of binders that can be dissolved in water. The high polarity of water limits the range of resins compared to that for resins that can be used for high solids applications because of solubility difficulties. Resin classes that have been used successfully include epoxies, acrylics, polyesters, and polyurethanes. These resins differ from their solvent-borne counterparts used in high solids coating through the addition of extra hydrophilic groups such as carboxylic acids and

Table 7.11. Advantages and drawbacks to water-borne coatings.

Advantages	Disadvantages
Inexpensive	High freezing point
Environmentally benign	High latent heat of vaporization
Nontoxic	Often need new equipment
Liquid form	Extra precautions with electrostatic paint applications systems
	Limited material compatibility for delivery systems
	Can exhibit high water permeability
	Pigment flocculation

amines. General overviews of water-reducible polymers have been outlined (Padget, 1994; Paul, 1996).

If desired paint properties cannot be obtained using water-soluble resins, formulations using a surfactant to emulsify appropriate resins may be effective. These are often referred to as latex paints. The polymer is most commonly based on acrylate esters, vinyl acetate, or copolymers with styrene. The polymeric resin is prepared in situ in an emulsion polymerization resulting in latex-type paint. The emulsions may contain up to 15% organic solvent as a stabilizer resulting in a low VOC coating. It is also worth mentioning that many water-reducible coatings contain small amounts of cosolvent such as a glycol ether or alcohol to aid in coating handling (Bittner and Epple, 1996).

Specific examples of tailored resins for water-borne coatings abound:

- Two-pack polyurethane paints exhibit film properties comparable to those of solvent-borne polyurethane coatings (Bittner and Epple, 1996; Mirgel, 1993).
- Waterborne polyurethanes that have the performance of solvent-based systems can be made via tailored emulsion polymerization (Hagernrother and Ruttmann, 1990).
- Aromatic polycarbodiimides act as very efficient cross-linkers in waterborne emulsion systems and have the added advantage that they are much less toxic than traditional polyaziridines (Brown, 1995).
- Cross-linking of the epoxy films results in a coating that is more resistant to humidity and mechanical impact (Eslinger, 1995).
- Water-borne fluoroelastomeric coatings for aggressive condition have been developed (Poggio et al., 1995).
- The automotive industry, a large paint consumer, has recently implemented metallic water-based coatings (Neimann, 1992).
- Finally, some waterborne coatings incorporated reactive diluents, as in high solids coatings. For example, Blank (1992) describes using a urethane diol as a reactive diluent to replace glycol ether cosolvents in emulsion coatings.

Case studies illustrate that waterborne paints are indeed feasible for many applications:

- Waterborne paints can reduce the amount of solvent used in vehicle painting from 42.4 to 7.3 kg (Clancy, 1994).
- Republic Container Co. (Nitro, West Va.), a company that supplies steel drums, switched from a solvent-based paint to a water-based paint, reducing their VOC emissions to 2.8 lb/gal and saving over $10,000 in costs.

- Cornwell illustrates many successful cases of water-borne paint use for steel coating, a substrate not traditionally coated with water-based paints because of difficulties with rusting (Cornwell, 1994).

Novel coating additives are also being studied as a way to ameliorate the disadvantages that have become synonymous with waterborne paints:

- Foaming, undesirable rheology, and poor glossiness due to agglomeration of the pigment can be eliminated (Bieleman, 1996) .
- Pigment dispersion can be discussed from the fundamental aspects of molecular interactions between water and the pigment (Kobayashi, 1996).
- Latex paint formulations can be formulated without the glycols that are usually added as stabilizers but that may be toxic and contribute to the VOC content of paint (Klein, 1993).

7.5.5.3 Supercritical Carbon Dioxide Formulations

$SCCO_2$ is used in spray paint formulation and application because it is nontoxic, inexpensive, and has the added advantage that it has high solvation power for many polymers. Since CO_2 is so volatile, it is mixed with the coating resin immediately prior to application and the resulting mixture sprayed onto the substrate. It has been demonstrated that up to 80% of the organic solvent used to formulate an acrylic spray paint can be replaced by $SCCO_2$ without compromising the coating homogeneity (Donohue et al., 1996). In addition, CO_2 is such a fast evaporating solvent that the paint dries quickly. Furthermore, it does not generate additional CO_2 like solvent-containing paints that can oxidize to form 2.3 to 3 kg CO_2/kg solvent. White reached conclusions similar to those of Donohue for a variety of resin-pigment combinations (White, 1991). Other researchers have patented their work with supercritical diluents for spray painting applications and demonstrated reductions in the amount of solvent required for adequate coating application (Nielsen and Glancy, 1996; Lee et al., 1990).

The process for spraying paints and other coatings which reduces atmospheric emissions of environmentally harmful VOCs. The liquid solvents of conventional coating have been replaced by $SCCO_2$. The carbon dioxide not only reduces viscosity, but provides additional benefits. The spray takes on a parabolic shape, is more finely atomized than conventional sprays, and has a narrower range of droplet sizes. The resulting coatings have uniform thickness and excellent coalescence. While much remains to be learned about the thermodynamics and rheology of polymers mixed with supercritical fluids, it appears that this technology can be used with nearly all paints and coatings that currently are sprayed using organic solvents (Donohue et al., 1996; Lewis et al., 1997).

7.5.5.4 Solvent-free Formulations

As with cleaning, many researchers are looking toward solvent-free coatings as the answer to solvent replacement.

- Powder coatings rely on thermosetting plastics to be sprayed on a surface at high temperature. This method produces high-gloss even coatings but requires specialized equipment and is limited to metal surfaces that can withstand the high-melt temperatures (Elvers et al., 1985).

- Ultraviolet (UV) curable coatings are another solvent-free alternative. In this case reactive monomers such as ethers and styrene are used to coat the surface of interest and UV light is used to initiate an in situ polymerization. Because the cure rate depends directly on the distance of the item to be coated from the UV source, this coating technique is best suited to flat sheets (Marrion, 1994). A limitation is that it is difficult to incorporate pigment in UV-cure coatings, as the pigments usually tend to absorb UV light.
- Many novel coatings technologies are discussed in the review by McGinniss (McGinniss, 1996) who discusses advances made in environmentally benign coatings that include silicon oxides, silica fillers, and hybrid waterborne/UV-curable systems.
- Linear oligoester diols can be used for solventless coatings (Jones, 1996).

7.5.6 Drop-in Replacements

As with other applications, the approach requiring the fewest modifications to already existing synthetic processes is to find a drop-in replacement for the conventional solvent. For example, it is common to replace extremely flammable diethyl ether with methyl *tert*-butyl ether (Budavari et al., 1989) or carcinogenic benzene with toluene (Femec and McAffrey, 1994). Such facile substitutions are not always available, however, and experimentation is often required to find a suitable replacement. Some examples of effective solvent substitutions are given in table 7.12. In the synthesis of phosphonitrilic hydroquinone prepolymers, the carcinogenic and ozone-depleting solvent carbon tetrachloride was replaced with cyclohexane with a slight increase in yield (Femec and McAffrey, 1994). Chloroform was considered an explosive hazard in solvating Schmidt reactions involving azides, and it was replaced with dimethoxyethane (Galvez et al., 1996). Dichloromethane, or methylene chloride, is one of the most popular synthesis solvents, but it is a suspected carcinogen and is highly volatile (bp = 40°C). Ogawa and Curran demonstrated that benzotrifluoride (low toxicity, bp = 102°C) can be an effective replacement for dichloromethane in many reactions, with similar yields (Ogawa and Curran, 1997).

Tetrahydrofuran (THF) is another important process solvent often used to solvate reactions involving strong bases. The workup of strong base reactions often includes an aqueous extraction, creating the problem of contaminated aqueous waste because THF is completely water-miscible. Typically, elaborate steps such as solvent exchange by distillation are taken to avoid THF contact with water. This is an energy-intensive process, and a more economical solution is desirable. Hatton's group has examined the

Table 7.12. Drop-in solvents for synthesis.

Solvent	Problem	Replacement
Diethyl ether	Flammable, flash point = –40°C	Methyl t-butyl ether
Benzene	Carcinogenic	Toluene
Carbon tetrachloride	Carcinogenic, ozone depleting	Cyclohexane
Chloroform	Explosive hazard with azides	Dimethoxy ethane
Dichloromethane	Suspected carcinogen, volatile	Benzotrifluoride

use of THF derivatives that have similar solvating characteristics but are essentially nonvolatile and water insoluble as reaction solvents (Molnar et al., 1996). A particularly effective solvent is n-octyl tetrahydrofurfuryl ether, which has been shown to be a satisfactory replacement for THF in a series of reactions in the synthesis of the human immunodeficiency virus (HIV) protease inhibitor Crixivan. These solvents therefore satisfy the criteria for green processing in that they are less prone to enter the environment and that a number of energy intensive separations and solvent exchanges can be avoided (Molnar et al., 1996).

In Illinois, engineers have devised a new way of halving the cost of manufacturing ethyl lactate. The new process uses a fine membrane to efficiently remove water, which is produced as a reaction byproduct, and allows the production of lactate esters that are almost pure. This method of production will make the environmentally benign ethyl lactate a cheap replacement for the harmful solvents used for paints, glues, inks, and dyes (Knight, 1998).

The products developed by several additive and specialty chemical suppliers to replace volatile solvents are reviewed. Such solvents have been integral to the coatings equation for a long time. Paints and coatings formulators have become aware of the role that additives and specialty chemicals play in eliminating these solvents (Chemical Week Assoc., 1994).

7.5.7 Ionic Liquids

Industrial exploitation of ionic liquids is in its early days (Freemantle, 2000). The use of ionic liquids in industry is seen as being highly speculative, but progress is being made. Room temperature ionic liquids have been studied actively since their discovery in the 1970s, predominantly for their possible application as battery electrolytes. Work on the exploitation of ionic liquids as reaction media started in the early 1980s, but only recently has it attracted industrial interest.

A few patents associated with the chemical applications of ionic liquids have emerged over the past couple of years, revealing the beginnings of industrial interest (Freemantle, 1998). However, little has entered the public domain concerning the use of ionic liquids on an industrial scale, and nothing has been claimed, even in general terms, to suggest that room-temperature ionic liquids are being used in a viable chemical process being operated commercially.

Other groups are working on the use of ionic liquids for chemical and industrial processes. In order to push the development of the industrial application of ionic liquids, a European consortium was formed several years ago (Seddon, 1999). This three-year arrangement between academics and industry has three major goals:

- Manufacture ionic liquids and make them commercially available;
- Explore the use of ionic liquids as catalysts for aromatic alkylation reactions;
- Use ionic liquids as catalysts for producing fine chemicals intermediates.

A study of the use of room temperature ionic liquids as a new class of nonaqueous solvents for 2-phase catalytic hydrocarbon transformations. The liquids investigated were mixtures of quarternary ammonium salts and organo-aluminum compounds. They were found to be very effective solvents for metal-catalyzed olefin dimerization and metathesis reactions. Their complexing ability and acidity can be tuned as re-

quired, and they provide many physical properties, including density, viscosity, melting points, and an extensive range of miscibilities. In oil exploration surveys, ionic liquids dissolve kerogen from geologic samples. The only other solvent known to do so is hydrofluoric acid. Ionic liquids are also being investigated for use in liquid–liquid extractions. A potential application for this is in the separation and processing of spent nuclear fuel and other nuclear waste (Chauvin and Helene, 1995).

The use of ionic liquids in most applications is still in development. The chemical industry in Europe is showing increasing interest in them, particularly for olefin dimerizations and Friedel-Crafts reactions. A two-phase "loop" reactor has been designed for large-scale preparations which allows for continuous reaction, separation of the product, and recycling of the ionic liquid (Chauvin and Helene, 1995).

Ionic liquids are successfully being used as replacements for hydrofluoric acid for the commercial oil exploration application discussed previously (Chauvin and Helene, 1995). As we saw in the previous chapter, ionic liquids have potential as extractants in recovery of butyl alcohol from fermentation broth (Fadeev and Meagher, 2001).

7.5.8 Water

Water is an ideal candidate as a replacement solvent. It is nontoxic, nonflammable, readily available, inexpensive, and easy to handle. Unfortunately, switching from organic to aqueous solvents is not a simple task. As with coating applications, the high polarity of water offers many difficulties in its implementation as a reaction medium because many organic compounds do not exhibit good aqueous solubility. Nonetheless, significant progress has been made in developing reaction chemistries that take place in substantially aqueous environments.

- Phase transfer catalysis takes advantage of the solvating properties of biphasic systems. Rearrangements are solvated in the organic and aqueous phases and a phase transfer catalyst is used to bring them to react in the organic phase (Goldberg, 1989).
- Aqueous alkali hydroxides can be used to replace flammable bases of sodium metal, sodium hydride, sodamide, and other alkoxides. The reaction temperature is lowered while the reaction rate improves because the increased reactivity of anions in the nonpolar solvent (Goldberg, 1989; Dehmlow and Dehmlow, 1993; Starks et al., 1994) as have asymmetric phase-transfer reactions (O'Donnell, 1993).
- Perform the reaction at the organic-aqueous interface. Reagents are moved from the organic to the aqueous phase but remain localized near the interface, and thus the reagents need not be significantly water-soluble. Catalysts are either solvated homogeneously in a supported thin aqueous film or at the interface by surface active ligands (Dartt and Davis, 1994; Lim and Zhong, 1996; Tenbrink et al., 1998).
- Exploiting the properties of aqueous surfactant solutions in which the surfactants aggregate to form micelles consisting of apolar cores comprised of the hydrophobic tail groups stabilized by coronae formed by the hydrophilic surfactant heads (Fendler and Fendler, 1975; Bunton, 1991). The apolar core plays the role of the organic solvent, whereas the palisade layer can provide a medium of intermediate polarity.

- Monflier showed that solvent-free telomerization of butadiene with water to form octadienols could be carried out effectively in the presence of a nonionic surfactant; the conventional process is performed in the solvent sulfolane (Monflier et al., 1995).
- Replacement of the organic phase with surfactants to exploit micellar phase transfer catalysis principles (Battal et al., 1997) for the alkylation of phenol and aniline. This group had previously demonstrated the synthesis of a surfactant by micellar autocatalysis, whereby the surfactant product itself catalyses the reaction (Kust and Rathman, 1995).
- The use of micellar solvent phases can be avoided and the reactions can be carried out in an entirely aqueous medium. For water-soluble reagents, catalytic reactions such as hydrogenations and hydroformylations may be carried out homogeneously in the aqueous phase with water-soluble ligands such as triphenylphosphinotrisulsulfonate (Tenbrink et al., 1998).
- Barbier-Grignard-type reactions in water (Li, 1996) between allyl halides and carbonyl compounds can be mediated by metals of tin, zinc, or indium. Usually the generation of the organometallic reagent takes place in anhydrous organic solvents, but using softer metals allows this reaction to take place in water.
- Epoxidation of cyclooctene has been shown, using ozone in water where the products were easily recovered by phase separation (Shu et al., 1995).
- Brominations are performed readily in water instead of in carbon tetrachloride (Shaw et al., 1997).

These examples indicate the potential minimization of solvent usage by the development of new water-based chemistries for green processing.

7.6 Alternative Solvents for Separation Processes

The application of organic solvents and organic solutions with carrier compounds for the separation of organic substances and metal ions from different sources is well known. These separations are usually performed by extracting the target compound into the organic phase for purification, enrichment, and pollution remediation. As with cleaning, coating, and synthetic applications, it is advantageous to replace the organic solvents used in liquid extractions with solvents that are environmentally friendly. In some cases it is beneficial to implement new separation techniques that reduce the need for large volumes of organic solvents. Among these, liquid extraction techniques employing supercritical fluids and aqueous formulations containing surfactants or soluble polymers are most frequently considered because of their environmentally friendly characteristics and because they often afford increased extracting strength.

7.6.1 Recrystallization/Cooling Solvents

The development of a successful crystallization process for purification and isolation of an organic compound requires the selection of a suitable solvent or solvent mixture; to date, no logical method has been established for determining the best solvent com-

bination. The process chemist or engineer often employs a trial-and-error procedure to identify an appropriate solvent system, the success of which is dependent on experience and intuition. A strategy for choosing crystallization solvents can be based upon equilibrium limits. The approach utilizes a group contribution method (UNIFAC) to predict a value for the activity coefficient of the solute in a given solvent system at the saturation point. Implementation of this strategy will reduce product cycle time, minimize solvent usage, and allow identification of cheaper solvent alternatives (Nass, 1994).

7.6.2 Supercritical Fluid Extraction

The characteristics of supercritical fluids make them ideal for the recovery of natural products (Molero et al., 1996). As a result, the food industry was among the first to implement supercritical fluid extraction (SFE) widely using CO_2. Not only is this process environmentally benign, it is also nontoxic, a primary concern when manufacturing edible products.

SFE has also replaced many regulated solvents in analytical chemistry applications in recent years, primarily because it provides a more reliable measure of the concentrations of environmental contaminants and can play an important role in pollution assessment, abatement, and control. Advantages have been shown for using SFE compared to the conventional Soxhlet extraction with toluene for determining the presence of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans in ashes from a municipal incinerator (Dolezal et al., 1995). SFE allows the complete extraction of the analytes from the sample, whereas conventional extraction results in an incomplete, and hence, inferior extraction.

- Analysis of agrochemical samples from soils after extraction by Soxhlet methods are now replaced by analysis following supercritical extractions (Clement et al., 1997).
- Alzaga et al. extracted Pirimicarb (a pesticide present in sediments of rivers) using supercritical CO_2 modified with triethylamine and compared the results to those obtained with the conventional Soxhlet method (Alzaga et al., 1995). The supercritical fluid method offered increased precision, shorter analysis time, and a 10-fold reduction in solvent usage.
- Reighard et al. used CO_2 enhanced by the addition of methanol (cosolvent) to extract nitroaromatic and phenolics, environmental pollutants (Reighard and Olesik, 1996). An attractive interim option from an environmental standpoint is the use of HFCs or HCFCs.
- At supercritical conditions these solvents effectively extract relatively polar compounds such as polychlorinated biphenyls, dibenzo-p-dioxins, and dibenzofurans without the use of a cosolvent (Roth, 1996).

7.6.3 Aqueous Surfactant and Macromolecular Solutions

Removal of organic or heavy metal ion contaminants from aqueous streams can be achieved using a variety of different separation strategies, one of which is solvent extraction. Potential counter-contamination of the streams being treated with the ex-

tracting solvent can be avoided by eliminating the organic solvent altogether in favor aqueous-based solvent systems that rely for their effectiveness on the presence of dissolved surfactant micelles or polymers. These aggregates or polymers can solubilize organic solutes with the aqueous phase or form complexes with the metal ions to be removed. Christian and Scamehorn (1989) studied the use of ultrafiltration for the retention of the surfactant micelles, whereas Hurter and Hatton (Hurter and Haton, 1992) examined the efficient separations could be obtained by exploiting the countercurrent principles within in chemical engineering unit operations.

A particularly important class of surfactants for the solubilization of organic compounds in aqueous solution is the polyethylene oxide-polypropylene oxide-polyethene oxide family of block copolymers (Hurter and Haton, 1992; Nagarajzan et al., 1986). These polymers form polymeric micelles that have a high capacity for the solubilization of organic compounds. Recovery of polyaromatic hydrocarbons (PAHs) by using block copolymer micelles in hollow-fiber membrane extraction was examined by Hurter et al. (1993). The high capacity of block copolymer micelles for trace contaminants offers the possibility of tailored design of block copolymers for future separations. An advantage of these polymeric micellar systems is that the micelles form only above a certain temperature, called the critical micelle temperature (CMT). These results and concepts have been confirmed by the more recent work of Lebens and Keurentjes (1996).

Water-based solvent systems originally developed for the separation and purification of proteins and other biomaterials (Walter et al., 1985) have been studied for the treatment of contaminated aqueous waste streams. Certain pairs of water-soluble polymers are incompatible in solution together, and this can lead to phase separation in which two phases are formed. Both phases are predominantly water, and each contains only one of the two polymers. Similar phase behavior results with some polymers and high concentrations of organic salts. The properties of the two phases ensure that the environment-afforded targeted species is different in the two phases. This provides the driving force for separation of different species. A commonly used phase-forming polymer is polyethylene glycol (PEG), which may or may not be derivatized to impart added selectivity to the separation (Rogers and Zhang, 1997; Rogers et al., 1996). The removal of color from textile wastes can be achieved using such systems. As solvent replacements, then, PEG-based aqueous biphasic polymer systems are an environmentally favorable alternative to traditional organic solvent phases.

Solvent-coated magnetic particles dispersed within the feed phase can be used to process metal waste solutions (Kaminski et al., 1997; Nunez et al., 1996). Once the desired solutes have been removed by extraction, these particles can be recovered conveniently using magnetic filtration.

7.7 Military Solvents

Most people associate the military with environmental problems rather than solutions. However, Stephen Andersen, E. Thomas Morehouse, Jr., and Alan Miller describe how the military has sped the adoption of new, environmentally friendlier technologies and, working with U.S. industry, has eliminated its need for ozone-depleting substances (Andersen et al., 1994).

40 CFR Part 63, Subpart GG, the National Emission Standard for Hazardous Air Pollutants for Aerospace Manufacturing and Rework Facilities, commonly referred to as the Aerospace NESHAP, required compliance by September 1, 1998. The regulation affects any facility that manufactures or reworks commercial, civil, or military aircraft vehicles or components and is a major source of HAPs. The regulation targets reducing VOC and HAP emissions to the atmosphere. Processes affected by the new regulation include aircraft painting, paint stripping, chemical milling masking, solvent cleaning, and spray gun cleaning. Strategies to reduce compliance costs and minimize record-keeping burdens have been developed (Bauer et al., 1997).

Even explosives must conform to regulations. Polymer bound explosives (PBXs) and Class 1.1 military propellants have been reformulated for use in the mining industry. There is a minimal waste stream (Wulfman et al., 1997).

The current fuel system icing inhibitor (FSII) additives used for commercial and military aircraft are ethylene glycol mono methyl ether (EGME) and diethylene glycol mono methyl ether (DiEGME). Propylene glycol is used for wing deicing. Fuel deicing additives are required in military fuels and optional in commercial fuels with wing deicing being weather dependent. The acetals and ketals of reduced sugars are being synthesized and modeled computationally because they are less toxic and more environmentally benign than EGME and DiEGME. Each compound is being evaluated with an emphasis on deicing effectiveness, human toxicity, and environmental hazard (Mushrush et al., 1997).

Increasingly stringent environmental regulations imposed on both the military and civilian sectors has created a growing demand for alternative abatement methods for a variety of hazardous compounds. One alternative, the nonthermal plasma, shows promise of providing an efficient means for the destruction of dilute concentrations of hazardous air pollutants. Promising results have been obtained for toluene, methylene chloride, and dichlorodifluoromethane in air at concentrations of a few hundred parts per million. The device has been operated at voltages up to 30 kV, pulse repetition rates up to 1.4 kHz, and flow rates up to 60 l/min (Korzekwa et al., 1998).

An epoxy resin formulation completely free of organic solvent was applied to carbon steel coupons using supercritical carbon dioxide (CO_2) as the volatile solvent. Sleet coupons coated in this manner were compared to coupons coated with a standard military specification marine primer (MIL-P-24441) during exposure to aerated 0.5 nrl sodium chloride (NaCl). The solvent-free coating protected the steel from corrosion in this environment as well, if not better than, the solvent-based primer (Kendig et al., 1999).

The high temperature and high loads of the military jet afterburner have resulted in the use of perfluorinated polyether (PFPE) greases which are chemically inert, high temperature resistant, and have good resistance to flow. These properties make removing the lubricant for inspection and repair difficult. Traditional cleaning for PFPE greases was the use of chlorofluorocarbons (CFCs) and a lot of elbow grease. With the phase-out of CFCs, new cleaning procedures have become necessary. These new procedures require a solvent which is safe to use, fast, and can be used in a variety of applications, ranging from flight line inspections to complete system overhaul. Investigations have determined the hydrofluorocarbons (HFCs), specifically the 8-carbon chain length HFCs, are an excellent replacement for CFCs (Thom, 1995).

7.8 Future of Industrial Solvents

7.8.1 Challenges

The chemical industry faces heightened challenges as it enters the twenty-first century. Five major forces are among those shaping the topography of its business landscape (National Research Council, 1996):

- increasing globalization of markets;
- societal demands for higher environmental performance;
- financial market demands for increased profitability and capital productivity;
- higher customer expectations; and
- changing work force requirements.

How the industry meets these challenges will affect the entire American economy. The U.S. chemical industry is the world's largest producer of chemicals (value shipped, $367.5 billion in 1995), contributing the largest trade surplus of any non–defense-related sector to the U.S. economy ($20.4 billion in 1995), representing 10 percent of all U.S. manufacturing, and employing more than 1 million Americans. The chemical industry, faced with an ever-changing business environment, must work individually and collectively to remain a world leader.

7.8.2 Meeting the Challenge

The chemical industry in the United States must confront these new market pressures head-on. With the goal of creating a technology "roadmap" for the chemical industry to follow, the chemical industry must accomplish five broad goals over the next 25 years. It must

- improve operations, with a focus on better management of the supply chain;
- improve efficiency in the use of raw materials, the reuse of recycled materials, and the generation and use of energy;
- continue to play a leadership role in balancing environmental and economic considerations;
- aggressively commit to longer term investment in R&D; and
- balance investments in technology by leveraging the capabilities of government, academe, and the chemical industry as a whole through targeted collaborative efforts in R&D.

7.8.2.1 Steps

To meet its goals, the U.S. chemical industry should accomplish the following:

- generate and use new knowledge by supporting R&D focused on new chemical science and engineering technologies to develop more cost-efficient and higher performing products and processes;

- capitalize on information technology by working with academia, federal and national laboratories, and software companies to ensure compatibility and to integrate computational tools used by the chemical industry;
- encourage the elimination of barriers to collaborative precompetitive research by understanding legislation and regulations that allow companies to work together during the initial stages of development;
- work to improve the legislative and regulatory climate by the reform of programs to emphasize performance rather than a specific method of regulatory compliance, and a greater consideration of cost, benefits, and relative risk;
- improve logistics efficiencies by developing new methods for managing the supply chain and by sponsoring an effort to shape information technology and standards to meet the industry's manufacturing and distribution needs;
- increase agility in manufacturing by planning manufacturing facilities capable of responding quickly to changes in the marketplace using state-of-the-art measurement tools and other technologies for design, development, scale-up, and optimization of production;
- harmonize standards, where appropriate, by working with governments within the United States and internationally, and with independent standards groups on nomenclature, documentation, product labeling, testing, and packaging requirements;
- create momentum for partnering by encouraging companies, government, and academia to leverage each sector's unique technical, management, and R&D capabilities to increase the competitive position of the chemical industry;
- encourage educational improvements through the advancement of strong educational systems and by encouraging the academic community to foster interdisciplinary, collaborative research and provide baccalaureate and vocational training through curricula that meet the changing demands of the industry.

7.8.3 Technical Recommendations

7.8.3.1 New Chemical Science and Engineering Technology

Chemical science is the most fundamental driver of advances within the chemical industry. Maintaining and improving the competitiveness of the U.S. chemical industry requires advances in three areas of chemical science: chemical synthesis, bioprocesses and biotechnology, and materials technology.

7.8.3.2 Chemistry

7.8.3.2.1 Chemical Synthesis The traditional tools of chemical synthesis in use today are organic and inorganic synthesis and catalysis. Synthesis is the efficient conversion of raw materials such as minerals, petroleum, natural gases, coal, and biomass into more useful molecules and products; catalysis is the process by which chemical reactions are either accelerated or slowed by the addition of a substance that is not changed in the chemical reaction. Catalysis-based chemical syntheses account for 60% of today's chemical products and 90% of current chemical processes (Collins, 2001).

To take full advantage of the potential offered in chemical syntheses, industry should work to accomplish the following:

- develop new synthesis techniques;
- enhance R&D collaborations in surface and catalytic science;
- promote enhanced understanding of the fundamentals in synthesis, processing, and fabrication; and
- support fundamental studies to advance the development of chemistry in alternative reaction media (gas phase, water, supercritical fluid, etc.).

7.8.3.2.2 Bioprocesses and Biotechnology Humans have used biologically based processes (bioprocesses) since they first made cheese, leavened bread, and brewed spirits. Bioprocesses are increasingly used to produce chemical products, and there is a whole world of potential biocatalysts to be discovered.

Each sector of the chemical enterprise has a role to play in advancing the use of biotechnology.

- Industry should define the R&D necessary to discover, develop, and provide more powerful and efficient biocatalysts, more effective process technology, and low-cost raw materials for bioprocesses.
- Academia should broaden the knowledge base relevant to industrial bioprocesses and use results of biotechnology research in health and agriculture to seek discoveries in bioprocessing.
- Government should encourage, support, and participate in precompetitive biotechnology R&D, while supporting long-term, high-risk technology development and demonstration.

7.8.3.2.3 Materials Technology The development of new synthetic materials has fueled the growth of the chemical industry and revolutionized our society in the twentieth century. Replacement of traditional materials such as metals, wood, glass, and natural fibers with synthetic polymers and composite materials has resulted in products with lower weight, better energy efficiency, higher performance and durability, and increased design and manufacturing flexibility.

7.8.3.3 Enabling Technologies

7.8.3.3.1 Process Science and Engineering Technology Process science and engineering technology (PS&ET)—which includes engineering technologies; engineering science; and engineering design, scale-up, and construction—dates back to the 1930s and is the foundation for the development, scale-up, and design of chemical manufacturing facilities. When effectively integrated with basic science and enabling technologies, PS&ET offers great potential for bringing science and quantitative understanding to the service of the chemical industry, permitting much higher capital utilization, improved yields, reduced waste production, and improved protection of human health, safety, and the environment.

To exploit the potential of PS&ET, industry should do the following:

- work with government and academia to develop relevant process software and real-time measurement tools;
- support engineering research in nontraditional reaction and separation systems (e.g., plasma, microwave, photochemical, biochemical, supercritical, cryogenic, reactive extraction and distillation, and membrane reactors); and
- pursue the development of new concepts in flexible manufacturing, process technology for high-performance materials and structures, disassembly and reuse of materials, solids processing, and "smart" processes.

7.8.3.3.2 Chemical Measurement Chemical analysis is a critically important enabling technology essential to every phase of chemical science, product and process development, and manufacturing control. New knowledge and insight provided through chemical measurement greatly accelerate progress in chemical science, biotechnology, materials science, and process engineering by providing reliable data to evaluate current and emerging technologies.

7.8.3.3.3 Computational Technologies Computational technologies have a broad range of applications, from molecular modeling to process simulation and control. Today, these technologies are embodied in almost every aspect of chemical research, development, design, and manufacture. Those most critical to the chemical industry include computational molecular science, computational fluid dynamics (CFD), process modeling, simulation, operations optimization, and control.

7.8.4 Supply Chain Management

The chemical industry has concentrated on science and production and also has given substantial attention to manufacturing. But it has given less attention to the supply chain, defined as the critical link between the supplier, the producer, and the customer. This is an important component of green chemistry.

7.8.5 Information Systems

Throughout the chemical industry, the ways in which data are turned into information and used, managed, transmitted, and stored will be critical to its ability to compete. Improved and enhanced information systems are at the very heart of the vision, which sees the chemical industry operating highly efficiently and economically.

7.8.6 Manufacturing Operations

The revenue-generating capability of the chemical industry is derived from its capability to deliver chemicals and materials that satisfy customer needs. Manufacturing operations play a key role in that activity. Maintaining and improving the competitiveness of the U.S. chemical industry will require advances in six areas of manufacturing operations:

- customer focus;
- production capability;
- information and process control;

- engineering design and construction;
- improved supply chain management; and
- global expansion.

To achieve improvements in these areas, the industry should

- encourage customer and supplier focus in a partnering fashion with emphasis on reliability of supply, continuous improvements in product quality and consistency, and responsiveness to change;
- encourage improvement in production capabilities to continuously improve process safety, reduce the impact of manufacturing processes and products on the environment, and speed up access to product and process information, thus enabling quick response to change and easing management of improvements;
- develop the technology to build plants in a shorter time and at lower cost to allow reconfiguration of plants as markets change;
- enhance the supply chain enterprise system by giving it a chemical industry focus;
- expand the capability for global operations and commerce.

8

Green Solvents for Practical and Ordinary Chemical Usage

8.1 Why This Area?

This area is broad and some current work will be highlighted. The chapter culminates by presenting the Cleaner Technologies Substitutes Assessment (CTSA) as a means for individuals and organizations to evaluate solvents. Creating safe indoor environments is an area in need of much basic research. There appears to be very little known about the cumulative effects of the many materials, products, and other environmental impacts of working in office building and living in homes constructed of relatively new materials. Science and technology can contribute by helping define risks to human health and the environment and defining cost-effective solutions to prevent risks or reduce risks to acceptable levels.

The study of toxins in the environment grew out of the post–World War II industrial age and the associated increase in use of synthetic pesticides, fertilizers, detergents and their additives, fossil fuels, derived industrial products, fissionable materials, and their generated waste products. Many innovations in biological and ecological experimentation accompanied this increased awareness; these developments dramatically improved our ability to screen for detrimental toxins in the environment, estimate toxic impacts on biological systems, and assess the risks of toxic exposures to ecosystems and the organisms that inhabit them. With the advent of these advanced experimental methods has come the need for sophisticated statistical procedures to analyze the data they generate (Piegorsch and Bailer, 1997).

The generation of household and "everyday" wastes is a major issue (Shorten et al., 1995). The National Academy of Sciences (1997) prepared a report explicitly for

use by the professional toxicologist engaged in either of two roles. The report should assist the administrator in developing and recommending strategies for testing compounds and products (mixtures) for the purpose of rendering hazard/safety assessments for human exposure. The report also should assist the toxicological investigator who translates guidelines into protocols and operational manuals for the various subspecialty areas of toxicology.

Society has only recently acknowledged that health problems can result from trace substances in our environment and that there is a need to prevent uncontrolled release of even small quantities of such substances into our environment. Environmental chemical agents can include elements and both natural and synthetic organic and inorganic compounds. The organic compounds are emphasized as a central theme and focus throughout this book, but the book is not limited to the organics, and this emphasis on organics does not reflect a lesser importance of inorganics as potential environmental human health hazards (McKinney, 1981).

A mathematical model was developed for the purpose of predicting the fate and transport of down-the-drain household chemicals in septic systems. Model simulations were in good agreement with field data for the laundry detergent builders tartrate monosuccinate (TMS) and tartrate dissuccinate (TDS). The model was also independently verified with phosphate data collected from the study site. Results from this study support that this model is satisfactory as a screening level tool for predicting the fate and transport of household chemicals in septic systems.

The principles and procedures described are applicable to testing chemicals used both inside and outside the home, such as solvents, pesticides, industrial compounds, food additives, and environmental pollutants. The important aspect is the development of design strategies to address properly whatever problems are at issue. The potential routes of human exposure and intoxication, as well as the anticipated magnitude of exposure, must be accurately determined or closely approximated before a design strategy is selected.

Risk assessment and epidemiology could be successfully combined to analyze environmental health risks. Exposure assessments estimate concentrations of toxic chemicals in the environment that could be transferred to humans by ingestion, inhalation, or dermal absorption. In the future, there will be a greater need for agreement on how best to simultaneously assess societal risks involved with damage to both ecosystems and the human population (Ruttenber, 1993).

8.1.1 Anthropogenic Chemical Products

New chemical products intended as pharmaceuticals and pharmaceutical carriers (and their important metabolites) are extensively tested under rules of the Food and Drug Administration (FDA). The FDA tests cover a wide variety of toxicity but concentrate on human effects. New discoveries intended for pest control or for use as agricultural insecticides, fungicides, or herbicides are subject to somewhat less rigorous testing required by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The FIFRA tests concentrate on predictors of human carcinogenic effects, with increasing attention to effects on "off-target" beneficial species, such as birds. Costs of testing a chemical under FIFRA can be tens of millions of dollars; costs of FDA testing can be even more.

New chemical products not under the FDA or FIDRA are covered by the Toxic Substances Control Act (TSCA). If these chemicals are intended to become articles of commerce, they are subject only to submission to the EPA of a request for a "Pre-Marketing Notice" (PMN). The EPA has 90 days to respond to such a request and often, in the absence of extensive data, relies on structure-activity relationship (SAR) predictions.

These chemicals can be subject to much more testing under the Occupational Safety and Health Act (OSHA) if they are known to be present in the workplace and a risk has been identified. In Europe, new chemicals are subject to more testing but still far less than that required for new drug or agricultural applications (National Research Council, 1996).

8.1.2 Anthropogenic Chemical Byproducts

Many anthropogenic chemicals end up in incinerators or wastewater treatment facilities. We need to be concerned about the reaction by products formed in such treatment facilities.

Chemicals that are disposed of in landfills (where they might leak from containment), are deliberately emitted (as in the case of hairspray or paint solvent), or are merely discarded will end up in the air or in surface runoff or in groundwater, or will simply reside on land.

Today, these chemicals, their degradation products, and the by-products of their production are, for the most part, investigated only when someone suggests an environmental hazard on the basis of anecdotal environmental monitoring, local tests, or calculations. Under TSCA and OSHA, much more testing of this chemical by-product can be required, once they are identified. This identification is unlikely to occur without better knowledge of what by-products might be formed from anthropogenic chemical production, and the use and effects such byproducts may have on the environment (National Research Council, 1996).

8.1.3 Long-term Effects of Chemicals

There is increasing concern about the health effects of chemicals we encounter in our daily lives. The carcinogenic properties of many compounds have been widely described, but less is known about the more subtle effects of exposure to certain substances. Damage to the endocrine, immune, and nervous systems has been observed in wildlife and laboratory animals, reflecting the need for a major epidemiological study to better assess toxic and biological effects on humans. The potential dangers have been highlighted by the National Research Council, which estimates that one-third of the chemicals that U.S. workers are exposed to could be neurotoxic. No information exists on the possible toxic effects of 80% of the industrial chemicals used in the United States, and limited information has been collected on the remaining 20 percent (Misch, 1993).

The health risks associated with ozone depletion will principally be those due to increased ultraviolet-B (UV-B) radiation in the environment, that is, increased damage to the eyes, the immune system, and the skin. Some new risks may also be introduced with the increased use of alternatives to the ozone-depleting substances (ODS). Quantitative risk estimates are available for some of the UV-B–associated

effects, for example, cataract and skin cancer; however, the data are insufficient to develop similar estimates for effects such as immunosuppression and the toxicity of alternatives. Ocular damage from UV exposures includes effects on the cornea, lens, iris, and associated epithelial and conjunctival tissues. Testing of a number of the chlorofluorocarbon (CFC) alternatives indicates that most of these chemicals have low acute toxicity, and low to moderate chronic toxicity. Some chemicals that were originally proposed as alternatives have been dropped from consideration because these tests raised concerns about toxicity and/or manufacturing difficulties. In one instance, high accidental occupational exposure was associated with liver damage, underlining the need for care in the use of these substitutes. Recent quantitative risk estimates have been developed for cataract, melanoma, and all skin cancers combined. These estimates indicate that under the Montreal Adjustments, cataract and skin-cancer incidence will peak midcentury at additional incidences of just under 3 per 100,000 and about 7 per 100,000, respectively (Longstreth et al., 1998).

A current review of the existing and projected chemical reactions in the stratosphere was given by Tang and co-workers (Tang et al., 1998).

8.1.4 Common Solvents in Cosmetics

Table 8.1 contains a list of 101 solvents commonly found in cosmetics (Ash and Ash, 1996). The list is not exhaustive, but it gives illustrates the enormous role solvents play in our lives.

8.2 Ordinary Solvent Usage

Nearly everyone uses cleaning products and deodorants and consumes food with artificial coloring and preservatives. The out-gassing of formaldehyde from furniture and flooring, chemicals released by freshly cleaned clothing, and even backyard grilling, surround us. We are all exposed.

In addition to the traditional aspects of chemical design, which focus largely on commercial usefulness and ease of synthesis, modern chemists are now expected to develop commercial chemical substances that are safe to human health and the environment, as well. The most effective way for chemists to meet this challenge is to design chemicals such that they will have minimal toxicity. There are several approaches to reducing toxicity: reducing absorption; understanding toxic mechanisms; using structure-activity relationships, retrometabolism, and isosterism; eliminating the need for associated toxic substances; and identifying equally useful, less toxic substitutes of another chemical class. A paper by DeVito provides chemists and chemical users with a strategic framework for the rational design of safer chemicals from the standpoint of pollution prevention and green chemistry (DeVito, 1996).

Since everything is composed of chemicals we have to realize that there are two sides to this story. Many, if not most chemicals, when used in appropriate amounts for the correct use, are beneficial to us. Problems develop with excessive exposure and inappropriate uses. That is why labeling is so important. We can protect ourselves from unnecessary chemical exposure only if we have the facts.

Table 8.1. Solvents found in common cosmetics.

Acetamide MEA	PPG-2 myristyl ethe propionate
Ammonium xylenesulfonate	PPG-20
α-Terpineol	PPG-24-glycereth-24
Benzyl benzoate	PPG-26
Benzyl laurate	PPG-3 methyl ether
Butyl alcohol	PPG-30
Butyl benzoate	PPG-40 diethylmonium chloride
Butyl stearate	PPG-55 glyceryl ether
C10-11 isoparaffin	PPG-9
C10-13 isoparaffin	Propylene glycol caprylate
C11-12 isoparaffin	Propylene glycol dicaprylate
C13-14 isoparaffin	Propylene glycol dicaprylate/dicaprate
Carbomer	Propylene glycol dioctanoate
Cetearyl alcohol	Propylene glycol dipelargonate
Cetearyl octanote	Propylene glycol ethyl ether
Cocoa butter	Propylene glycol ethyl ether acetate
Decyl oleate	Propylene glycol n-propyl ether
Dibutyl phthalate	Shea butter
Diethyl phthalate	Sucrose palmitate
Diisobutyl adipate	Tallow alcohol
Diisopropyl sebacate	Tridecyl neopentanoate
Dimethicone copolyol undecylenate	Walnut oil
Dimethyl isosorbide	Wheat germ oil
Dipropylene glycol	PPG-2 myristyl ethe propionate
Dipropylene glycol butyl ether	PPG-20
Ethoxydiglycol	PPG-24-glycereth-24
Ethylene glycol propyl ether	PPG-26
Formic acid	PPG-3 methyl ether
Glycereth-7 triacetate	PPG-30
Glyceryl formal	PPG-40 diethylmonium chloride
Isocetyl alcohol	PPG-55 glyceryl ether
Isocetyl salicylate	PPG-9
Isodecyl isononanoate	Propylene glycol caprylate
Isodecyl oleate	Propylene glycol dicaprylate
Isododecane	Propylene glycol dicaprylate/dicaprate
Isononyl isononanoate	Propylene glycol dioctanoate
Isooctyl stearate	Propylene glycol dipelargonate
Isopropyl laurate	Propylene glycol ethyl ether
Isopropyl palmitate	Propylene glycol ethyl ether acetate
Isopropyl stearate	Propylene glycol n-propyl ether
Isostearyl alcohol	Shea butter
Isostearyl isostearate	Sucrose palmitate
Isostearyl lactate	Tallow alcohol
Isotridecyl isononanoate	Tridecyl neopentanoate
Laneth-10	Walnut oil
Laneth-15	Wheat germ oil
Lanolin	PPG-2 myristyl ethe propionate
Lanolin oil	PPG-20
Methoxyethanol	PPG-24-glycereth-24
Methoxyisopropanol	PPG-26
Methyl benzoate	PPG-3 methyl ether
Mineral oil	PPG-30
Myristyl propionate	PPG-40 diethylmonium chloride
Neopentyl glycol dicaprate	PPG-55 glyceryl ether
Neopentyl glycol dioctanoate	PPG-9
Octyl hydroxystearate	Propylene glycol caprylate

Table 8.1. Continued.

Oleth-2	Propylene glycol dicaprylate
Oleyl alcohol	Propylene glycol dicaprylate/dicaprate
Oleyl oleate	Propylene glycol dioctanoate
PEG-10 lanolate	Propylene glycol dipelargonate
PEG-10 methyl ether	Propylene glycol ethyl ether
PEG-16	Propylene glycol ethyl ether acetate
PEG-20 lanolate	Propylene glycol n-propyl ether
PEG-20 oleate	Shea butter
PEG-4 dilaurate	Sucrose palmitate
PEG-4 dioleate	Tallow alcohol
PEG-5 lanolate	Tridecyl neopentanoate
PEG-6 methyl ether	Walnut oil
PEG-8 dilaurate	Wheat germ oil
PEG-8 oleate	PPG-2 myristyl ethe propionate
Petrolatum	PPG-20
Poloxamer 181	PPG-24-glycereth-24
Polysorbate 60	PPG-26
Potassium hydroxide	PPG-3 methyl ether
PPG-10 glyceryl ether	PPG-30
PPG-15 stearyl ether methyl ether	PPG-40 diethylmonium chloride
PPG-17	PPG-55 glyceryl ether
PPG-2 methyl ether	PPG-9

8.2.1 Public Health

Occupational and toxicological studies have demonstrated adverse health effects from exposure to toxic contaminants. Emissions data from stationary and mobile sources are used in an atmospheric dispersion model to estimate outdoor concentrations of 148 toxic contaminants for each of the 60,803 census tracts in the contiguous United States for 1990. Approximately 10% of all census tracts had estimated concentrations of one or more carcinogenic HAPs at a greater than 1-in-10,000 risk level. Twenty-two pollutants with chronic toxicity benchmark concentrations had modeled concentrations in excess of these benchmarks, and approximately 200 census tracts had a modeled concentration 100 times the benchmark for at least one of these pollutants. This comprehensive assessment of air toxics concentrations across the United States indicates hazardous air pollutants may pose a potential public health problem (Woodruff et al., 1998).

As an example of future concerns, although popular for their alleged ability to reduce wrinkles, spots, and other signs of aging, cosmetics containing α-hydroxy acids (AHAs) carry some risks. AHAs, chemicals derived from fruit and milk sugars, are thought to be milder versions of chemicals that plastic surgeons and dermatologists have long used to peel off the outer layer of skin. Little is known about the long-term side effects of cosmetic versions. Moreover, one industry-sponsored study has found that AHA cosmetic use can cause increased sun sensitivity. Furthermore, in 1997, the cosmetic industry's self-regulatory body, the Cosmetic Ingredient Review Panel, issued manufacturing guidelines for AHA products, and the FDA advised AHA users to regularly use sunscreen products (Foltz-Gray, 1992).

Both too much and too little ozone can be harmful, depending on where the ozone is. When everything is going smoothly, there is a natural balance that maintains a stratospheric ozone layer as a protective sunblock and dissipates concentrations of ground-level ozone that can harm human health and the living environment. However, the expanding world population is beginning to distort this delicate balance. Lifestyle changes are required to ensure an ozone-healthy world (Close and Greg, 1997).

8.2.2 Children

Several soil ingestion studies have indicated that some children ingest substantial amounts of soil on any given day. Although the U.S. EPA has assumed that 95% of children ingest 200 mg of soil per day or less for exposure assessment purposes, some children have been observed to ingest as much as 25–60 g of soil during a single day. In light of the potential for children to ingest such large amounts of soil, an assessment was made of the possibility for soil pica episodes to result in acute intoxication from contaminant concentrations that EPA regards as representing conservative screening values (i.e., U.S. EPA soil screening levels and U.S. EPA Region III risk-based concentrations for residential soils). For a set of 13 chemicals included in the analysis, contaminant doses resulting from a one-time soil pica episode (5 to 50 g of soil ingested) were compared with acute dosages shown to produce toxicity in humans in clinical studies or case reports. For four of these chemicals, a soil pica episode was found to result in a contaminant dose approximating or exceeding the acute human lethal dose. For five of the remaining chemicals, the contaminant dose from a soil pica episode was well within the reported dose range in humans for toxicity other than lethality (Calabrese et al., 1999).

The risk to children arising from the indoor use of pesticides has also been studied. A study by Gurunathan and colleagues in the January Environmental Health Perspectives indicated that the indoor use of pesticides can unintentionally expose small children to significant amounts of toxic chemicals, as vapors can contaminate toys and household objects that children later handle or place in their mouths (Brody, 1998).

Factors that should be considered when formulating measures to protect children from environmental health threats have been examined. Children are particularly susceptible to chemical injury before birth, as well as in their early months and years of life, when their consumption of food and drink, relative to body weight, greatly exceeds that of adults. Moreover, children's metabolic pathways are immature and are less able to detoxify potentially harmful environmental chemicals than adults. Several chemicals that are deleterious to children's health have been identified by the Agency for Toxic Substances and Disease Registry, and an EPA report has proposed a national agenda to protect children from environmental health threats (Wiant, 1997).

8.2.3 Sources of Information

A book by Lewis tries to summarize some of the available literature on a number of the most commonly used solvents in chemistry (Lewis, 1994). Solvents may have many chemicophysical properties in common, but there are also many differences in chemical structure, and in metabolism, leading to the formation of different metabolites having different toxicity. These similarities and differences may explain some of

the complexity of the findings. Thus, some symptoms and signs common to various solvents should be expected, but so should definite differences in symptomatology and the location of the major sites of action, as well as in mechanisms (Arlien-Soborg, 1992).

The ultimate objective of those working on assessing toxic hazards associated with chemicals, which must be to provide a sound body of knowledge underpinned by validated theory, is still some way off. Nevertheless, the scientist responsible for recommending acceptable or safe levels of exposure to particular substances must use to best advantage present knowledge, which, although it may be incomplete, is still considerable. Another book gives information and advice from many of those concerned with research, application and legislation relevant to toxic hazards and should materially assist in the formulation of such recommendations (Richardson, 1986).

Regarding solvents in ordinary usage, two important things to consider are how much of a product is used and how often it is used. For instance, a teaspoon of vinegar is safe to use on a salad, but if a person drank several cupfuls daily it could cause serious harm. So we can say "the dose makes the poison." In everyday products the amounts used are at safe levels for the average person. The consumer would usually not apply or eat enough of the chemical to be hazardous. However, when misused, used by children in appropriate amounts, or by people who have particular allergies or sensitivities, there is reason for concern.

Chemical research is an ongoing activity, with new information available everyday. As a result, the present book does not indicate everything known about every chemical. More information on each chemical is available in books like those listed in this book's bibliography, via online computer databases like Info Trac and Medline, and from poison control centers or a library.

8.3 Household Solvents

Interpretation of ecotoxicity is still more of an art than a science. Perhaps the greatest advances in this area will come from increasing understanding of the structure-activity correlations for chemicals. However, further effort is necessary to integrate the wide range of different types of assessment currently employed, which range over almost every scientific discipline. In the strictest sense, the laboratory methods described can permit only comparative evaluation of chemicals under the test conditions. Extrapolation from laboratory results to predict what will happen when chemicals enter the natural environment must be improved (Duffus, 1986).

Household Hazardous Waste (HHW) is defined by the U.S. EPA as solid wastes, discarded from homes or similar sources, that are either hazardous wastes or wastes that exhibit any of the following characteristics: ignitability, corrosivity, reactivity, or toxicity. A significant fraction of HHW is generated by home mechanics who use such products as motor oil, cleaners and solvents, refrigerants, and batteries. The results indicate that most of the survey respondents perceive automotive products to pose significant health and environmental risks, and they tend to dispose of these wastes in an environmentally conscious manner. There is quite often a discrepancy between human perception and scientific reality (see table 8.2) (Shorten et al., 1995).

Table 8.2. Examples of common household solvents.

Solvent	CAS Number	Use	Products	Health Effects
Acetal	105-57-7	Solvent and odorant	Cosmetics, jasmine perfumes, fruit flavors	Highly flammable; moderately toxic: narcotic
Acetaldehyde	75-07-0	Solvent and flavoring	Perfume, food, cosmetics, adhesives, and glues	Moderately toxic: skin and eye irritant
Acetic Acid	64-19-7	Flavor enhancer, pickling agent, and solvent	Many foods, skin bleaching cosmetics, hair coloring products	Moderately toxic: strong irritant to skin and tissue; eye irritant
Acetone	67-64-1	Solvent; to clean and dry	Nail polish remover, markers, airplane glue, solvent, fabric cement, cleaning fluids, paint varnish, lacquer	Flammable; moderately toxic: skin and eye irritant; narcotic
β-hydroxy butyraldehyde		Solvent	Perfume, dyes, sedative (drugs)	Skin irritant in concentrated form
Amyl Acetate	628-63-7	Solvent or Flavoring agent	Nail polish, polish remover, leather polish, shoe polish, perfume odorant, food	Systemic effects; mildly toxic: skin and eye irritation; flammable
Amyl formate	638-49-3	Solvent, odorant, Flavoring	Films, coating, leather, perfume	Flammable; toxic by swallowing and breathing; skin irritant

8.4 Recreational and Transportation Solvents

Lior reviews some leading novel energy conversion approaches which are aimed at improving power generation efficiency and/or reducing harmful emissions. Included would be solvent use and conservation (Lior, 1997).

Thermophotovoltaic systems convert the radiant energy produced by fuel combustion directly into electricity. Such systems can potentially attain high overall conversion efficiencies. Because they may use renewable as well as fossil fuels, they permit a smooth pathway for an environmentally benign method of electrical energy generation (Catalano, 1996).

Many changes have been made to fuel composition. A number of these changes have been made with the intention of improving the environment by altering exhaust emissions. On some occasions it appears that refiners may have removed one hazard only to create another. A typical example is the introduction of oxygenates at the expense of aromatics. This will reduce benzene and aromatic emissions but will increase aldehyde emissions. The use of catalytic converters minimizes many of these fuel effects but in many countries the catalytic vehicle population is small and these fuel changes may have significant effects if the fuels are used in cars not fitted with exhaust treatment devices. Concern grows regarding vehicular emissions as the number of vehicles continues to rise. It becomes even more important that we understand

the environmental effects that changing fuel compositions will have. The increase in the use of aromatics in fuel appears to be particularly indicated. This leads to an increase in the known carcinogen benzene and polynuclear aromatics, as well as contributing to photochemical smog. Yet the approach of reducing aromatics and increasing oxygenates may not necessarily be the best option for vehicles without some form of exhaust treatment system. Additionally, raising the alkene content of fuel has been shown to increase 1,3-butadiene emissions but increasing the alkane concentration leads to the formation of photochemically active alkenes. Solving the problem of making fuel changes to give the lowest-risk emissions will require the many competing interactions in fuel systems to be understood so the best, most environmentally benign, solution can be achieved (McGinty and Dent, 1995).

Fuel cells and other advanced electric-generation technologies have not experienced a record of successful commercialization efforts. To lower costs for these technologies requires substantial production volumes with a significant investment in manufacturing facilities, all dependent on developer confidence in the ultimate market. Yet, market acceptance by buyers requires an adequate demonstration of technical performance and an assurance that these lower costs can be reached. In addition to this fundamental commercialization challenge, there are significant external factors that are greatly influencing the market's (utility's) future implementation of new alternative energy-generating technologies. The factor that has possibly the greatest impact today is the public demand for environmentally benign and renewable resource technologies. There is a growing trend of involvement by consumers, regulators, and intervenors in the business and utility industry that is shifting the economic playing field by which industries make resource decisions. Competitive requirements to reduce the cost of utility service are leading to business decisions that provide both opportunities and problems for increased use of alternative energy-generating technologies, like fuel cells, and/or renewables, such as wind and solar photovoltaics. Bringing new energy technologies to market is very expensive and this financial burden cannot be shouldered by the market, manufacturers, or federal government alone. Further, for the market to assume a key position in early commercialization, the technology must offer a strategic and competitive advantage to early buyers. In order to break this problematic cycle of investments depending on market assurance and of market reluctance until cost goals are met, fresh approaches must be sought to address the unique challenges of each commercialization effort. Market-driven collaborations in which potential buyers, such as electric utilities, work together to define and implement a commercialization program that meets the market's requirements, with one or more suppliers, and with the federal government as a catalyst, provide perhaps the best opportunity for further commercialization of renewable energy and energy-efficient technologies. The key is that the market—not government agencies—determines the objectives and manages the resulting program (Serfass et al., 1994).

Transportation is an industry that is dependent upon solvents. There is an application of fuzzy logic to the risk assessment of the transport of hazardous materials by road and pipeline in order to evaluate the uncertainties affecting both individual and societal risk estimates. In evaluating uncertainty by fuzzy logic, the uncertain input parameters are described by fuzzy numbers and calculations are performed using fuzzy arithmetic; the outputs will also be fuzzy numbers. This work is an attempt to justify some of the questions the use of fuzzy logic in the field of risk analysis stimu-

lates. Test results of combined uncertainty and sensitivity analysis in the risk evaluation of a toxic gas release show which effect each uncertain input has on the output uncertainty (Bonvicini et al., 1998).

Although there have been several studies examining emissions of criteria pollutants from in-use alternative fuel vehicles (AFVs), little is known about emissions of hazardous air pollutants (HAPs) from these vehicles. Winerbake and Deaton (1999) explore HAP tailpipe emissions from a variety of AFVs operating in the federal government fleet and compares these emissions to emissions from identical vehicles operating on reformulated gasoline. Emissions estimates are presented for a variety of fuel/model combinations and on four HAPs (acetaldehyde, 1,3-butadiene, benzene, and formaldehyde). The results indicate that all AFVs tested offer reduced emissions of HAPs, with the following exceptions: ethanol fueled vehicles emit more acetaldehyde than RFG vehicles, and ethanol- and methanol-fueled vehicles emit more formaldehyde than RFG vehicles. Results can lead to more accurate emissions factors for HAPs, thus improving HAP inventory and associated risk estimates for both AFVs and conventional vehicles.

8.4.1 Household Solvents

Zero-emission mandates are opening commercial markets for battery-powered electric vehicles. Although these vehicles do not produce tailpipe emissions, recent assessments have raised concerns that emissions generated by recycling lead-acid batteries used in electric vehicles may create a major environmental impact. The authors used an abridged life-cycle assessment, which produces easily comprehended information about each life stage of a product, to analyze environmental impacts associated with recycling and waste management of four battery technologies likely to be used in electric vehicles over the next 5–10 years. They ranked recycling and waste-management impacts and emphasized environmental consequences associated with design factors. Their results suggest that nickel-metal hydride batteries are the most environmentally benign; however, an infrastructure for recycling these batteries does not exist. Lead-acid and nickel-cadmium batteries are highly recyclable, but the question of significant toxicity remains (Steele and Allen, 1998).

8.4.2 Hygiene Solvents

The use of biotechnology for the production of specialty chemicals, such as those used by the pharmaceutical industry to make chiral drugs, is a reality currently being pursued by many companies. A significant advantage that biocatalysts offers is high efficiency and high selectivity. Although the cost of using biocatalysts today is also high, this cost can be absorbed by the high selling price that the final product (e.g., a drug) commands on the market. The use of biocatalysts can have an even greater environmental impact in the production of commodity organic chemicals because of the sheer volume of toxic chemicals generated from the current use of fossil feedstocks. Unfortunately, unlike specialty chemicals, profit margins in commodity chemical production are very narrow; processes must therefore be as economical as possible to compete with the lower up-front cost of well-entrenched petrochemicals. Currently, this is not the case (Webster et al., 1996).

8.4.3 Food, Cooking, and Nourishment Solvents

The safe and effective use of chemicals within the live production phases of the poultry industry requires the implementation of integrated health programs. Chemical programs will vary with regard to phase, intended usage, and method and frequency of application. The term "chemicals" herein presented excludes drugs and nonnutritive feed additives, with primary emphasis on sanitation products (i.e., detergents, disinfectants, sanitizers, deodorizers, descalers, and possible combinations), and pesticides (i.e., insecticides and rodenticides). Products that are effective, environmentally and user friendly, and applied within label specification will provide for safe, economical, and long-term success of poultry health programs. Such programs must be supported by management and maintained through education and product stewardship administered cooperatively with chemical suppliers, technical consultants, and end users (Eckman, 1994).

8.5 Evaluating Chemistries

Pollution prevention has become a hot topic in the last few years and it is being touted as a way of achieving "sustainable development." A methodology should encourage agencies to use less hazardous products and to minimize the number of products to keep in inventory. Additionally, the method may be used to identify safer household products (Quan, 1996).

8.5.1 Cleaner Technologies Substitutes Assessment

This section presents the methods and resources needed to conduct a Cleaner Technologies Substitutes Assessment (CTSA), a methodology for evaluating the comparative risk, performance, cost, and resource conservation of alternatives to chemicals currently used by specific industry sectors (Kincaid et al., 1996). The CTSA methodology was developed by the U.S. EPA Design for the Environment (DfE) Program, the University of Tennessee Center for Clean Products and Clean Technologies, and other partners in voluntary, cooperative, industry-specific pilot projects.

A publication by Kincaid et al. (1996) is intended for trade associations, businesses, citizen groups, or government agencies interested in learning about, initiating, or participating in a CTSA. The goal is to provide the CTSA methodology to anyone who can benefit from the increased efficiency and reduced environmental risk that results from using a cleaner product, process, or technology. The full article presents sources of data, analytical models, and previously published guidance that can be used in a CTSA. A companion publication, "Design for the Environment (DfE): Building Partnerships for Environmental Improvement" (EPA, 1995a), describes other aspects of DfE industry projects, including how DfE projects are organized and how DfE partnerships disseminate project results.

8.5.2 Background

Businesses operating in the twenty-first century face a variety of competing demands—maintaining high quality at low cost, staying competitive in a global mar-

ketplace, and meeting consumer preferences and regulatory demands for reduced environmental impacts. Designing for the environment is an effective strategy for organizing and managing these challenging demands.

The CTSA methodology has grown out of DfE industry projects, which are cooperative, joint efforts with trade associations, businesses, public-interest groups, and academia to assist businesses in specific industries to select more environmentally sound products, processes, and technologies. A CTSA does not recommend alternatives or make value judgements concerning an alternative. Instead, the goal is to provide business and individuals with information to make environmentally informed choices and design for the environment.

8.5.2.1 EPA's Design for the Environment Program

The DfE Program in EPA's Office of Pollution Prevention and Toxics was created in 1991 to promote the incorporation of environmental considerations into the design and redesign of products, processes, and technical and management systems. By developing and providing businesses with information on designing for the environment, the program aims to encourage pollution prevention and efficient risk reduction in a wide variety of activities. Under the DfE Program, EPA works through voluntary partnerships with industry, professional organizations, state and local governments, other federal agencies, and the public, including environmental and community groups.

The DfE Program aims to turn pollution prevention into both a corporate and an environmental asset, by helping businesses incorporate environmental considerations into the product or process design and decision-making process. The program has three goals:

- Encourage voluntary reduction of the use of specific hazardous chemicals by businesses, governments, and other organizations through actual design or redesign of products, processes, and technical and management systems.
- Change the way businesses, governments, and other organizations view and manage for environmental protection by demonstrating the benefits of incorporating environmental considerations into the up-front design and redesign of products, processes, and technical and management systems.
- Develop effective voluntary partnerships with businesses, labor organizations, government agencies, and environmental/community groups to implement DfE projects and other pollution prevention activities.

DfE projects include three distinct project types:

- Institutional projects include environmental accounting, curriculum development, green chemistry, and insurance projects.
- Cooperative industry projects are joint efforts with trade associations, businesses, public interest groups, and academia.
- Cooperative government projects are joint efforts with government organizations to promote the use of environmentally preferred products by organizations.

8.5.2.2 What Is a Cleaner Technologies Substitute Assessment?

The CTSA methodology is a means of systematically evaluating the comparative human health and environmental risk, competitiveness (e.g., performance, cost, etc.), and

resource conservation of traditional and alternative chemicals' manufacturing methods and technologies. A CTSA document is the repository for the technical information developed by a DfE industry project, including risk, performance, cost, and resource conservation data. A use cluster is a product- or process-specific application in which a set of chemical products, technologies, or processes can substitute for one another to perform a particular function.

A CTSA does not recommend alternatives. Instead, the goal is to promote informed decisions that integrate risk, performance, and cost concerns by providing businesses with easily accessible information.

8.5.3 Steps in a Cleaner Technologies Substitutes Assessment Project

8.5.3.1 Identifying Substitutes

A substitutes *tree* is developed. This is a graphical depiction of the substitute or alternative chemical products, technologies, or processes that form the use cluster and their relationship to each other with the functional category defined by the use cluster.

8.5.3.2 Information Modules

A CTSA uses information modules to develop as complete and systematic a picture as possible of the comparative risk, competitiveness (i.e., performance, cost, etc.), and resource conservation of the substitutes in a use cluster. An information module is a standard analysis or set of data designed to build on or feed into other information modules to form an overall assessment of the substitutes.

Figure 8.1 describes the basic process for developing a CTSA. The technical work typically starts with the collection of basic chemical properties and process information, followed by the collection of risk, competitiveness, and conservation data. At the same time, the project team develops methodologies for data analysis to ensure that all necessary data are collected. The next step is to analyze the collected data to determine the relative human health and environmental risk, competitiveness, and resource conservation of alternatives.

Since the CTSA process is applicable to numerous industry sectors, the module descriptions were developed to provide basic information suitable for a wide audience with a broad range of information needs (see fig. 8.2 and tables 8.3 through 8.8).

8.5.3.3 Benefits of a Cleaner Technologies Substitutes Assessment

DfE partnerships developed the CTSA methodology to help business decision-makers achieve the tangible benefits that result from using a cleaner product or technology. CTSA results give businesses the information needed to improve their bottom line by evaluating and documenting voluntary changes a business can make to prevent pollution and reduce risk. Pollution prevention often lowers cost by reducing the amount of materials used in production processes, the amount of waste streams that must be treated and disposed, and by improving worker health and safety. In addition, a CTSA

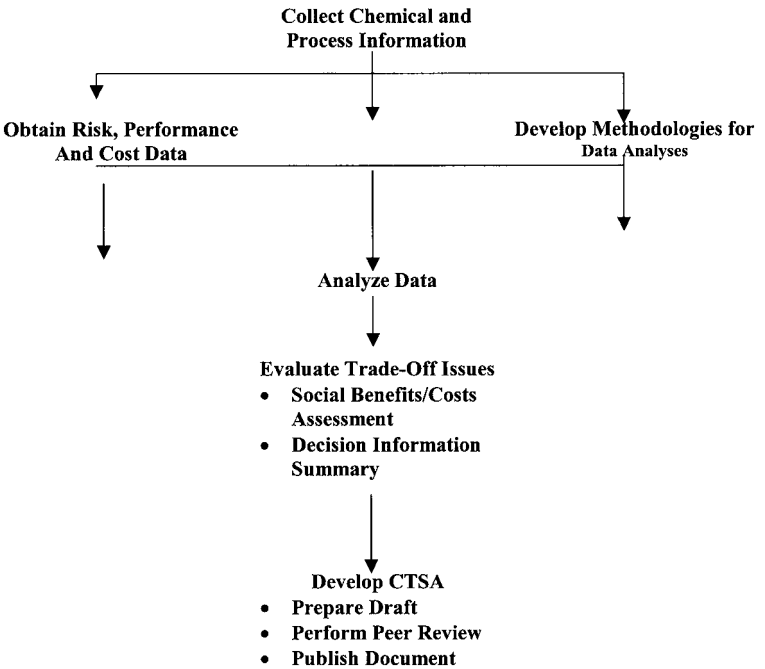


Figure 8.1 Steps to Develop a CTSA.

provides the necessary information for companies to make informed business decisions that may reduce their regulatory burden or potential liability costs. Also, companies that make voluntary changes to prevent pollution or reduce risk may enjoy increased acceptance and market share from environmentally conscious consumers. Businesses that participate in voluntary DfE initiatives demonstrate their commitment to continuous environmental improvement. Company employees involved in day-to-day operations ensure the project team understands the process constraints that need to be considered in the design of environmentally preferable options. Stakeholder communities outside the company provide unique perspectives and ideas to broaden the evaluation beyond standard industry concerns.

CTSA results also promote environmental competitiveness. Many companies are discovering that proactive environmental business policies are necessary to remain competitive in today's global marketplace. In addition to the benefits of an improved company image, businesses are finding that they can no longer afford to waste energy or other precious resources or pollute the environment.

8.5.4 Value of CTSA

Stakeholder partnerships promote consensus options or solutions to address complex environmental problems that are far more effective and productive than those obtained by any group acting alone.

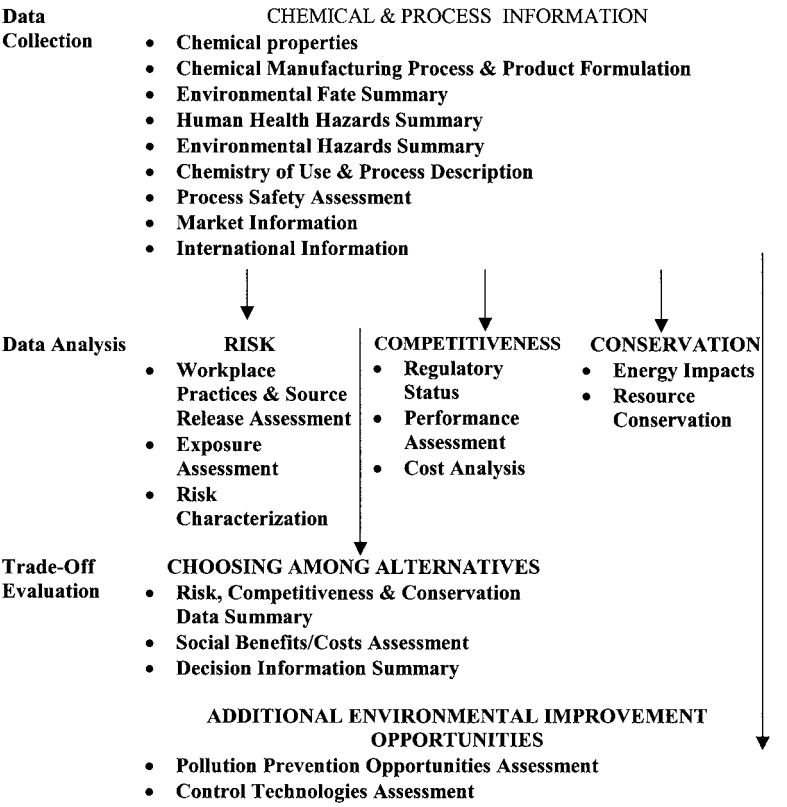


Figure 8.2 CTSA Information Flows.

1. Industry
   a. perspective on industry concerns and priorities
   b. knowledge of industry infrastructure
   c. expertise and data on industry technologies, products, practices, cost, and performance
   d. access to industry communication channels and networks
   e. industry credibility
2. Research/Education
   a. expertise and facilities for:
      i. research and analysis
      ii. tests and demonstrations
      iii. information/technology transfer
      iv. training resources and expertise
   b. public credibility
3. Public Interest Groups
   a. perspective on constituents' concerns
   b. access to channels and networks for communicating to constituents

Table 8.3. Overview of each of the information modules: Chemical and process information.

Overview of CTSA Information Modules		
Component	Module	Overview
Chemical & process information	Chemical properties	The chemical and physical properties of a substance are characteristics which identify it from other substances. The physical and chemical characteristics of the chemicals in the use cluster are detailed.
	Chemical manufacturing process & product formulation	The chemical manufacturing process & product formulation module describes: 1) the process for manufacturing the chemicals in the use cluster; and 2) the chemical product formulation process, if applicable.
	Environmental fate summary	The environmental fate of chemicals describes the processes by which chemicals move and are transformed in the environment. Some of the processes that should be addressed include: persistence in air, water, and oil; reactivity and degradation; migration in groundwater; removal from effluents by standard wastewater treatment methods; and bioaccumulation in aquatic or terrestrial organisms.
	Human health hazards summary	Human health hazards assessment is the process of identifying the potential effects that chemical may have on humans who are exposed to it, and of determining the levels at which these effects may occur. Human health toxicity data are compared with data from the exposure assessment module to assess human health risk in the risk characterization module.
	Environmental hazards summary	Environmental hazards assessment is the process of identifying the adverse effects that a chemical may have on organisms in the environment. Currently, the CTSA process for environmental hazards assessment focuses on aquatic toxicity.
	Chemistry of use & process description	Chemistry of use & process description module identifies: 1) the chemical/physical properties which contribute to the effectiveness of the chemicals in the use cluster; and 2) the process in which the chemicals are used.
	Process safety assessment	The process safety assessment module screens potential chemical substitutes to determine if they could potentially pose a safety hazard in the workplace.
	Market information	The market information module contains economic data used to evaluate the importance of the target industry sector to the overall market and conversely, the economic importance of the alternatives to the industry sector.

Table 8.3. Continued.

Overview of CTSA Information Modules		
Component	Module	Overview
	International information	The international information module collects data pertaining to the use or production of alternatives in other parts of the world, the impact of international trade on the selection of alternatives, and the impacts of switching to an alternative on international trade.

Table 8.4. Overview of each of the information modules: Risk.

Risk	Workplace practices & source release assessment	The workplace practices & source release assessment module identifies: 1) the workplace practices that contribute to environmental releases and worker exposure; and 2) the sources, amounts, and characteristics of environmental releases
	Exposure assessment	Exposure assessment is the quantitative or qualitative evaluation of the contact an organism (human or environmental) may have with a chemical or physical agent, which describes the magnitude, frequency, duration, and route of contact.
	Risk characterization	Risk characterization (also referred to in the CTSA process as risk integration) is the integration of hazard and exposure information to quantitatively or qualitatively assess risk.

Table 8.5. Overview of each of the information modules: Competitiveness.

Competitiveness	Regulatory status	The regulatory status module determines the statutes and regulations that govern a particular chemical or industrial process.
	Performance assessment	The performance assessment module measures how well a substitute performs to meet the functional requirements of the use cluster.
	Cost analysis	The cost analysis module identifies the costs associated with the baseline process, as well as suitable substitutes, and calculates comparative costs between the baseline process and the substitutes.

Table 8.6. Overview of each of the information modules: Conservation.

Conservation	Energy impacts	Energy consumption, either during the manufacture of a chemical or the use of a substitute product, process, or technology can vary with a selected chemical or process change.
	Resource conservation	Resource conservation is the process of selecting and using products, processes, or technologies that minimize the overall consumption of resources while effectively achieving a desired function.

Table 8.7. Overview of each of the information modules: Additional environmental improvement opportunities.

Additional environmental improvement opportunities	Pollution prevention opportunities assessment	Pollution prevention is the process of reducing or preventing pollution at the source through changes in production, operation, and raw materials use.
	Control technologies assessment	Control technologies are methods, which can be used to minimize the toxicity and volume of pollutants.

Table 8.8. Overview of each of the information modules: Choosing among alternatives.

Choosing among alternatives	Risk, competitiveness & conservation data summary	The risk, competitiveness & conservation data summary module organizes data from the risk, competitiveness, and conservation components of a CTSA together with data from the process safety assessment, market information, and international information modules to: 1) identify the tradeoff issues associated with any one substitute; and 2) compare the tradeoff issues across substitutes.
	Social benefits/costs assessment	Social benefits/costs assessment is the process of qualitatively and systematically evaluating the impacts made on all society by individual decisions.
	Decision information summary	The decision information summary is the final module of a CTSA. It combines the results of the risk, competitiveness & conservation data summary with the social benefits/costs assessment to identify the overall advantages and disadvantages of the baseline and the substitutes from both an individual business perspective and a societal perspective.

   d. risk data
   e. ideas about alternatives
4. Government
   a. perspective on government and public concerns and priorities
   b. risk expertise and data
   c. regulatory information
   d. public credibility
   e. ability to mediate divergent stakeholder interests
   f. ability to convene stakeholder groups

A goal is to provide businesses, public interest groups, and other stakeholders the information they need to perform comparative evaluations with or without the direct participation of the EPA.

8.5.4.1 Why Participate in a Cleaner Technologies Substitutes Assessment?

An unforeseen consequence of recent regulation is that pollutants are often shuffled from one environmental medium to another, with little net environmental improvement. In other cases, regulation has caused industry to substitute materials, which in turn may become subject to regulation. While the current regulatory system has reduced risk and improved the environment, it has in some cases been inefficient and unnecessarily costly in achieving environmental goals.

DfE partnerships developed the CTSA methodology to help business decision-makers achieve the tangible benefits that result from using a cleaner product or technology:

- CTSA results can improve businesses' bottom line: A CTSA provides a systematic methodology for evaluating voluntary changes to prevent pollution and reduce risk. A CTSA provides the necessary information for companies to make informed business decisions that may reduce their regulatory burden or potential liability costs or avoid regulation altogether.
- CTSA projects promote effective, efficient change through constructive partnerships: Businesses that participate in voluntary DfE initiatives demonstrate their commitment to continuous environmental improvement. The result is effective and efficient change founded in the requisite expertise to identify innovative solutions.

Environmental evaluation and setting priorities for change involve value judgements. No simple metric exists that encompasses the range of environmental issues or addresses the concerns of all stakeholders.

- CTSA results promote environmental competitiveness in a global marketplace: Companies and businesses throughout the world must practice proactive environmental improvement to remain competitive in today's global marketplace.

In short, government, industry, and public interest groups alike are recognizing that voluntary changes to reduce risks by preventing pollution are good for business and good for the environment.

9

Green Solvents: Ecology and Economics

9.1 Place of Green Solvents in Chemistry Practices

The use of solvents in the chemical industry and chemical-related industries is ubiquitous. In 1991, the production of the 25 most commonly used solvents was more than 26 million tons per year. According to EPCRA section 313 data, of the chemicals and chemical categories tracked by the program in 1994, five of the top 10 chemicals released or disposed of were solvents, and included methanol, toluene, xylene, methyl ethyl ketone, and dichloromethane. The total quantity of these chemicals released or disposed of was over 687 million pounds, which accounts for 27 per cent of the total quantity of TRI-listed chemicals released and disposed of in that year (Sullivan, 1997).

There is an increased awareness of the need to reduce or eliminate toxic chemical waste and/or byproducts that arise in the course of chemical synthesis and manufacture. A fundamental change in the philosophy of chemical synthesis, processing and usage is needed wherein the priority is placed upon health and environmental impact rather than just the efficiency associated with the chemical use. Certainly one aspect of synthesis in which dramatic advances in pollution prevention can be realized entails replacing many of the toxic, environmentally threatening solvents utilized in most chemical processes with nontoxic, "environmentally benign" alternatives (Tanko et al., 1994). Supercritical carbon dioxide ($SCCO_2$), as we have seen, represents an inexpensive, environmentally benign alternative to conventional solvents for chemical synthesis (Morgenstern et al., 1996). It has also been used in processes such as spraying paints and other coatings, which reduces atmospheric emissions of environmentally harmful volatile organic compounds (VOCs) (Morgenstern et al., 1996).

As will happen, for example, with perfluorotriethylamine, a substance that is a good alternative reaction medium may be found for reactions and it can be easily recycled by simple extractive workup (Nakano and Kitazume, 1999). One of the most important issues in twenty-first century scientific society is the environmental problem. Thus far, there have been increasing demands for substitutes for toxic and/or harmful solvents like CH_2Cl_2. Recently, inert and less toxic fluorous (perfluorinated) fluids have been recognized and are attracting attention as new alternative solvents (Fish, 1999). This fact shows the need to survey the scope and limitations of the utility of these liquids as alternative reaction media for reactions, which are of great current interest due to their unique reactivities and selectivities.

Assuredly, one way to reduce pollution at the source is to design safer chemicals. Chemicals that persist in the environment remain available to exert toxic effects and may bioaccumulate. Since microbial degradation is the major loss mechanism for most organic chemicals in soil, water, and sewage treatment, biodegradability should be included as a factor in solvent considerations along with function and economics. Biodegradability has been an important consideration for down-the-drain consumer products like laundry detergents for more than 40 years, but not for chemicals used mainly in commerce. The relationship between molecular structure and biodegradability is generally well enough understood to make its application feasible in solvent selection (Boethling, 1996). We must extend the benign-by-design concept to commercial chemicals because:

- Production volume and thus release may increase with time;
- New uses may develop and with them, the potential for greater release;
- We cannot know in advance all of the possible toxic effects of released chemicals.

9.2 Green Solvents: Epilogue

Solvent replacement technology is a diverse field that affects many industries. It is a field driven by regulations implemented to protect our environment and health rather than for purely economic or scientific reasons. However, these regulations often translate to economic incentives and have given rise to many exciting and innovative technologies that otherwise might never have been developed.

In the cleaning and coatings industries, heavy government regulation has prompted the development of greener products, although the selection process for these new commercial products seems to be one of trial and error until a cost-effective solution is found. For synthetic applications, regulations are not as stringent, although it is recognized that significant processing advantages may be gained by using alternative solvents for existing processes or by developing new chemical routes to desired products that can exploit more benign solvent systems. Rational design and implementation of these solvents can lead to significant decreases in the environmental burden associated with solvent losses through vapor emissions and aqueous discharge streams and in energy usage through the simplification of process flow-sheets. Water-based systems are gaining attention, particularly in separations operations where in some

instances aqueous surfactant and polymer solutions show considerable promise in emulating conventional organic solvents. These technologies, although many still in their infancy, seem promising as greener alternatives in their niche applications.

Finally, it is clear that many experimental efforts do not take advantage of the wealth of available computer databases and simulation techniques that may aid in selecting an appropriate replacement with minimal testing. The problem of finding suitable solvent substitutions has led to the development of several computer programs and databases to assist in the process. Of these computer-assisted techniques, several programs are publicly available, and for others the algorithms have been described. The literature contains several examples of how these tools have been used to aid researchers in the selection of solvent alternatives for a number of applications. Specific tools have been developed to assist in the molecular design of solvent replacement molecules, to predict physical properties from molecular structure, to predict activities such as toxicity and carcinogenicity, and to assist in the design of alternative synthetic pathways.

It is important, however, to remember that there is a great danger in seeing technology alone as the answer to the environmental crisis. In fact, the idea that new technology is the solution to all our problems is central to the faulty way of thinking that created the crisis in the first place.

Unless we come to a better understanding of both the potential and the danger of technology, the addition of more technological power simply ensures further degradation of the environment, and no matter what new technologies we discover, no matter how cleverly and efficiently we manage to get them into the hands of people throughout the world, the underlying crisis will worsen unless, at the same time, we redefine our relationship to the environment, stabilize human population, and use every possible means to bring the earth back into balance (Gore, 1992).

Still, the dissemination of new, appropriate technologies will likely be critical to our success in saving the environment. Individuals, corporations, social institutions, even entire cultures, adapt to the requirements of their technologies, in the process making such large investments of wealth, effort, time, and experience as to render any thought of change impractical or even unimaginable. And the elaborate web of economic incentives and disincentives that grow up around these technologies and their related activities serves as a further barrier.

New technologies should not be embraced too eagerly, either; careful study of their environmental impact is essential. CFCs offer a case in point. Originally developed as substitutes for an earlier generation of chemicals that were harmful on contact, CFCs were determined to be nontoxic before they were introduced. Ironically, they do not react chemically to human contact because of their stability as molecules, which also enables them to float steadily upward—unimpeded by any transforming reaction in the lower atmosphere—until they rise all the way to the stratosphere, where the sun's ultraviolet rays slice them apart and touch off the destruction they cause to the ozone layer. Although no amount of research can determine every possible impact of a technology, our experience with CFCs reminds us of the importance of caution when marveling over the magical powers of any new tool or technology.

During the debates over the Montreal Protocol, spokesmen for the CFC industry said that it was futile for the world to expect substitutes anytime soon; the good news, however, is that—for most uses—replacement chemicals are already being found.

Moreover, under the protocol, the substitutes will be made available to developing countries, which will ensure that this technology spreads as rapidly as possible.

Green chemistry and the design and development of green solvents and processes, as described in the chapters of this book, follow the same tradition of scientific discovery and understanding that has characterized chemistry from its origins. Green chemistry simply utilizes the information that is now available to the scientific community about the toxicity and other hazards posed by certain chemicals in order to fully evaluate the negative as well as positive impact of the chemistry being designed. Databases of information on the hazardous properties of chemicals have only recently been available. It is the responsibility of chemists and the chemical community to use this information.

Just as chemists are needed to fully understand the nature and source of environmental problems that result from certain chemicals of concern released to the environment, chemists are also required to use that understanding in preventing problems from occurring in the first place. For a wide array of chemicals, the activity of a chemical of concern in the environment can be related to the molecular structure of the chemical, that is, how the atoms of the molecule are connected. Through a combination of knowledge of the nature of a chemical's hazardous properties with the ability to manipulate the chemical's structure, chemists possess the ability and skill to mitigate the hazard.

The presentations in this book have provided material that will enable the better-informed selection of solvents. This selection will in turn lead to the selection of chemicals that will have reduced hazardous properties, can lead to reduced waste generation, improved product selectivity and reaction efficiency, and more prudent use of quantities.

9.3 Economics and Ecology

The economic evaluation of engineering projects typically involves estimation of equipment, installation, raw material, energy, and maintenance costs. Disposal and pollution control costs are often factored into these calculations in determining economic rates of return, but other regulatory and social costs are not. These evaluations generally overlook some of the costs of waste generation. A more complete accounting of environmental costs is referred to as *total cost assessment* (Allen and Rosselot, 1997). In this work they identified four types of costs, labeled tier 0, tier 1, tier 2, and tier 3. Tier 0 costs are the "usual" costs that are included in a conventional analysis of a project. Tier 1 costs include permitting, reporting, monitoring, manifesting, and insurance costs and are often referred to as "hidden" costs because they are usually treated as overhead costs and are not directly charged to a project. Waste-disposal costs are sometimes treated as overhead costs as well. Tier 2 costs include future liabilities, which are extremely difficult to accurately evaluate. Even more difficult to evaluate are tier 3 costs, which include consumer responses, employee relations, and public image. All four cost tiers provide information for financial analysis methods, where measures such as rate of return and payback periods are evaluated.

Marvin (1997) explored the relationship between telecommunications systems and urban environmental policy. It challenged the powerful, and often taken for granted,

assumption that telecommunications improve the environmental performance of cities because the technologies are "inherently environmentally benign" and that they simply "substitute" for travel, inevitably leading toward the dematerialisation of the contemporary city. Instead the paper argues that telecommunications raise serious environmental problems and act as powerful materializers, particularly as a generator of new demands for travel. It shows that the environmental implications of telecommunications are undoubtedly move complex and contradictory than is often assumed. This will be true as green chemistry spreads.

9.3.1 Evaluating Hidden Costs

As mentioned above, tier 1 costs are often charged to overhead accounts, and as a consequence are regarded as "hidden." As a result, very simple opportunities for waste reduction, and therefore cost avoidance, are sometimes not exploited. For example, replacing an environmentally hazardous material with a more benign alternative may be difficult to justify if there are not direct cost savings. However, if the substitute material eliminates the need for reporting in the TRI, as well as the need for manifesting residues that are regulated under the Resource Conservation and Recovery Act, the actual cost savings associated with the alternate material may be substantial.

9.3.2 Less Tangible Costs

The least tangible of the economic factors that might be considered in evaluating pollution prevention projects are grouped into the third tier of costs. Consumer responses to improved product quality or improved corporate image, employee responses to improved environmental stewardship, and potential improvements in worker health and safety due to pollution prevention could all be considered. Such factors are even more difficult to quantitatively evaluate than tier 1 and tier 2 costs.

9.3.3 Comprehensive Methods of Economic Analysis

Several well-documented methodologies for economic evaluation of pollution prevention projects are publicly available. Some have been critically reviewed (Tellus Institute, 1991).

9.4 Future Steps

9.4.1 Computer Simulations

As computers become more pervasive and increasingly powerful, specialized programs and databases are being developed to assist in a wide variety of research efforts. This is true in the search for solvent alternatives, and in this section we review the application of computers to solvent substitution studies and cover computer-aided molecular design of new solvents, methods developed for the prediction of physical properties, methods for predicting less precise chemical characteristics such as toxicity and carcinogenicity, and computer-aided design of alternative synthetic pathways.

These tools may assist the scientist in two ways. First, the design process can be optimized with the use of more complex constraints than could otherwise be handled. Second, in some cases the need for time-consuming and costly physical or chemical property measurements can be eliminated with the use of estimation techniques for properties of interest.

New manufacturing software could give product designers instant information on how to avoid pollution. Called the Expert Process Advisory System, the software's aim is to instantaneously present designers with information about the environmental ramifications of their design options. The "expert" part of the software is a database containing wisdom harvested from Boeing's most experienced design engineers, together with data about environmental regulations and life-cycle costs (Betts, 1998).

New process simulation tools being developed for pollution prevention have been discussed by Hilaly and Sikdar (Hilaly and Sikdar, 1996). A process simulator is a large computer program that simulates chemical and related operations and provides an overall integrated mathematical model of the commonly used process units. Although all of the simulators furnish a user-friendly interface, only some furnish optimization tools. Among the new methodologies being developed for pollution prevention are the Clean Process Advisory System, the Waste Reduction algorithm, the Program for Assisting the Replacement of Industrial Solvents, the Mass Exchange Network methodology, and the Environmentally Acceptable Reaction methodology. A recent workshop on improving process simulation tools for pollution prevented conducted by the U.S. EPA, the Department of Energy, and the American Institute of Chemical Engineers was summarized.

Spent solvents constitute a major source of pollution in the chemical and pharmaceutical industries. Much of this pollution can be prevented by substituting solvents that are more environmentally compatible or possess higher performance, thus reducing the amount used. However, identifying replacement solvents is often a difficult process performed in an ad hoc manner (Joback, 1994).

9.4.1.1 Computer-Aided Selection of Replacement Solvents

Several methods have been proposed to guide the solvent replacement process for the many applications described in the chemical literature. These efforts attempt to build an organized framework for this process and provide a substantial improvement over previously ad hoc or trial-and-error approaches to solvent replacement. Joback outlines a methodology for the selection of replacement solvents for various processes such as extraction or cleaning (Joback, 1994). There are basically four steps to this process: identify constraints on important solvent properties, compile data for all properties, rank solvents satisfying the target constraints, and evaluate top solvent candidates using simulation.

Constraints on the selection of a solvent are diverse. Environmental, safety, health, reactivity, stability, and regulatory considerations must be considered (Zakrzewski, 1991). These should be added to the model. For many applications, conventional organic solvents are highly desirable because of familiarity, low cost, ease of handling, and ease of disposal. To satisfy the needs of these applications a large variety of new, alternative solvents are being offered. Because there are no exact drop-in replacements, a systematic evaluation of solvent substitutes must be performed.

In-depth examination of this subsample led to the conclusion that enough toxicity and exposure information for a complete health-hazard assessment are lacking. By inference, similar conclusions were made for the select universe from which the sample and the subsample were drawn. This report presents criteria for selecting substances and determining toxicity-testing needs, provides estimates of those needs, and describes some useful criteria for assigning priorities for toxicity testing.

Toxicity data collected under standardized test conditions may be of the utmost importance in health risk assessment, in which human exposure limits are often derived from laboratory experiments. A standardized approach to data collection is also important for evaluating the sensitivity and specificity of test methods used to determine toxic potential. The results showed that the chemicals produced markedly different qualitative patterns of effect on systemic, neurological, and developmental indices of toxicity. Differences in the pattern of systemic and neurological effects were also obtained that depended on dosing duration. Quantitative analyses indicated that the highest ineffective dose as well as the lowest effective dose could vary by as much as two orders of magnitude across the different indices of toxicity. These results clearly show that a test battery focused on a single endpoint of toxicity cannot be used to accurately predict either qualitatively or quantitatively a chemical's systemic, neurological, and developmental toxicity profile (Macphail et al., 1995).

9.4.2 Solvent Profile

The following solvent profile (see fig. 9.1) developed both from reading Joback (Joback, 1987) and subsequent discussions. It provides one possible alternative way to begin to select solvents.

9.4.2.1 Step 1: Identification of Constraints

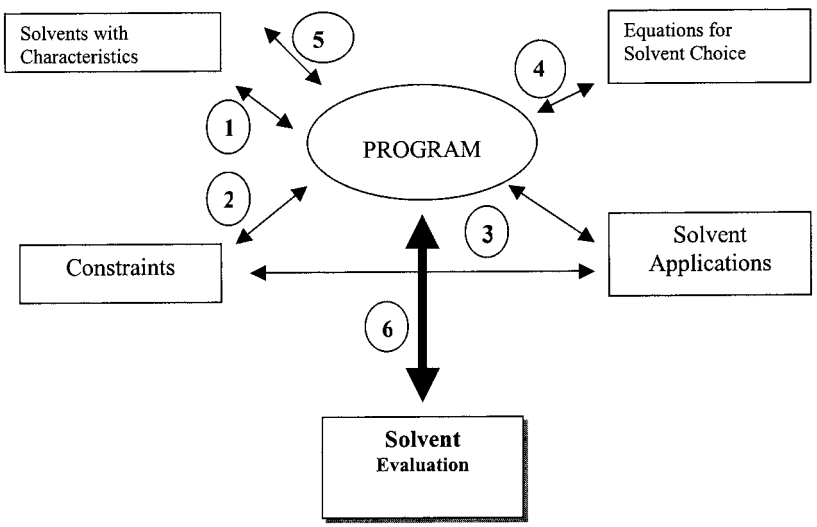
The first step of the possible methodology is to identify the physical chemical properties the solvent must possess for a given application. A detailed engineering analysis of the application will yield many performance constraints. Constraints are also obtained considering the solvent's entire life cycle.

Each constraint needs to be quantified in terms of physical and chemical properties or restrictions on composition or molecular structure. The following paragraphs list a number of constraints found in typical solvent applications:

9.4.2.1.1 Performance Constraints A major use of solvents facilitates separation via liquid–liquid extraction, azeotropic distillation, crystallization, and absorption. A solvent's capacity, selectivity, and distribution can all be related to its activity coefficients.

9.4.2.1.2 Environmental/Health/Safety Constraints Combination effects include both synergism and antagonism. These constraints combine the following activities:

- the development and application of statistically designed experiments combined with multivariate data analysis and modeling in vitro and in vivo studies on a wide variety of chemicals such as petroleum hydrocarbons, aldehydes, food contaminants, industrial solvents, and mycotoxins;



Key to Solvent Profile Schematic

Step	*Description*
1	Define complete range of characteristics (uniform format and units) to characterize solvents (physical, computed and "fuzzy")
2	Define constraint categories
3	For each constraint category, define desirable characteristics for each class of solvents
4	Define equations that will enable solvent choice
5	Select solvent possibilities
6	Evaluate potential solvents: a. pure, existent; then test, b. solvent mixture, formulate, then test, c. unknown, then synthesize or predict.

Figure 9.1 Profile schematic.

- development of safety evaluation strategies for mixtures such as the use of toxic equivalence factors or alternatives;
- fractionation followed by recombination of the mixture in combination with a mixture design; and
- quantitative structure-activity relationship analysis combined with lumping analysis and physiologically based pharmacokinetic or pharmacodynamic modeling for studying complex mixtures.

Other examples are carcinogenicity studies on complex mixtures (petroleum middle distillates, foundry fumes, pesticides, heterocyclic amines, diesel exhaust, and solid particles); neurotoxicity studies of mixtures of solvents alone or in combination with exposure to physical factors; and toxicity studies of outdoor air pollutants, focusing

on particulates. Toxicologists and regulators clearly have a growing interest in the toxicology and risk assessment of chemical mixtures (Feron et al., 1998).

Equipment design, operating procedures, and operator training often address environmental, health, and safety constraints. Eliminating fugitive emissions, removing workers from potential chemical exposure, and ensuring that flammable concentrations never occur are just a few of the approaches used.

Solvent properties, which must be considered, include biological oxygen demand, global warming potential, ozone-degradation potential, vapor pressure, toxicity, flammability limits, and flashpoint. Special attention must be given to all ways in which the solvent will be used to identify possible constraint violations. Although a solvent mixture might be of a nonflammable composition, a leak in the process stream could preferentially release a flammable component.

9.4.2.1.3 Recovery Constraints Distillation is a primary means of solvent recovery. In a separation process the chosen solvent must be easily distilled from the extracted solute. The relative volatility should be large to ensure easy separation. The enthalpy of vaporization should be low for reduced energy consumption.

Even in applications where the solvent is not recovered, such as some cleaning operations, volatility and vaporization constraints are still important.

9.4.2.1.4 Reactivity Constraints The majority of applications require solvents to be stable and nonreactive. Solvent stability in the presence of air and water must be considered.

Reactivity in the environment must be considered. A prime example is chlorinated solvents, which are nonreactive in most applications but break down in the upper atmosphere thereby catalyzing ozone degradation.

Most reactivity constraints can be directly quantified in terms of the presence or absence of molecular substructures such as −COOH, −OH, −Cl, or −Br. These constraints can be easily used to screen candidate solvents.

9.4.2.1.5 Regulatory Constraints The presence or absence of a solvent on various regulatory lists, for example, SARA 313, can either restrict or increase the cost of its use.

9.4.2.1.6 Cost Considerations Cost is an objective in solvent selection. A solvent with a low cost but unacceptable performance is not a viable candidate.

Numerous other application-specific properties such as density, viscosity, surface tension, enthalpy of combustion, freezing point, purity, and availability must also be considered.

9.4.2.1.7 Current Solvent Constraints Another major source of constraints on substituted solvents comes from the solvent currently being used. Extracting constraints from the currently used solvent is of course based on the assumption that the current solvent was chosen wisely.

9.4.2.2 Step 2: Data Compilation The result of step 1 will be a set of constraints on solvent properties. The second step of the methodology is to obtain values for

these properties for each of the solvent candidates being considered. When solvent property data can not be found estimation techniques must be used.

Physical property estimation techniques fall into two major categories, equation based and structure based. Equation-based techniques determine the value of an unknown physical property from the values of one or more known physical properties. Structure-based techniques determine the value of an unknown physical property from a function of molecular structure.

The Riedel method is an example of an equation oriented estimation technique for predicting the enthalpy of vaporization at the solvent's normal boiling point (Reid et al., 1987):

$$\Delta H_{vb} = 1.093RT_c\ (T_{br}(\ln P_c - 12.539)/(0.930 - T_{br}))$$

Group contribution techniques relate the physical property of a molecule to that molecule's structure. Each molecular structure fragment or group is assumed to contribute a certain amount to the molecule's total property. Totaling the contributions for all groups provides an estimate of the molecule's property. For example, table 9.1 shows group contributions for the normal boiling point (Joback and Reid, 1987). Estimating the normal boiling point for isopropyl alcohol we begin by decomposing its molecular structure into groups:

Group	Occurrences
$-CH_3$	2
>CH−	1
−OH	1

Totaling the contributions in the table gives

$$T_b = 2(23.58) + 1(21.74) + 1(92.88) + 198.12 = 359.9K$$

This is in good agreement with the literature value of 355.41K (Daubert and Danner, 1992). There are numerous techniques which provide good accuracy for thermodynamic and transport properties. Techniques for estimating environmental properties and health effects have lower accuracy.

One very important property in solvent selection is the activity coefficient. Many techniques exist for estimating activity coefficients (Fredenslund et al., 1977). In addition to these detailed techniques, a number of simpler approaches have been found to be very effective. These include infinite dilution activity coefficients (Thomas and Eckert, 1984), critical solution temperatures (Francis, 1944), and solubility parameters (Barton, 1983). In implementing the above system the authors chose to use a three term solubility parameter model.

The three terms of the solubility parameter, δ_d, δ_p, and δ_h, represent measures of dispersive forces, polar forces, and hydrogen-bonding forces, respectively. Two liquids with similar solubility parameters are soluble.

Similarity of solubility parameters can be measured using a Euclidean distance metric. For two molecules A and B, the distance between their solubility parameters is given by:

Table 9.1. Programs developed for property prediction, solvent replacement studies, and reaction design (Sherman et al., 1998).

Program Name	Application	Reference
	Organic Synthesis	
CAMEO	Organic reaction product prediction	*www.chem.leeds.ac.uk*
LHASA	Organic synthetic route design	*www.chem.leeds.ac.uk*
SYNGEN	Organic synthetic route design	*www.biobrandeis.edu/faculty01/hendrickson.html*
	Process Simulation	
KEMDS	Liquid-liquid extraction	
Aspen Plus	Steady-state process simulation	*www.aspentec.com*
ChemCAD III	Steady-state process simulation	*www.phoenix.net*
HYSIM	Steady-state process simulation	*www.hyprotech.com*
PRO II	Steady-state process simulation	*www.simsci.com*
SPEEDUP	Dynamics and plant optimization	*www.aspentec.com*
	Property Prediction	
UNIFAC	VLE prediction	*http://chemistry.berkeley.edu/index.shtml*
ADAPT	General property prediction	*http://research.chem.psu.edu.pcjgroup*
CODESSA	General property prediction	*www.semichem.com/codessa.html*
MOLCONN	Topological descriptor calculation	*www.eslc.vabiotech.com/molconn*
Henry, BIODEG, $\log K_{ow}$, etc.	Several codes	Syracuse Research Corporation (nonprofit)
ACD/BP, etc.	Property prediction	*www.acdlabs.com*
DEREK	Toxicity prediction	*www.chem.leeds.ac.uk*
TOPKAT	Toxicity prediction	*http:www.accelrys.com/products/topkat*
Paris II	Solvent prediction	*http://www.tds-tds.com/*

Note: All links in this table can be found in *web.mit.edu/huibers/www/greenchem.html* (Sherman et al., 1998).

$$((\delta^A{}_d - \delta^B{}_d)^2 + (\delta^A{}_p - \delta^B{}_p) + (\delta^A{}_h - \delta^B{}_h))^{1/2}$$

where δ^A are the solubility parameters for molecule A and δ^B are the solubility parameters for molecule B. The authors used the estimation techniques described in Barton for solvents with missing solubility parameter data (Barton, 1983).

The major advantage of using the solubility parameter approach is that it is consistent with our methodology of matching solvent properties with application properties. In fact, the use of a distance measure can be extended to include all properties.

9.4.2.3 Step 3: Candidate Ranking

Once physical properties are determined for each candidate solvent they can be compared against the constraints compiled in step 1. Only those candidates that satisfy the

constraints are retained for further consideration. This screening of candidates will in general have two results: Either all candidates will be rejected, or several candidates will succeed.

If all candidates are rejected, an analysis of the constraints must be done. Constraints may be too tight or in conflict with one another. Constraints which are too tight can be easily identified by examining the result of applying the individual constraint. Conflicting physical property constraints can be difficult to identify because of the interrelationships between physical properties. A standard technique in statistical analysis to find such interrelationships is to create plots of all pairs of variables.

When several candidates satisfy our target constraints, a ranking must be performed. Price is often used as the criteria to rank satisfactory solvents. However, one must be very careful to realize that price is often a poor indicator of the final cost of using a solvent. The cost of operation, disposal, regulation, and so on (i.e., its life cycle) must be considered.

Unfortunately, many of these costs cannot be easily quantified in dollar amounts. However, we must remember that to rank our candidate solvents it is not necessary to know their absolute costs but only a relative cost. Relative cost can be inferred from physical property values. For example, a solvent with a lower enthalpy of vaporization will in general have a lower recovery cost, assuming recovery is done by distillation. A solvent with a higher enthalpy of combustion will have a lower disposal cost, assuming disposal is done by incineration.

In the above methodology each solvent is given a "score of satisfaction" on each constraint. This score is simply the distance from the constraint's limit. For example, if the target was $T_b > 300K$, toluene, with a T_b of 383.78 K, would receive a score of 83.78 while hexanol, with a T_b of 430.55, would receive a score of 130.55.

These raw scores are next normalized using a simple utility function: $U = 100$ (score/max), where max is the maximum score of all solvents on this constraint. This function simply translates all values onto a 0 to 100 range. This translation assists in comparing solvents against several constraints.

A total score is obtained by a simple weighted summation of the utility scores for each constraint for each solvent. These total scores are used as a means to rank candidate solvents. The best candidates are then examined in greater detail by simulation.

9.4.2.4 Step 4: Simulation

The final step of the methodology is to analyze the performance of the top candidates in the specific application being investigated. One of the advantages of using physical properties in the selection process is that many of these properties are required for process simulation. For example, in the selection of alternative liquid–liquid equilibrium solvents the density, viscosity, solubility, and distribution coefficients are properties needed both for selection and process simulation.

The software used to evaluate solvents through simulation is generally a commercially available process simulator software package such as Aspen Plus or Pro II, (see table 9.1). These programs allow the simulation of engineering and operating problems from the unit scale to full plant simulations. The impact on the entire plant of a proposed solvent substitution can be estimated using such a program.

A subgrid-scale plume model has been developed for a better treatment of dynamics of the emissions from concentrated emission sources in air quality models. The model is based on the Gaussian model description of the dispersion of NOx emissions from the power plants. Detailed inorganic and, if desired, organic atmospheric chemistry is included in the model. Results from the simulation with the detailed organic chemistry found little difference than the detailed inorganic chemistry, though significant local differences were found between those and the simplified NOx chemistry or the calculation without the subgrid-scale treatment (Kumar and Russell, 1996).

9.4.3 Process Simulation

There are a number of forces driving the U.S. chemical industry as it moves into the twenty-first century including shareholder return (economics), globalization, efficient use of capital, minimization of environmental impact, improved return on investment, improved and more efficient use of research, and efficient use of people. As the chemical industry strives to achieve these goals, it is investigating the use and application of new technologies. A critical new technology that is beginning and will continue to have an impact on the chemical industry is modeling and simulation. This area of science and technology is piggybacking on the revolution that is occurring in computer technologies and in the development of new software and the corresponding algorithmic advances. Two major driving forces of the industry are the desire to improve manufacturing processes and the need to rationally design new materials. The goal of developing green manufacturing processes that minimize both energy utilization and waste-stream production will drive the need to develop news technologies as will the goal of more rapidly designing new materials with the required properties including minimal environmental impact. Modeling and simulation is a critical technology for achieving these goals as it can be used to reduce cost and cycle time. A critical subdomain of modeling and simulation that will have real impact is computational chemistry/molecular modeling (Dixon and Feller, 1999). The utilization of advanced software, as described in Dixon and Feller, indicates how the process simulation incorporating green solvents might improve the environmental performance of chemical processes.

9.4.4 Modeling Solvents

Much current research on solvent substitution takes the process a step further than a simple screening of existing solvents by using an approach consisting of building new molecules from substituent molecular subgroups and using methods for predicting molecular properties from structure. This is done in the framework of a system in which the rules for the constraints to the solvent selection are defined and an optimization is performed.

The theory of solvent effects on the electronic structure of a given solute leads to a representation of the subsystem embedded in a larger one with the help of effective Hamiltonians, wave functions, and eigenvalues. Since the whole electronic system is quantum mechanical in nature, and in principle nonseparable, the theory for the ground electronic state permits defining under which conditions the solute and solvent separability is an acceptable hypothesis. It is possible to distinguish passive from

active solvent effects on chemical reactions. Passive solvent effects do not change the quantum nature of the interconversion step, while it may change the relative energies of the corresponding spectra. The active solvent effects involve a specific action of the solvent in the chemical interconversion step leading to a change of mechanism or to a surrogate mechanism. This may include general/specific acid or base catalysis by the solvent molecules. For a chemical reaction having different mechanism to accomplish the chemistry, a passive solvent may change the relative probabilities between channels but not the actual mechanisms. From the computational viewpoint, in the supermolecule approach such a distinction is seldom retained. Small solvent clusters treated at any level of electronic theory cannot be expected to provide an adequate description of the characteristic many-body effects (Tapia et al., 1996). Active solvent effects can be treated as a passive one if by including minimal (critical) number of solvent molecules the interconversion step is correctly described as a supermolecule, the remaining solvent can be considered as passive. It is to this type of system that the theory would apply.

Contemporary computer-assisted molecular simulation methods and modern computer technology has contributed to the actual numerical calculation of solvent effects on chemical reactions and molecular equilibria. Classical statistical mechanics and quantum mechanics are basic pillars on which practical approaches are based. On top of these, numerical methods borrowed from different fields of physics and engineering and computer graphics techniques have been integrated into computer programs running in graphics workstations and modern supercomputers (Zhao et al., 2000).

9.4.4.1 General Discussion

The most abundant compound on our planet is water at the liquid state. Because of its diffusion and its solvating properties, a large number of chemical reactions important both in life and in industrial processes take place in aqueous solution.

From a computational viewpoint, chemical reactions in solution present a not-yet solved challenge. On one hand, some of the solvent effects can be approximated as if the solute molecule would be in a continuum with a given dielectric characterization of the liquid. On the other hand, the continuum model fails totally when one is interested in the specific interactions of the first solvation shell with the solute; clearly, if a hydrogen rather than an oxygen atom points toward a specific atom of the solute molecule, the energetics of the interaction is drastically different. This leads to the need to represent the first shell in a detailed way, recognizing explicitly the solvent molecules at the atomic level.

It is clear from the above that the continuum model can simulate only those aspects of the solvent which are somewhat independent from hydrophobicity, hydrophyllicity, generally the first solvation shell, and specific interactions with the solute. The physical problem is a general one; namely, it relates to the validity to use quantities, correctly described and defined at the macroscopic level, in the discrete description of matter at the atomic level. For such study, one needs explicit consideration of the solvent, for example the molecules of water. This can be done either at the quantum-mechanical level, as in cluster computations. Another approach is to simulate the system at the molecular dynamics (or Monte Carlo) level; these techniques allow us to consider

very large systems and, if one assumes periodic boundary conditions, even infinitely large systems.

The motions of a molecular system, for example a solution, occur on many time scales. There are very fast electronic motions, the basic mechanism in chemical reactions. Then, there are the nuclear motions—vibrations, rotations, and translations (diffusion).

The two avenues above, namely ab-initio computations on clusters and molecular dynamics on the one hand and continuum model on the other, are somewhat bridged by those techniques where the solvent is included in the Hamiltonian at the electrostatic level with a discrete representation.

9.4.4.2 Specific Examples of Molecular Modeling

The basis of the UNIFAC approach is the definition of submolecular groups (e.g., CH_2, CH_3, CH_3O, CH_2Cl, OH) and the fitting of a given molecular property or activity coefficient to a sum of contributions based on the subgroup molecular volume and interaction terms between the groups.

Continuum models are the most efficient way to include condensed-phase effects into quantum-mechanical calculations, and this is typically accomplished by using the self-consistent reaction field (SCRF) approach for the electrostatic component. Therefore it is very common to replace the quantal problem by a classical one in which the electronic energy plus the coulombic interactions of the nuclei, taken together, are modeled by a classical force field—this approach usually called molecular mechanics (MM) (Cramer and Truhlar, 1996).

When structural and dynamical information about the solvent molecules themselves is not of primary interest, the solute–solvent system may be made simpler by modeling the secondary subsystem as an infinite (usually isotropic) medium characterized by the same dielectric constant as the bulk solvent, that is, a dielectric continuum. Theoretical interpretation of chemical reaction rates has a long history already. Until recently, however, only the chemical reactions of systems containing a few atoms in the gas phase could be studied using molecular quantum mechanics due to computational expense. Fortunately, very important advances have been made in the power of computer-simulation techniques for chemical reactions in the condensed phase, accompanied by an impressive progress in computer speed (Gonzalez-Lafont et al., 1996).

To microscopically model a reaction in solution, one needs to include a very large number of solvent molecules in the system to represent the bulk. The problem stems from the fact that it is computationally impossible with our current capabilities to locate the transition-state structure of the reaction on the complete quantum-mechanical potential energy hypersurface, if all the degrees of freedom are explicitly included. Moreover, the effect of thermal statistical averaging should be incorporated. Then, classical mechanical computer simulation techniques appear to be the most suitable procedures to attack the above problems.

A systematic procedure can select optimal solvent blends for nonreactive, multicomponent absorption processes accounting for plant-wide point source environmental interactions. This approach, based on the optimal design technique for pure solvents, involves the identification of all agent-based operations (such as gas absorption and

liquid extraction) within the process of interest, the determination of a list of candidate solvent blends satisfying separation task operational and environmental constraints, and the selection of an optimal solvent blend candidate based on global plant-wide process and environmental constraints (Buxton et al., 1999).

Separation processes (both liquid–liquid and gas–liquid) are a key element in many industrial processes. For this application, solvent molecules are built from UNIFAC submolecular groups, and the relevant properties of the new molecules such as distribution coefficients and selectivities are estimated. Strategies for the design of solvents for separation processes were initially formulated and later extended to better model the processes of solvent synthesis, solvent evaluation, and solvent screening. A method for solvent design for liquid–liquid extraction has been developed.

For example, the search for potential solvents for liquid extraction and extractive distillation is carried out through a group contribution molecular design of solvents (MOLDES) approach (Pretel et al., 1994).

A general methodology for computer aided product design (CAPD) with specified property constraints which is capable of solving a large range of problems is possible. The methodology employs the group contribution approach, generates acyclic, cyclic, and aromatic compounds of various degrees of complexity (including isomers) and size (including polymers) and provides accurate and consistent estimation of properties. The application range of the methodology has been enlarged and the validity of the predictions improved through the incorporation of a new group contribution based method for estimation of properties. Finally, a computer program based on the extended methodology has been developed and the results from five case studies highlighting various features of the methodology (Constantinou et al., 1996).

A review of the literature available that will help analysts to select alternative solvents, with particular emphasis on solvent extraction and liquid chromatography, has been done. Methods of classifying solvents are discussed and tables of solvent properties are given. Strategies for optimizing mobile phases for high-performance liquid chromatography are described in detail (Barwick, 1997).

Computer-aided molecular design (CAMD) provides a means for determining molecules or mixtures of molecules having a desirable set of physicochemical properties. The application range of CAMD is restricted due to limitations on the complexity of the generated molecular structures and on the availability of suitable models for property prediction. A new CAMD methodology that addresses this issue by combining molecular modeling techniques with a traditional CAMD approach is shown. The method includes a new molecular/atomic structure generation algorithm, a large collection of property estimation methods, and a link to molecular modeling tools (Harper et al., 1999).

Computer-aided molecular design is a strategy in which a set of structural groups are systematically combined to form molecules with desired properties. Duverdi and Achenie demonstrated a computer-aided molecular strategy to design environmentally safe refrigerants. In this paper, a mathematical programming-based approach to computer-aided molecular design is presented. Using a set of structural groups, the problem is formulated as a mixed integer nonlinear program in which discrete variables represent the number of each type of structural groups present in the candidate compound (Duvedi and Achenie, 1996).

Meniai and Newsham (Meniai and Newsham, 1996) applied Monte Carlo simulations to develop relationships between the solute binding energy and both the solvent

selectivity and the partition coefficient. This method is useful in designing liquid–liquid extraction processes.

A paper by Marcoulaki and Kokossis (Marcoulaki and Kokossis, 1998) presents optimization technology for the computer-aided design of molecules. The approach combines stochastic optimization and group contribution methods to select chemicals with optimized properties. Each molecule is represented as a set of functional groups. The work reports novel molecular structures and significant improvements over conventional techniques.

9.4.5 Prediction of Physical Properties from Molecular Structure

At the core of many of these algorithms for solvent substitution is a method for predicting the properties of proposed molecules, given only the molecular structure. Much work has been done in this area alone, and several programs have been developed to guide this process. Some of these programs are listed in table 9.1. Additionally, process simulation software such as Aspen Plus contain several different approaches for the prediction of properties from molecular structure.

Molecular mechanics calculations in vacuum were used to examine the influence of the structures of alkyl chains R of dialkyl phosphoric acids ($(RO)_2PO_2H$ noted HL) on liquid–liquid extraction of lanthanide(III). Several models were proposed to investigate the partage, the dimerization of ligands, their interfacial areas, and the stability of $Ln(HLL)_3$ complexes, Ln varying from La to Lu. The presence of branched alkyl chains increases van der Waals interactions between extractants in the complex and between alkyl chains in the dimer $(HL)_2$. The solvent accessible surfaces of ligands (SHL) and complexes (Scplx) are estimated and empirical relations between partition constants (PHL) and SHL are proposed. The results obtained have shown that all calculated $Ln(HLL)_3$ complexes can probably exist without high constraints caused by steric effects (Sella et al., 1997).

Zhao and Cabezas have contributed an important tool in solvent design (Zhao and Cabezas, 1998). The use of physical properties and fluid behavior from molecular thermodynamics can lead to better decision making in the design of substitute solvents and can greatly reduce the expense and time required to find substitutes compared to designing substitute solvents by experiment. This paper systematically discusses the equilibrium and dynamic properties and the fluid behavior which are important for designing substitute solvents. The rationale for using the property, the current level of understanding from molecular thermodynamics, the general methodology for estimating the property for single chemicals, and suggested methods for liquid mixtures.

A template effect by solvent was found in the synthesis of self-assembled capsules. Experimental evidence is presented that the solvent molecules control the covalent bond formation through molecular recognition within the monomeric tetrahedral intermediate. It is proposed that solvation effects can be treated as a subset of molecular recognition events (Tokunaga et al., 1998).

The findings of computer simulations on aqueous solutions could be summarized as follows (Efremov et al., 1999):

- Structural and energetic properties of studied molecules strongly depend on the solvent; membrane-mimetic media significantly promote formation of α-helices capable of traversing the bilayer, whereas a polar environment destabilizes α-helical conformation via reduction of solvent-exposed surface area and packing.
- The structures calculated in a membrane-like environment agree with the experimental ones.
- Noticeable differences in conformation of surfactant lipoprotein assessed via Monte Carte simulation with implicit solvent and molecular dynamics in explicit solvent were observed.
- In vacuo simulations do not correctly reproduce protein-membrane interactions, and hence should be avoided in modeling membrane proteins.

Oil–water partitioning, solubilities, and vapor-pressure experiments on small-molecule compounds are often used as models to obtain energies for biomolecular modeling. For example, measured partition coefficients, K, are often inserted into the formula-RT ln K to obtain quantities thought to represent microscopic contact interaction free energies (Chan and Dill, 1997).

Thermolysin-catalyzed peptide synthesis using N-(benzyloxycarbonyl)-L-phenylalanine (Z-Phe) and L-phenylalanine methyl ester (Phe-OMe) as substrates was done mainly in a water-organic one-phase solvent system. The organic solvent content used was less than the saturation concentration in buffer. With organic solvents with high log P values, the enzymatic activity increased as the organic solvent content increased; but further increases in the organic solvent content decreased the enzymatic activity, showing an "organic activity" profile. On the other hand, with organic solvents of low log P values, the enzymatic reaction was inhibited even by the initial addition of organic solvents. When a correlation between maximum activities and log P values or Hildebrand solubility parameters was investigated, a linear correlation was obtained among the same category of organic solvents, but not between categories. This suggests that the direct effect of organic solvents on the microenvironment of the enzyme largely depends on the molecular structure of the solvents (Inagaki et al., 1994).

A mean field theory for the study of solvent effects considers polarizable solvent molecules. The model, which combines quantum chemistry and simulation calculations, splits the system into three parts:

- the solute, treated quantum mechanically;
- polarizable solvent molecules, whose positions are obtained from molecular dynamics data;
- a dielectric continuum.

An averaged solvent electrostatic potential, obtained by averaging over the solvent configurations, is included in the solute Hamiltonian and electric and energy properties are obtained. The method provides results for the dipole moment and solute–solvent interaction which agree with the experimental values and with the results obtained by other workers (Mendoza et al., 1998).

The topological approach is an extension of simpler group contribution efforts, as it can include contributions of higher order, where group contributions are essentially

modified by contributions from nearest neighbors and beyond. Several other types of topological descriptors have been developed and applied to property prediction. Several research groups have taken the topological descriptors along with other types of molecular descriptors (geometrical, electrostatic, quantum chemical) and arrived at multiple linear regressions what allow the prediction of properties.

9.4.6 Prediction of Toxicology and Related Parameters

Environmental chemical agents can include elements and both natural and synthetic organic and inorganic compounds. However, the majority of chemicals in the biotic environment recognized to be hazardous are low- to medium-molecular-weight lipophilic organic compounds. On the contrary, it suggests the need for enhanced research effort in this area, particularly to enhance our understanding of the effects of toxic trace metals and their relevant species in the environment (McKinney, 1981).

Process simulation is a key tool in computer-assisted solvent substitution. More complicated than the prediction of physical and chemical properties is the prediction of more loosely defined molecular characteristics such as toxicity. These properties are not traditionally included in process simulation software, so special attention must be paid to their prediction.

Traditionally, synthetic chemists focused on ease of synthesis and commercial use in chemical design. With ever-increasing attention being paid to environmental impact and toxicity, addition constraints are being placed on the chemical design process DeVito (DeVito, 1996a, 1996b) outlines some of the approaches that chemists may consider for the design of safer substances; these include reducing absorption, understanding toxic mechanisms, using structure-property relationships, retrometabolism, isosterism, eliminating the need for associated toxic substances, and identifying equally useful but less toxic chemicals of another chemical class. The basis of chemical carcinogenesis is discussed by Lai et al. (1996), who proposed a molecular design method to reduce the carcinogenicity of compounds. The hazy science behind environmental risk assessments currently relies much more on general principles and experience than on a detailed understanding of how specific chemicals cause cancer or other adverse effects. Without those mechanistic details, risk assessments suffer from being sketchy and uncertain—a blurred picture that is open to interpretation (Patlak, 1998).

Prediction of chemical toxicity using a computer can save time and money (because of the high cost of toxicology studies) either by eliminating toxicological testing or by reducing the use of laboratory animals by improving the order of priorities for testing. Several approaches have been used to estimate toxicity of a given compound. Some approaches derive parameters from the molecular structure, and correlate those parameters with different common measures of toxicity. Others correlate toxicity with known chemical structures. Various computer methods used to predict toxicity from molecular structure have been summarized. Medicinal chemists have known for some time that toxicity, bioavailability, and other important parameters that gauge the interaction of chemical compounds with humans and animals correlate well with the octanol-water partition coefficient (Milne et al., 1996). Oil–water partitioning, solubilities, and vapor pressure experiments on small-molecule compounds are often used as models to obtain energies for biomolecular modeling (Chan and Dill, 1997).

An attractive aspect of this approach is that an actual purified sample of the compound of interest is not necessary for property estimation, and no other measured properties are necessary, as the toxicity is correlated with molecular descriptors derived solely from molecular structure.

An example of another approach is DEREK, a publicly available expert system designed to assist chemists and toxicologists in predicting toxicological hazards based on analysis of chemical structure (see table 9.1). DEREK differs from other computer methods for toxicity prediction in that it makes qualitative rather than quantitative predictions and does not rely on algebraic or statistical relationships.

A variety of different approaches to the prediction of toxicity have been developed under the sponsorship of the Predictive Toxicology Evaluation project of the National Institute of Environmental Health Sciences. The widespread application of computational techniques to studies in biology, chemistry, and environmental sciences has led to a quest for important, characteristic molecular parameters that may be directly derived from these computational methods. Theoretical linear solvation energy relationships combine computational molecular orbital parameters with the linear solvation energy relationship of Kamlet and Taft to characterize, understand, and predict biological, chemical, and physical properties of chemical compounds (Famini and Wilson, 1997).

Assessment of environmental and health hazards from chemicals requires a multidisciplinary approach. One needs to consider chemical economics, production, usage, and so on; environmental release; monitoring data; environmental behavior; health; and environmental effects. Often events concerning environmental and health hazards can be predicted based on structure and activity relationships and physical-chemical characteristics. The first volume of their publication has made available current information in several important areas of chemical hazard assessment (Saxena and Fisher, 1981; Saxena, 1983; Saxena, 1984).

Acute, sublethal neurotoxicity data for the neurotropic effects of some common solvents were subjected to quantitative structure-activity relationship (QSAR) analysis. Hydrophobicity was found to be important in modeling neurotoxicity; however, highly significant QSARs from regression analysis were not obtained, which may imply that metabolic activity and differing mechanisms of action play an important role in neurotoxicity. It is proposed that hydrophobicity could be used to predict a "minimal" neurotoxic effect level, above which there will be a neurotoxic effect. This was successful when parameters describing hydrophobicity, molecular volume and size, melting and boiling point were included and provides a potential method to predict whether a compound is highly neurotoxic. This suggests that in addition to partitioning through a membrane, aqueous solubility and volatility are also important factors governing neurotoxicity (Cronin, 1996; Borman, 1990; Hansch et al., 1996).

9.4.7 Computer-Aided Design of Alternative Synthetic Pathways

A complicated problem is that of solvent substitution for organic reaction optimization. The solvent is important in organic synthesis, and several solvent polarity scales have been developed to attempt to quantify this, specifically work by Reichardt (Reichardt, 1988).

Table 9.2. Solvent substitution resources on the World Wide Web.

Name & Sponsor	Description	Address
Enviroene U.S. EPA, DoD SERDP	A single repository for pollution prevention, compliance assurance, and enforcement information databases; has the database umbrella architecture for solvent alternatives solvent substitution data systems	*http://es.epa.gov* *http://es.epa.gov/ssds/ssds.html*
	Integrated Solvent Substitution Data System (ISSDS)	*http://es.epa.gov.gov/issds.html*
	Hazardous Solvent Substitution Data System; on-line product information, material safety data sheets	*http://es.epa.gov/ssds/hssdstel.html*
	Solvent Handbook Database System	*http://wastenot.inel.gov/shds*
	Solvents Database	*http://solvdb.ncms.org*
Research Triangle Institute, Research Triangle Park, N.C.	Solvent Alternatives Guide (SAGE): provides alternatives to solvent cleaning	*http://clean.rti.org*
	Coatings Alternatives Guide (CAGE) provides summarized information on recommended alternatives for coating technologies	*http://cage.rti.org*
Naval Facilities Engineering Service Center, Port Hueneme, CA	Pollution Prevention Handbook, P2 Equipment book, and "Environmental Products Catalog"	*http://enviro.nfesc.navy.mil/p2library*
Pacific Northwest Pollution Prevention Resource Center, Seattle, Wash.	Contains review which cover alternative pollution prevention technologies that have proven successful; offers links to other relevant Internet sites	*http://pprc.gov/*
Waste Reduction Resource Center, Raleigh, N.C.	Clearinghouse providing access to and collecting of waste reduction information, including on-line solvents guide	*http://www.p2pays.org/wrrc*
Environmental Software Cooperative, Ventura, Cal.	Database application containing information on approximately 2200 software products for the environmental management field	*http://www.esp-net.com/products/index.html*
Battelle Seattle Research Centers	Brief survey of P2 software: Survey which identified gaps in the available packages that represent opportunities for software development	*http://www.seattle.battelle.org/*
National Center for Clean Industrial and Treatment Technologies, Houghton, Mich.;	Clean Process Advisory System (CPAS) is a system of software for efficiently delivering information on clean technologies and P2 methodologies	*http://cpas.mtu.edu*

Table 9.2. Continued.

Name & Sponsor	Description	Address
The AIChE/Center for Waste Reduction Technologies, NY; National Center for Manufacturing Sciences GZA GeoEnvironmental Technologies, Inc., Newton, Mass.	Links to federal government agencies; federal regulations references; health and safety issues; professional associations; etc.	*http://www.clay.net*
Tec-Com, Inc., Knoxville, Tenn.	International WWW publication covering news and vies on risk assessment and risk management	*http://www.riskworld.com*
Illinois Waste Management and Research Center Champaign, Ill.	Information on pollution prevention, with pages on green chemistry and alternative cleaning technologies	*http://www.wmrc.uiuc.edu*
U.S. Environmental Protection Agency, Washington, D.C.	USEPA Green Chemistry Program, including the Green Chemistry Expert System	*http://www.epa.gov/greenchemistry*
The Toxics Use Reduction Institute, University of Massachusetts, Lowell, Mass.	The Toxics Use Reduction Institute (TURI) sponsors and conducts research, organizes education and training programs and provides technical support to promote reduction in the use or generation of toxic chemicals	*http://www.cleaning.org/*
Minnesota Office of Environmental Assistance to the University of Minnesota, School of Public Health	Free technical assistance tailored to individual businesses. MnTAP helps Minnesota companies become more efficient and find alternatives to using hazardous materials.	*http://www.mntap.umn.edu*
Northeast Business Environmental Network, Lawrence, Mass.	Environmental networking	*http://www.nben.org*
Society of Environmental Toxicology and Chemistry (SETAC) Pensacola, Fla.	The Society of Environmental Toxicology and Chemistry (SETAC) is an independent, nonprofit professional society that provides a forum for study of environmental issues	*http://setac.org/1setac.html*
	Cleaner Technologies Substitutes Assessment	*http://www.epa.gov/opptintr/dfe/tools/ctsa/contents.htm*
European Chemical Industry Council	The European Chemical Industry Homepage	*http://www.cefic.be*
The Questor Centre, The Queen's University of Belfast	Questor Centre industry-university cooperative environmental research outside the United States	*http://questor.qub.ac.uk*

Note: U.S. EPA: U.S. Environmental Protection Agency; DoD SERDP: Department of Defense Strategic Environmental Research and Development Program.

Several programs have been developed to assist in this process. The CAMEO program (table 9.1) uses a mechanistic approach to make predictions and does not rely on data tables of specific reactions. Consequently, it is capable of predicting novel chemistry. Given the reactant molecules and reaction conditions, CAMEO evaluates the reactions and suggests products. Another program, LHASA (table 9.1), uses a chemical knowledge base that consists of an extensive library of reaction descriptors (transforms) based on reviews of the chemical literature. These transforms define the scope and limitations of each reaction type. The knowledge base is not just a restricted reaction database but enables LHASA to suggest new and innovative synthetic routes to chemists. Another program, SYNGEN (table 9.1), automatically generates the shortest, most economic organic synthesis routes for a given target compound.

Several other approaches for automated design of synthetic pathways are discussed in the literature. Crabtree and El-Halwagi (1994) develop the concept of environmentally acceptable reactions in which an optimization is done considering reactants and by products in an economic model toward the production of a certain product. Anastas defines computer-assisted organic synthesis and describes software developed to identify alternative and potentially more benign reaction pathways for the synthesis of commercial chemicals (see Anastas and Farris, 1994). Optimization of both solvent design and reaction path design within the context of their previously defined methodology for environmental impact minimization is addressed by Stefanis et al. (1996).

SMART (Solvent Measurement, Assessment, and Revamping Tool) is a software program that allows assessment of solvents used for batch processing based on both empirical data and property estimation methods (Modi et al., 1996). This system includes a new conjugation based method for the estimation of reaction rates in solution, which is based on the concept that the absolute reaction rate coefficient can be obtained from a function dependent on the change in molecular charge distribution between reactants and activated complex (Sherman et al., 1998). Table 9.2 provides a list of solvent substitution resources available on the World Wide Web.

Appendix A

Table A1. Green solvents.

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
10	064741-41-9	#489–0			188	0.775
20	000075-45-6a	(F-22) Anti-Static Super Freeze 1503-12			–40.6	1.194
30	000460-73-1	1,1,1,3,3-Pentafluoropropane			15.3	
40	000680-00-2	1,1,2,2,3,3-Hexafluoropropane	152.04	–159	12.6	
50	000679-86-7	1,1,2,2,3-Pentafluoropropane	134.05	–73.4	24.96	1.336
60	000079-01-6	1,1,2-Trichloroethylene	131.38	–73	86.7	1.46
70	000076-14-2	1,2-Dichlorotetrafluoroethane	170.92	–93.9	3.3	
80	000627-92-9	1,2-Propanediol, 3-(3-methylbutoxy)-	162.14	29	260	
90	000624-52-2	1,2-Propanediol, 3-butoxy-	148.13			
100	000623-39-2	1,2-Propanediol, 3-methoxy-	106.08	–3.8	197	
110	000460-12-8	1,3-Butadiyne	50.26	–36.4	10.3	
120	000107-88-0	1,3-Butanedio1	90.12	–50	207.5	1
130	000111-32-0	1,3-Butylene glycol methyl ether	104.17			
140	000542-92-7	1,3-Cyclopentadiene	66.1	–85	41.7	0.8
150	000504-60-9	1,3-Pentadiene	68.2	–108	42	
160	000123-91-1	1,4-Dioxane	88.12	11.8	101.32	1.03
170	000591-93-5	1,4-Pentadiene	68.12	–148	26	
180	001115-08-8	1,4-Pentadiene, 3-methyl-	82.15	–108.5	55	
190	002396-65-8	1,8-Nonadiyne	120.19	–21	55	0.799

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
200	000071-36-3	1-Butanol	74.14	−88.62	117.2	0.81
210	000563-46-2	1-Butene, 2-methyl-	70.14	−137	31	
220	000558-37-2	1-Butene, 3,3-dimethyl-	84.16	−115	41	
230	000111-70-6	1-Heptanol	116.23	−36	176	
240	000111-27-3	1-Hexanol	102.17	−52	157	0.85
250	019430-93-4	1-Hexene, 3,3,4,4,5,5,6,6,6-nonafluoro-	246.08	−111	59	
260	000107-98-2	1-Methoxy-2-propano1	90.14	−142	118	1
270	000111-87-5	1-Octanol	130.23	−14.97	194	0.82
280	000071-41-0	1-Pentanol	88.17	−78.2	137.8	0.811
290	000109-67-1	1-Pentene	70.13	−165	29.9	0.635
300	000691-37-2	1-Pentene, 4-methyl-	84.15	−153	53	0.67
310	000627-19-0	1-Pentyne	68.12	−106	40	0.69
320	000071-23-8	1-Propanol	60.11	−127	97.2	0.799
330	000584-84-9	2,4-Toluenediisocyanate	174.17	21	251	1.22
340	000110-13-4	2,5-Hexanedione	114.14	−9	188	0.737
350	000112-34-5	2-(2-n-Butoxyethoxy)ethanol	162.26	−68.1	230.6	0.95
360	000078-92-2	2-Butanol	74.14	−115	99.512	0.81
370	000513-35-9	2-Butene, 2-methyl-	70.13	−124	37.5	
380	000112-07-2	2-Butoxyethanol acetate	160.24	−64	192	0.94
390	000503-17-3	2-Butyne	54.09	−32	27	
400	000100-37-8	2-Diethylaminoethanol	117.22	−70	162.7	0.884
410	000110-80-5	2-Ethoxyethano1	90.122	−100	135.5	0.925
420	000111-15-9	2-Ethoxyethanol acetate	132.159	−61.7	156.1	0.97
430	000110-43-0	2-Heptanone	114.21	−35	151.1	0.81
440	000591-78-6	2-Hexanone	100.18	−55.8	127.58	0.81
450	000598-82-3	2-Hydroxypropanoic acid	90.08	16.8	83.5	1.206
460	000109-86-4	2-Methoxyethanol	76.11	−85	124	0.966
470	000109-83-1	2-Methylaminoethanol	75.11	−4.5	155	0.94
480	000078-83-1	2-Methylpropanol	88.2	−117	132	0.8
490	000123-96-6	2-Octanol	130.26	−32	179.8	0.82
500	000107-87-9	2-Pentanone	86.13	−76.9	102	0.81
510	000109-68-2	2-Pentene	70.13	−135	35.85	0.65
520	000626-78-8	2-Propanol, 1,3-bis(3-methylbutoxy)-	232.22	31	287	
530	000623-69-8	2-Propanol, 1,3-dimethoxy-	120.15	−27	162	
540	000111-35-3	3-Ethoxy-1-propanol	104.17			
550	000563-80-4	3-Methyl-2-butanone	86.15	−92	94	0.81
560	000108-11-2	4-Methyl-2-pentanol	102.17	−90	131.7	0.8
570	000110-12-3	5-Methyl-2-hexanone	114.21	−73.8	143.89	0.81
580	000541-85-5	5-Methyl-3-heptanone	128.24	−42	157	0.82
590	064742-47-8c	Actrel 116OL cleaner		−20	211	0.8
600	064742-48-9d	Actrel 3338L cleaner		−60	165.27	0.75
610	064742-48-9e	Actrel 3349L cleaner		0	180.83	0.76
620	064742-48-9c	Actrel 3360L cleaner		−1	188	0.77
630	064771-72-8	Actrel 4493L cleaner	72.15	−3.88	234.99	0.76
640	000064-19-7	Acetic acid	60.06	16.66	117.1	1.044
650	000108-65-6	Acetic acid, 2-methoxy-1-methylethyl ester	132.16	−55	146	
660	000628-63-7	Acetic acid, amyl ester	130.186	−70.8	149.25	0.87
670	000108-21-4	Acetic acid, isopropyl ester	102.15	−69	90	0.872
680	000105-46-4	Acetic acid, sec-butyl ester	116.16	−73.3	112.34	0.87
690	000067-64-1	Acetone	58.08	−94.7	56	0.784
700	000107-02-8	Acrolein	56.07	−86.95	52.69	0.84

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
710	005989-27-5a	Biogenic SE 373	0	0	154.44	0.854
720	000071-43-2	Benzene	78.11	5.5	80	0.874
730	002366-52-1	Butane, 1-fluoro-	76.11	−134	32.5	6.7789
740	000075-83-2	Butane, 2,2-dimethyl-	86.18	−98.2	49.7	
750	000079-29-8	Butane, 2,3-dimethyl-	86.18	−135	57.9	
760	000078-78-4	Butane, 2-methyl-	72.15	−159.9	27.8	0.62
770	000111-76-2	Butoxyethanol	118.17	−75	170.2	0.896
780	000123-86-4	Butyl acetate	116.18	−73.5	124	0.88
790	000109-73-9	Butylamine	73.16	−49.1	77.07	0.737
800	000109-21-7	Butyric acid, butyl ester	144.21		165	
810	000623-42-7	Butyric acid, methyl ester	102.15	0	102	0.9
820	000120-80-9	Catechol	110.11	105	245	1.344
830	000075-45-6b	Chlorodifluoromethane	86.47	−146	−40.6	1.19
840	000074-87-3	Chloromethane	50.48	−81.7	−24.4	0.911
850	000076-15-3	Chloropentafluoroethane	154.47	−141.7	−38.88	
860	000075-72-9	Chlorotrifluoromethane	104.46	−189	−81.44	
870	000287-23-0	Cyclobutane	56.11	−50	12.9	
880	000110-82-7	Cyclohexane	84.16	6.6	80.7	0.77
890	000108-93-0	Cyclohexanol	100.18	22	161.1	0.95
900	000108-94-1	Cyclohexanone	98.16	−45	155.65	0.9
910	000287-92-3	Cyclopentane	70.134	−93.8	49.3	0.75
920	000142-29-0	Cyclopentene	68.12	−135.1	44.2	
930	001191-96-4	Cyclopropane, ethyl-	70.14	−96	34.5	
940	000123-42-2	Diacetone alcohol	116.18	−42.8	168.1	0.934
950	000693-65-2	Diamyl ether	158.28	−69.4	186.8	0.78
960	000142-96-1	Dibutyl ether	130.23	−95.2	140.3	0.764
970	002050-60-4	Dibutyl oxalate	202.25	−29	239	0.99
980	000084-74-2	Dibutyl phthalate	278.38	−35	340	1.05
990	000075-71-8	Dichlorodifluoromethane	120.91	−158.2	−30	1.35
1000	000075-43-4	Dichlorofluoromethane	102.92	−135	8.9	1.37
1010	000111-42-2	Diethanolamine	105.14	27.9	268.3	1.1
1020	000095-92-1	Diethyl oxalate	146.14	−40.6	185.4	1.07
1030	000111-46-6	Diethylene glycol	106.12	−7.8	245	1.12
1040	000112-73-2	Diethylene glycol dibutyl ether	218.336	−60	254.6	0.88
1050	000112-36-7	Diethylene glycol diethyl ether	162.23	−44.3	188.9	0.91
1060	000111-96-6	Diethylene glycol dimethyl ether	134.17	−64	159.8	0.94
1070	000124-17-4	Diethylene glycol monobutyl ether acetate	204.3	−32	245	
1080	000111-90-0	Diethylene glycol monoethyl ether	134.17	−76	202	0.98
1090	000112-15-2	Diethylene glycol monoethyl ether acetate	176.21	−25	217.4	1.01
1100	000111-77-3	Diethylene glycol monomethyl ether	120.15	−84	193	1.0167
1110	000629-38-9	Diethylene glycol monomethyl ether acetate	162.21	−9	209.1	
1120	000461-63-2	Difluoromethyl fluoromethyl ether			29.9	
1130	000108-83-8	Diisobutyl ketone	142.24	−46.04	168.24	0.8
1140	000108-20-3	Diisopropyl ether	102.17	−60	68.51	0.73
1150	000108-18-9	Diisopropylamine	101.19	−96	83.57	0.72

(*continued*)

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
1160	000067-68-5	Dimethyl sulfoxide	78.14	18.45	189	1.095
1170	000127-19-5	Dimethylacetamide	87.12	–20	165	0.94
1180	000124-40-3	Dimethylamine	45.084	–92.2	6.89	0.65
1190	000108-01-0	Dimethylethanolamine	89.16	40	133	0.89
1200	000138-86-3	Dipentene	136.26–	–95.5	176	0.84
1210	000101-84-8	Diphenyl ether	170.22–	27.8	258.06	1.08
1220	034590-94-8	Dipropylene glycol monomethyl ether	148.2—	–80	188.3	0.95
1230	088917-22-0	Dipropylene glycol monomethyl ether acetate	190.14–	–8	200	0.97
1240	068526-79-4	Exxal 6	130.23–	–53.88	154.44	
1250	108419-43-7	Exxate 1000 solvent		–60	235	0.87
1260	088230-35-7	Exxate 600 solvent	144.22	–60	166	0.87
1270	090438-79-2	Exxate 700 solvent		–60	180.05	0.87
1280	108419-32-5	Exxate 800 solvent	172.27	–60	202.5	
1290	108419-33-6	Exxate 900 solvent	186.3	–20	206	
1300	064742-47-8a	Exxsol D 3135 solvent		–54.44	166.38	0.77
1310	064742-47-8b	Exxsol D 60 naphtha		–43.33	198.05	0.76
1320	000071-55-6b	Ethane, 1,1,1-trichloro-	133.4	–30.4	73.9	1.33
1330	000354-58-5	Ethane, 1,1,1-trichloro-2,2,2-trifluoro-	187.88	13	46	
1340	000076-13-1a	Ethane, 1,1,2-trichloro-1,2,2-trifluoro-	187.38	–35	47.7	1.56
1350	000075-34-3	Ethane, 1,1-dichloro-	98.96	–97.2	57.3	1.17
1360	001717-00-6	Ethane, 1,1-dichloro-1-fluoro-	116.95	–103.5	32	
1370	000306-83-2	Ethane, 1,1-dichloro-2,2,2-trifluoro-	152.93	27.9	44.88	
1380	000124-73-2	Ethane, 1,2-dibromo-1,1,2,2-tetrafluoro-	259.82	–110.4	47.3	2.16
1390	001649-08-7	Ethane, 1,2-dichloro-1,1-difluoro-	134.94	–101.2	46.8	
1400	000624-72-6	Ethane, 1,2-difluoro-	66.05	–145	30.7	
1410	000076-12-0	Ethane, 1,2-difluoro-1,1,2,2-tetrachloro-	203.83	25	92.8	1.65
1420	013838-16-9	Ethane, 1-chloro-1,2,2-trifluoro, 2-difluoro-methoxy-	184.49	–108	56.5	1.52
1430	026675-46-7	Ethane, 1-chloro-2,2,2-trifluoro, 1-difluoromethoxy-	184.49	–108	48.5	
1440	003831-49-0	Ethane, 1-iodo-1,1,2,2-tetrafluoro-	227.93	–96	41	
1450	000151-67-7	Ethane, 2-bromo-2-chloro-1,1,1-trifluoro-	197.38	–118	50.2	
1460	000074-96-4	Ethane, bromo-	108.97	–118.6	38	1.45
1470	000075-00-3	Ethane, chloro-	64.52	–138.9	12.2	0.88
1480	000354-64-3	Ethane, pentafluoroiodo-	245.92	–95	12	2.085
1490	020602-86-2	Ethanedioic acid, dipentyl ester	230.18	54	163	1.15
1500	000064-17-5	Ethanol	46.1	–113.9	78	0.784
1510	000141-78-6	Ethyl acetate	88.11	–83.6	77.1	0.895
1520	000075-04-7	Ethyl amine	45.1	–81	16.6	0.69
1530	000060-29-7	Ethyl ether	74.12	–116	34	0.71

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
1540	000109-94-4	Ethyl formate	74.08	−79.6	54.4	0.92
1550	000105-37-3	Ethyl propionate	102.133	−73.85	99.1	0.884
1560	000100-41-4	Ethylbenzene	106.18	−94.975	136	0.87
1570	000107-21-1	Ethylene glycol	62.08	−12.6	197.5	1.11
1580	000112-48-1	Ethylene glycol dibutyl ether	174.28	−69.1	203.3	0.83
1590	000629-14-1	Ethylene glycol diethyl ether	118.176	−74	121.2	0.84
1600	000110-49-6	Ethylene glycol methyl ether acetate	118.15	−65	145	1.01
1610	000622-08-2	Ethylene glycol monobenzyl ether	152.21	33	265	1.07
1620	000122-99-6	Ethylene glycol monophenyl ether	138.18	14	245.2	1.11
1630	000075-21-8	Ethylene oxide	44.06	−111	10.5	0.82
1640	000060-00-4	Ethylenediaminetetraacetic acid	292.28	240	557.81	
1650	086508-42-1e	FC-104 Fluorinert	435		101	1.8
1660	086508-42-1c	FC-40 Fluorinert	650		155	1.9
1670	086508-42-1g	FC-43 Fluorinert	670		174	1.9
1680	086508-42-1h	FC-5312 Fluorinert	820		215	1.9
1690	086508-42-1i	FC-70 Fluorinert	820		215	1.9
1700	125061-94-1	FC-71 Fluorinert	774.14	33	253	2
1710	086508-42-1j	FC-72 Fluorinert	340		56	1.7
1720	086508-42-1k	FC-722 Fluorad			56	1.7
1730	086508-42-1l	FC-75 Fluorinert	420		102	1.8
1740	086508-42-1m	FC-77 Fluorinert	415		97	1.8
1750	086508-42-1d	FC-84 Fluorinert	388		80	1.7
1760	000050-00-0	Formaldehyde	30.03	−92	−21	1.1
1770	000064-18-6	Formic acid	46.03	8	100.5	1.214
1780	000110-00-9	Furan	68.08	−85.6	31.3	0.94
1790	000098-01-1	Furfura1	96.085	−36.5	161.8	1.16
1800	000098-00-0	Furfuryl alcoho1	98.11	15	171	1.1285
1810	000142-82-5	Heptane	100.21	−90.6	98.5	0.68
1820	000999-97-3	Hexamethyldisilazane	161.311	−58	125	0.77
1830	000822-06-0	Hexamethylene diisocyanate	168.22	−67	255	1.04
1840	000110-54-3	Hexane	86.18	−95.3	68.7	0.65
1850	000355-42-0	Hexane, tetradecafluoro-	338.04	−87.1	56.6	
1860	000123-31-9	Hydroquinone	110.11	173.5	285	1.33
1870	064742-48-9f	Isopar G solvent		−5	154	5.51
1880	064742-48-9b	Isopar H solvent		−60	176	0.76
1890	064742-48-9a	Isopar L solvent		−60	185	0.77
1900	026952-21-6	Isooctyl alcohol	130.26	−106	188	
1910	000078-79-5	Isoprene	68.12	−145.9	34	
1920	000067-63-0	Isopropyl alcohol	60.11	−88	83	0.781
1930	008008-20-6	Kerosene	170.01	−20	150	0.81
1940	086508-42-1f	L-12077			90	1.8
1950	006382-06-5	Lactic acid, amyl ester	160.13	6.6	112	
1960	000138-22-7	Lactic acid, butyl ester	146.19	−28	187.77	0.98
1970	000097-64-3	Lactic acid, ethyl ester	118.13	−27	153.88	1.03
1980	000547-64-8	Lactic acid, methyl ester	104.11	−39	144	1.09
1990	000076-13-1c	MS-177 Freon TE Solvent		−43	44.61	1.51
2000	000076-13-1b	MS-178 Freon TES Solvent		−44	44.4	
2010	000107-30-2	Methane, chloromethoxy-	80.51	−103.3	57	1.06
2020	000074-95-3	Methane, dibromo-	173.85	−52.5	95	
2030	000075-61-6	Methane, dibromodifluoro-	209.83	−146.1	24.4	2.29

(*continued*)

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
2040	000075-09-2	Methane, dichloro-	84.93	−95	39.4	1.32
2050	000593-53-3	Methane, fluoro-	34.03	−141.8	78.4	
2060	001493-03-4	Methane, iododifluoro-			21.6	3.24
2070	000373-53-5	Methane, iodofluoro-			53.4	2.37
2080	000056-23-5	Methane, tetrachloro-	153.82	−23	77	1.59
2090	000067-66-3	Methane, trichloro-	119.38	−63	61	1.48
2100	000075-69-4	Methane, trichlorofluoro-	137.37	−111.1	23.7	1.47
2110	000075-75-2	Methanesulfonic acid	96.11	20	167	
2120	000067-56-1	Methanol	46.1	−98	64	0.79
2130	000100-66-3	Methoxybenzene	108.15	−37.5	153.6	0.989
2140	000079-20-9	Methyl acetate	74.08	−98	56.8	0.93
2150	000078-93-3	Methyl ethyl ketone	72.12	−86	80	0.8
2160	000107-31-3	Methyl formate	60.05	−99	31.7	0.96
2170	000141-79-7	Methyl isobutenyl ketone	98.144	−52.8	129.76	0.85
2180	000108-10-1	Methyl isobutyl ketone	100.16	−84	117	0.8
2190	000554-12-1	Methyl propionate	88.12	−88	79.7	
2200	000557-17-5	Methyl propyl ether	74.12	−101	39.1	
2210	001634-04-4	Methyl tert-butyl ether	88.17	−109	55	0.7
2220	064475-85-0	Mineral spirits		−20	175	0.75
2230	000141-43-5	Monoethanolamine	61.08	10.3	170.8	1.013
2240	000074-89-5	Monomethylamine	31.07	−93.3	−6.1	0.67
2250	000872-50-4a	N-Methylpyrrolidone	99.132	−24	202	1.03
2260	000062-75-9	N-Nitrosodimethylamine	74.1	−39.07	152	1.005
2270	064742-49-9g	Patclin #427 cold degreaser			167	0.707
2280	086508-42-1b	PF-5050			33	1.6
2290	086508-42-1	PF-5060	588		56	1.7
2300	000422-05-9	Pentafluoropropyl alcohol	150.06	−82	80	1.51
2310	000109-66-0	Pentane	72.15	129.7	36	0.63
2320	000678-26-2	Pentane, dodecafluoro-	288.04	−10	29.2	
2330	025322-68-3b	Polyglycol E 200	200	−65	0	1.124
2340	025322-68-3c	Polyglycol E 400	400	3.9		1.1
2350	025322-68-3d	Polyglycol E 600	600	22	201	1.13
2360	025322-68-3e	Polyglycol E-1000	1000	37	201	1.01
2370	025322-68-3f	Polyglycol E-1450	1450	44		1.102
2380	025322-68-3g	Polyglycol E-3350	3350	54		1.2
2390	025322-68-3i	Polyglycol E-4500	4500	58		1.2
2400	025322-68-3h	Polyglycol E-8000	8000	60		1.2
2410	025322-68-3a	Polyglycol E-900	900	34	0	
2420	025322-69-4c	Polyglycol P 425		−30		1.004
2430	025322-69-4a	Polyglycol P-1200		−40		
2440	025322-69-4b	Polyglycol P-2000		−30		1.005
2450	000754-34-7	Propane, 1,1,1,2,2,3,3-heptafluoro-3-iodo-	295.91	−95	40	2.06
2460	000677-69-0	Propane, 1,1,1,2,3,3,3-heptafluoro-2-iodo-	295.92	−58	38	2.097
2470	000540-54-5	Propane, 1-chloro-	78.54	−122	46	0.89
2480	000075-29-6	Propane, 2-chloro-	78.54	−117	35	0.86
2490	000507-20-0	Propane, 2-chloro-2-methyl-	92.57	−26.5	51	
2500	000109-60-4	Propyl acetate	102.13	−95	101.6	0.88
2510	000108-32-7	Propylene carbonate	102.09	−54.5	241.7	1.19
2520	000057-55-6	Propylene glycol	76.11	−60	188.2	1.033
2530	004169-04-4	Propylene glycol monophenyl ether	152.21	12.78	242.7	
2540	000075-56-9	Propylene oxide	58.08	−104.4	33.9	0.83

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
2550	086508-42-1a	SF-2			70	1.7
2560	018395-30-7	SIL-ACT ATS-100	178.31	−34	155	0.933
2570	000872-50-4b	SVC-150		0	225	1.025
2580	064742-88-7	Solvent 140-66			155	0.9
2590	008052-41-3	Stoddard Solvent	0	−28	149	0.78
2600	000126-33-0	Sulfolane	120.171	28.45	287.3	1.26
2610	000127-18-4	Tetrachloroethylene	165.82	−22.35	121.07	1.61
2620	000112-60-7	Tetraethylene glycol	194.26	−4	327.3	1.13
2630	000112-57-2	Tetraethylene pentamine	189.36	−40	333	0.998
2640	000075-73-0	Tetrafluoromethane	88.01	−183.6	−127.8	
2650	000109-99-9	Tetrahydrofuran	72.107	−108.3	65	0.89
2660	000097-99-4	Tetrahydrofurfuryl alcohol	102.15	−80	178	1.0483
2670	000100-72-1	Tetrahydropyran-2-methanol	116.18	−70	187	1.03
2680	000108-88-3	Toluene	92.15	−94.991	110.63	0.86
2690	000102-71-6	Triethanolamine	149.189	21.57	335.4	1.12
2700	000121-44-8	Triethylamine	101.2	−115	88.9	0.72
2710	000112-27-6	Triethylene glycol	150.17	−4.3	287.4	1.12
2720	004499-99-4	Triethylene glycol diethyl ether	206.18	0	0	
2730	000112-49-2	Triethylene glycol dimethyl ether	178.23	−45	216	0.99
2740	000075-46-7	Trifluoromethane	70.01	−160	−84.4	
2750	000504-63-2	Trimethylene glycol	76.095	−26.7	214.4	1.05
2760	000110-88-3	Trioxane	90.09	64	114.5	1.17
2770	008006-64-2	Turpentine (steam distilled)	0	−40	153	
2780	008032-32-4	VM & P Naphtha	100	−73	94	0.73
2790	000071-55-6a	Vi-Chem VC-1 Cleaner		−35.8	71.11	
2800	001330-20-7	Xylene (mixed)	106.18	−45	137	0.857
2810	010482-56-1	alpha-Terpineol	154.25	37	217.5	0.94
2820	005989-27-5b	d-Limonene	136.24	−96	175	0.84
2830	000096-48-0	gamma-Butyrolactone	86.09	−43.53	204	1.1254
2840	000108-38-3	*m*-Xylene	106.18	−47.7	138.9	0.86
2850	000142-92-7	*n*-Hexyl acetate	144.22	−80	169.2	0.868
2860	000112-58-3	*n*-Hexyl ether	186.38		228	
2870	000095-47-6	o-Xylene	106.18	−25	144.429	0.876
2880	000106-42-3	p-Xylene	106.167	13.263	138.359	0.86
2890	000056-81-5	Glycerol	92.095	17.8	290	1.256
2900	000060-35-5	Acetamide	59.068	80	221.15	
2910	000062-53-3	Aniline	93.129	−5.98	183.9	1.02
2920	000068-12-2	N,N′-Dimethylformamide	73.11	−60.4	152.8	0.944
2930	000074-83-9	Methyl bromide	94.939	−93.66	3.3	1.66
2940	000074-88-4	Methyl iodide	141.94	−66.45	42.8	2.27
2950	000074-97-5	Chlorobromomethane	129.384	−86.7	68	1.93
2960	000074-98-6	Propane	44.11	−187.8	−42.1	0.493
2970	000075-01-4	Vinylchloride	62.5	−160	−13.8	0.9
2980	000075-03-6	Iodoethane	155.97	−108	72.4	1.92
2990	000075-05-8	Acetonitrile	41.05	−43.8	81.6	0.78
3000	000075-07-0	Acetaldehyde	44.05	−123	20	0.77
3010	000075-11-6	Methylene iodide	267.83	5	181	3.31
3020	000075-12-7	Formamide	45.041	2	210	1.13
3030	000075-15-0	Carbon disulfide	76.13	−111.6	46.5	1.26
3040	000075-18-3	Dimethylsulfide	62.14	−98.3	36.2	0.84
3050	000075-25-2	Bromoform	252.75	6	149.5	2.88
3060	000075-26-3	2-Bromopropane	122.993	−89	59	1.31

(*continued*)

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
3070	000075-28-5	2-Methylpropane	58.124	−159.4	−11.7	0.551
3080	000075-30-9	2-Iodopropane	169.994	−90	89	1.69
3090	000075-31-0	Isopropylamine	59.112	−95.2	31.8	0.68
3100	000075-35-4	1,1-Dichloroethene	96.944	−122.7	31.7	1.17
3110	000075-37-6	1,1-Difluoroethane	66.051	−117	−26.5	0.89
3120	000075-50-3	Trimethylamine	59.112	−117.2	2.8	
3130	000075-52-5	Nitromethane	61.041	−28.9	101.2	1.13
3140	000075-64-9	*t*-Butylamine	73.139	−67.5	44	
3150	000075-65-0	*t*-Butanol	74.1237	25.62	82.2	0.79
3160	000075-76-3	Tetramethyl silane	88.2262	−99	26.6	
3170	000075-79-6	Methyltrichlorosilane	149.4801	−77.8	66.4	
3180	000075-84-3	2,2-Dimethyl-1-propanol	88.1508	53	114	
3190	000075-85-4	2-Methyl-2-butanol	88.1508	−8.8	101.8	
3200	000075-89-8	2,2,2-Trifluoroethanol	100.0408	−43.5	74	
3210	000076-01-7	Pentachloroethane	202.3	−28.9	161	1.68
3220	000076-05-1	Trifluoroacetic acid	114.0243	−15.4	72.4	
3230	000078-40-0	Triethyl phosphate	182.1579	−56.4	215	
3240	000078-75-1	1,2-Dibromopropane	201.8893	−55	140	
3250	000078-76-2	2-Bromobutane	137.0203	−112	91.2	
3260	000078-81-9	Isobutylamine	73.139	−85	68	0.739
3270	000078-84-2	Isobutyraldehyde	72.1078	−65.9	64	0.783
3280	000078-86-4	2-Chlorobutane	92.5693	−140	68	
3290	000078-87-5	1,2-Dichloropropane	112.9873	−100.5	96.6	1.16
3300	000079-00-5	1,1,2-Trichloroethane	133.4052	−36.6	113.9	1.44
3310	000079-09-4	Propionic acid	74.09	−15	141.1	0.99
3320	000079-10-7	Acrylic acid	72.0641	12.78	141	1.05
3330	000079-16-3	N-Methylacetamide	73.11	28	205	
3340	000079-24-3	Nitroethane	75.0677	−89.5	113.88	1.05
3350	000079-27-6	1,1,2,2-Tetrabromoethane	345.6542	0	245.5	2.97
3360	000079-31-2	Isobutyric acid	88.1072	−47	152	
3370	000079-34-5	1,1,2,2-Tetrachloroethane	167.8502	−36	146	1.59
3380	000079-41-4	Methacrylic acid	86.0912	16	162.76	1.02
3390	000079-46-9	2-Nitropropane	89.0947	−92.8	120.25	0.99
3400	000080-56-8	α-Pinene	136.239	−55	155	0.863
3410	000080-62-6	Methyl methacrylate	100.1183	−48	101	0.94
3420	000087-62-7	2,6-Dimethylaniline	121.1836	10	215	
3430	000090-02-8	o-Hydroxybenzaldehyde	122.1247	−7	196	
3440	000090-11-9	1-Bromonaphthalene	207.0713	0.2	281	
3450	000090-12-0	1-Methylnaphthalene	142.2024	−22	244.7	
3460	000090-13-1	1-Chloronaphthalene	162.6203	−2.5	259.3	
3470	000091-16-7	1,2-Dimethoxybenzene	138.1677	22	206	
3480	000091-17-8	Decahydronaphthalene	138.255	−30.4	187	0.9
3490	000091-20-3	Naphthalene	128.1753	80	217.942	1.15
3500	000091-22-5	Quinoline	129.1628	−14.5	237.7	
3510	000091-23-6	2-Nitroanisole	153.15	9.4	277	
3520	000092-51-3	Dicyclohexyl	166.3091	4	238	
3530	000093-58-3	Benzoic acid, methyl ester	136.1518	−15	198	
3540	000093-89-0	Ethyl benzoate	150.1789	−34	211	1.02
3550	000094-96-2	2-Ethyl-1,3-hexandiol	146.2315	−40	243.1	0.93
3560	000095-48-7	*o*-Cresol	108.1412	30.944	191	1.05
3570	000095-49-8	2-Chlorotoluene	126.585	−35	159.99	1.08
3580	000095-50-1	1,2-Dichlorobenzene	147.0048	−17	180	1.3
3590	000095-51-2	2-Chloroaniline	127.573	−1.94	208.84	1.208
3600	000095-52-3	*o*-Fluorotoluene	110.1322	−62	114	0.99

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
3610	000095-53-4	*o*-Toluidine	107.1565	−16	200.4	0.99
3620	000095-65-8	3,4-Dimethylphenol	122.1683	65	226	1.13
3630	000095-68-1	2,4-Dimethylaniline	121.1836	−14.3	211.5	0.97
3640	000095-73-8	2,4-Dichlorotoluene	161.03	−13.5	199.6	1.24
3650	000095-75-0	3,4-Dichlorotoluene	161.03	−16	208.9	1.24
3660	000095-87-4	2,5-Dimethylphenol	122.166	74.85	211.1	1.189
3670	000096-14-0	3-Methylpentane	86.177	−118	63.2	0.65
3680	000096-18-4	1,2,3-Trichloropropane	147.4323	−14.4	156.8	1.33
3690	000096-22-0	3-Pentanone	86.1349	−42	101	0.81
3700	000096-33-3	Methyl acrylate	86.09	−76	80	0.96
3710	000096-37-7	Methylcyclopentane	84.161	−142.2	71.8	0.74
3720	000096-47-9	2-Methyltetrahydrofuran	86.13	−137.2	80	0.85
3730	000096-49-1	1,3-Dioxolan-2-one	88.0635	36.3	248	1.33
3740	000097-85-8	Isobutyl isobutyrate	144.2155	−80.7	147	
3750	000097-95-0	2-Ethyl-1-butanol	102.17	−114.5	146.3	0.82
3760	000098-06-6	*tR*-Butylbenzene	134.22	−57.8	169.1	0.86
3770	000098-07-7	Benzotrichloride	195.476	−4.4	213	1.38
3780	000098-08-8	Benzotrifluoride	146.112	−28.16	102	1.18
3790	000098-55-5	α-Terpineol	154.25	35	217	0.92
3800	000098-82-8	Cumene	120.196	−96.033	152	0.09
3810	000098-86-2	Acetophenone	120.15	19.62	201.7	1.03
3820	000098-95-3	Nitrobenzene	123.11	6	210	1.205
3830	000099-87-6	*p*-Cymene	134.2231	−67.935	176.5	0.855
3840	000099-94-5	*p*-Toluic acid	136.1518	180.5	274.5	
3850	000100-42-5	Styrene	104.153	−30.6	145	0.91
3860	000100-44-7	α-Chlorotoluene	126.5868	−45	179	1.1
3870	000100-47-0	Benzonitrile	103.12	−12.75	191.1	1
3880	000100-51-6	Benzyl alcohol	108.14	−15.3	206	1.04
3890	000100-52-7	Benzaldehyde	106.12	−55.6	178.75	1.1
3900	000100-61-8	N-Methylaniline	107.15	−57	194	0.99
3910	000102-76-1	Triacetin	218.2	−37	258	1.15
3920	000102-82-9	Tri N-butylamine	185.35	−70	214	0.77
3930	000103-09-3	2-Ethylhexylacetate	172.26	−93	198.6	0.87
3940	000103-36-6	Cinnamic acid, ethyl ester	176.2171	6.5	271	
3950	000103-50-4	Dibenzyl ether	198.26	3.6	288.3	1.04
3960	000103-73-1	Ethoxybenzene	122.16	−29.5	169.8	0.96
3970	000104-51-8	N-Butylbenzene	134.22	−87.8	183.1	0.85
3980	000104-75-6	2-Ethylhexylamine	129.24	−76	169	0.78
3990	000104-76-7	2-Ethyl-1-hexanol	130.23	−76	182	0.83
4000	000105-30-6	2-Methyl-1-pentanol	102.176		147.9	0.82
4010	000105-34-0	Methyl cyanoacetate	99.09	−13.1	205.1	1.12
4020	000105-45-3	Methyl acetoacetate	116.11	−80	171.7	1.07
4030	000105-53-3	Diethyl malonate	160.169	−48.9	198	1.05
4040	000105-54-4	Ethylbutyrate	116.16	−98	120	0.87
4050	000105-56-6	Ethyl cyanoacetate	113.117	−22	206	1.056
4060	000105-57-7	1,1-Diethoxyethane	118.175	−100	103	0.82
4070	000105-58-8	Diethyl carbonate	118.13	−43	126	0.97
4080	000105-60-2	Caprolactam	113.16	68.9	268.3	1.01
4090	000105-67-9	2,4-Dimethylphenol	122.16	24.5	210.9	1.02
4100	000105-76-0	Dibutyl maleate	228.29	−80	280	0.99
4110	000106-31-0	Butyric anhydride	158.19	−65.7	199.4	0.96
4120	000106-35-4	3-Heptanone	114.189	−39	147.4	0.81
4130	000106-43-4	*p*-Chlorotoluene	126.585	7.3	162	1.065
4140	000106-44-5	*p*-Cresol	108.14	34.739	201.9	1.15

(*continued*)

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
4150	000106-46-7	1,4-DIchlorobenzene	147.005	53.13	174.12	1.25
4160	000106-49-0	*p*-Toluidine	107.15	43.8	200	
4170	000106-69-4	1,2,6-Hexanetriol	134.18	−20	178	1.1
4180	000106-88-7	1,2-Butyleneoxide	72.1078	−150	63	0.83
4190	000106-93-4	1,2-Dibromoethane	187.862	9.79	131	2.17
4200	000106-94-5	1-Bromopropane	122.99	−108.1	70.9	1.34
4210	000106-97-8	*n*-Butane	58.124	−138.2	−0.5	0.57
4220	000106-98-9	1-Butene	56.1084	−185	−6.3	
4230	000107-04-0	1-Bromo-2-chloroethane	143.411	−16.7	106.7	1.73
4240	000107-05-1	3-Chloropropylene	76.526	−134.5	45.1	0.94
4250	000107-06-2	1,2-Dichloroethane	98.96	−35.66	83.85	1.24
4260	000107-07-3	2-Chloroethanol	80.515	−67	128	1.197
4270	000107-08-4	1-Iodopropane	169.994	−101	102	1.74
4280	000107-10-8	Propylamine	59.112	−83	47.2	0.71
4290	000107-11-9	Allylamine	57.096	−88	53	0.76
4300	000107-12-0	Propionitrile	55.08	−91.8	97.2	0.777
4310	000107-13-1	Acrylonitrile	53.06	−83.5	77	0.81
4320	000107-15-3	1,2-Diaminoethane	60.099	8.3	116.9	0.91
4330	000107-18-6	Allyl alcohol	58.08	−129	96	0.85
4340	000107-19-7	Propargyl alcohol	56.065	−51.8	113.6	0.97
4350	000107-41-5	2-Methyl-2,4-pentanediol	118.177	−50	196	0.92
4360	000107-83-5	2-Methylpentane	86.177	−96	60.27	0.66
4370	000107-92-6	Butyric acid	88.11	−5.2	163.7	0.95
4380	000108-03-2	1-Nitropropane	89.095	−103.9	131.2	1
4390	000108-05-4	Vinyl acetate	86.091	−58	72.5	0.93
4400	000108-08-7	2,4-Dimethylpentane	100.21	−119.2	80.4	0.67
4410	000108-24-7	Acetic anhydride	102.091	−73	139	1.08
4420	000108-39-4	*m*-Cresol	108.141	11	202.232	1.03
4430	000108-41-8	*m*-Chlorotoluene	126.58	−26.25	161.75	1.06
4440	000108-44-1	*m*-Toluidine	107.1565	−30.5	202.7	0.98
4450	000108-47-4	2,4-Dimethylpyridine	107.155	−63.9	158	0.927
4460	000108-48-5	2,6-Lutidine	107.155	−5.8	144	0.918
4470	000108-64-5	Ethyl isovalerate	130.18	−99	134.7	0.86
4480	000108-67-8	1,3,5-Trimethylbenzene	120.196	−44.6	164.7	0.86
4490	000108-68-9	3,5-Dimethylphenol	122.16	63.2	221.7	1.12
4500	000108-75-8	2,4,6-Collidine	121.18	−44	171	0.91
4510	000108-84-9	4-Methyl-2-pentyl acetate	144.21	−63.8	146	0.86
4520	000108-86-1	Bromobenzene	157.01	−30.6	155.9	1.488
4530	000108-87-2	1-Methylcyclohexane	98.18	−126.6	100.8	0.765
4540	000108-89-4	4-Methylpyridine	93.13	3.6	145	0.95
4550	000108-90-7	Chlorobenzene	112.56	−45	131.687	1.11
4560	000108-91-8	Cyclohexanamine	99.177	−17.7	134.5	0.9
4570	000108-95-2	Pheno1	94.114	43	181.839	1.06
4580	000108-98-5	Thiophenol	110.179	−14.9	168.9	1.08
4590	000108-99-6	3-Methylpyridine	93.129	−18.1	144	0.95
4600	000109-06-8	2-Methylpyridine	93.13	−66.7	129.3	0.939
4610	000109-43-3	Dibutyl sebacate	314.46	−10	344.5	0.94
4620	000109-52-4	Pentanoic acid	102.134	−33.6	185.5	0.93
4630	000109-65-9	1-Bromobutane	137.02	−112	101.3	1.27
4640	000109-69-3	1-Chlorobutane	92.57	−123.1	78.5	0.88
4650	000109-74-0	Butyronitrile	69.107	−111.9	117.62	0.78
4660	000109-78-4	Ethylene cyanohydrin	71.079	−46	220	1.04
4670	000109-79-5	1-Butanethio1	90.188	−115.6	98.4	0.83
4680	000109-87-5	Dimethoxymethane	76.09	−105	41.6	0.86
4690	000109-89-7	Diethylamine	73.138	−49.8	55.5	0.7

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
4700	000109-92-2	Ethyl vinyl ether	72.108	−115.8	35.5	0.75
4710	000109-97-7	Pyrrole	67.091	−23.4	129.8	0.966
4720	000110-01-0	Tetrahydrothiophene	88.167	−96.1	120.9	0.99
4730	000110-02-1	Thiophene	84.136	−38.3	84.1	1.06
4740	000110-19-0	*sec*-Butylacetate	116.161	−98.8	116.6	0.87
4750	000110-53-2	1-Bromopentane	151.047	−87.9	129.5	1.21
4760	000110-58-7	N-Pentylamine	87.166	−43.2	104	0.75
4770	000110-59-8	Valeronitrile	83.134	−96.2	141.3	0.795
4780	000110-61-2	Succinonitrile	80.089	57.15	265	0.99
4790	000110-63-4	1,4-Butanedio1	90.123	19.6	228	1.01
4800	000110-71-4	Ethylene-glycol dimethyl ether	90.122	−69	84	0.86
4810	000110-74-7	Propyl formate	88.106	−92.9	80.8	0.899
4820	000110-83-8	Cyclohexene	82.147	−103.5	83	0.81
4830	000110-86-1	Pyridine	79.102	−41.6	115	0.98
4840	000110-89-4	Piperidine	85.149	−10.5	106.3	0.857
4850	000110-91-8	Morpholine	87.122	−4.9	128.9	1.007
4860	000111-13-7	2-Octanone	128.216	−20.3	172	0.81
4870	000111-29-5	1,5-Pentanediol	104.149	−15.6	242	0.986
4880	000111-34-2	Butyl vinyl ether	100.16	−92	93.8	0.77
4890	000111-40-0	Diethylenetriamine	103.167	−39	206.9	0.96
4900	000111-43-3	Di(N-propyl) ether	102.176	−123.2	90.1	0.74
4910	000111-44-4	Bis(2-chloroethyl) ether	143.013	−46.8	178.75	1.21
4920	000111-48-8	2,2′-Thiobisethanol	122.187	−10.2	282	1.18
4930	000111-55-7	Ethylene glycol diacetate	146.144	−41	190	1.099
4940	000111-65-9	Octane	114.233	−56.8	125.6	0.699
4950	000111-66-0	1-Octene	112.214	−101.6	121	0.71
4960	000111-84-2	n-Nonane	128.257	−53.5	150.7	0.72
4970	000111-85-3	1-Chlorooctane	148.677	−57.8	181.5	0.87
4980	000111-92-2	Dibutylamine	129.247	−62	159.6	0.76
4990	000112-05-0	Nonanoic acid	158.243	12.5	255.6	0.9
5000	000112-29-8	1-Bromodecane	221.183	−29.2	240.6	1.06
5010	000112-40-3	Dodecane	170.337	−9.6	216.3	0.745
5020	000112-41-4	1-Dodecene	168.332	−35	213	0.75
5030	000112-62-9	Methyl oleate	296.498	−19.9	217	0.87
5040	000112-80-1	Oleic acid	282.46	13.4	286	0.89
5050	000115-10-6	Dimethyl ether	46.07	−141.5	−24.8	0.66
5060	000115-21-9	Ethyltrichlorosilane	163.507	−105.6	99.1	1.24
5070	000115-25-3	Perfluorocyclobutane	200.032	−38.7	−6	1.5
5080	000117-81-7	Bis(2-ethylhexyl)phthalate	390.57	−50	384	0.99
5090	000119-36-8	Methyl salicylate	152.151	−8	233	1.18
5100	000119-64-2	Tetralin	132.207	−35	207.2	0.966
5110	000119-65-3	Isoquinoline	129.163	26.48	243.25	1.09
5120	000120-51-4	Benzyl benzoate	212.248	19.4	323	1.112
5130	000120-92-3	Cyclopentanone	84.118	−51.3	130.6	0.94
5140	000121-69-7	N,N-Dimethylaniline	121.183	2.45	194.05	0.96
5150	000123-04-6	3-(Chloromethyl)heptane	148.67	−135	172	0.88
5160	000123-38-6	Propionaldehyde	58.081	−80	48	0.79
5170	000123-39-7	Methylformamide	59.068	−3.8	180	1
5180	000123-51-3	Isopentanol	88.151	−117.2	130.2	0.81
5190	000123-54-6	2,4-Pentanedione	100.118	−23	138.3	0.97
5200	000123-62-6	Propionic anhydride	130.145	−43	167	1.006
5210	000123-72-8	Butyraldehyde	72.108	−96.4	74.8	0.8
5220	000123-73-9	Trans-crotonaldehyde	70.092	−74	104	0.85

(*continued*)

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
5230	000123-75-1	Pyrrolidine	71.123	−57.8	86.5	0.85
5240	000123-92-2	Isoamyl acetate	130.188	−78.5	142.5	0.866
5250	000123-95-5	N-Butyl stearate	340.588	26.3	343	0.854
5260	000124-07-2	Octanoic acid	144.215	16.5	239.7	0.91
5270	000124-11-8	1-Nonene	126.244	−81.3	146.9	0.73
5280	000124-12-9	Octanenitrile	125.215	−45.6	205.2	0.81
5290	000124-18-5	n-Decane	142.287	−29.7	174.1	0.73
5300	000124-68-5	2-Amino-2-methyl-1-propano	89.138	30	165	
5310	000126-73-8	Tributylphosphate	266.32	−79	289	0.98
5320	000126-98-7	Methacrylonitrile	67.091	−35.8	90.3	0.8
5330	000127-91-3	α-Pinene	136.24	−61.5	166	0.867
5340	000135-98-8	*sec*-Butylbenzene	134.223	−75.5	173.5	0.86
5350	000137-32-6	2-Methyl-1-butanol	88.151	−69	128	0.82
5360	000140-11-4	Benzyl acetate	150.179	−51	213	1.05
5370	000140-29-4	Phenylacetonitrile	117.152	−23.8	233.5	1.01
5380	000140-88-5	Ethyl acrylate	100.118	−71.2	99.5	0.92
5390	000141-05-9	Diethyl maleate	172.182	−8.8	223	1.06
5400	000141-97-9	Acetoacetic ester	130.145	−39	180.8	1.02
5410	000142-62-1	Hexanoic acid	116.161	−3.44	205.02	0.923
5420	000142-68-7	Tetrahydropyran	86.135	−45	88	0.877
5430	000142-77-8	Butyl oleate	338.578	−15	204	0.86
5440	000142-84-7	Dipropylamine	101.193	−63	109.2	0.733
5450	000151-56-4	Aziridine	43.068	−78	57	0.832
5460	000156-59-2	*cis*-1,2-Dichloroethene	96.944	−80	60.1	1.28
5470	000156-60-5	*trans*-1,2-Dichloroethene	96.944	−49.8	47.7	1.25
5480	000311-89-7	Heptacosafluorotributylamine	671.097	−38	177	1.88
5490	000352-32-9	*p*-Fluorotoluene	110.132	−56	116.6	0.99
5500	000352-70-5	*m*-Fluorotoluene	110.132	−87	115	0.99
5510	000352-93-2	Diethylsulfide	90.188	−103.9	92.1	0.83
5520	000355-25-9	Decafluorobutane	238.029	−128.2	−2.2	1.51
5530	000392-56-3	Hexafluorobenzene	186.057	−11	80.2	1.61
5540	000420-46-2	1,1,1-Trifluoroethane	84.091	−111.3	−47.5	0.96
5550	000462-06-6	Fluorobenzene	96.105	−40	84.73	1.01
5560	000463-82-1	2,2-Dimethylpropane	72.151	−16.5	9.5	0.585
5570	000464-49-3	(1R,4R)-(+)-Camphor	152.238	178.8	207.4	0.99
5580	000470-82-6	1,8-Cineole	154.254	1.3	176	0.92
5590	000493-01-6	*cis*-Bicyclo(4.4.0)decane	138.25	−42.9	195.8	0.893
5600	000493-02-7	*trans*-Bicyclo(4.4.0)decane	138.25	−30.3	187.3	0.866
5610	000503-74-2	Isovaleric acid	102.1343	−37	176	
5620	000507-19-7	2-Bromo-2-methylpropane	137.02	−16.3	73.3	1.21
5630	000512-56-1	Trimethyl phosphate	140.076	−46	192.85	1.21
5640	000513-36-0	Isobutyl chloride	92.57	−131	68	0.88
5650	000513-38-2	1-Iodo-2-methylpropane	184.02	−90.7	120	1.6
5660	000513-85-9	2,3-Butanedio1	90.123	22.5	182	1
5670	000538-93-2	Isobutylbenzene	134.223	−51.4	172.7	0.85
5680	000539-30-0	Benzyl ethyl ether	136.195	−17	186	0.95
5690	000540-84-1	2,2,4-Trimethylpentane	114.233	−107.39	99.24	0.69
5700	000541-73-1	3-Dichlorobenzene	147.005	−24.76	173	1.28
5710	000542-54-1	4-Methylpentanitrile	97.161	−51	154	0.8
5720	000542-55-2	Isobutyl formate	102.134	−95	98	0.87
5730	000542-69-8	N-Butyl iodide	184.02	−103	130.4	1.61
5740	000543-49-7	2-Heptanol	116.205	−39	158	0.81
5750	000543-59-9	1-Chloropentane	106.596	−99	107.8	
5760	000544-01-4	Diisopentyl ether	158.286	−49	172	0.77
5770	000544-40-1	5-Thianonane	146.297	−75	182	0.83
5780	000554-14-3	2-Methylthiophene	98.168	−63.4	112.6	1.014
5790	000564-02-3	2,2,3-Trimethylpentane	114.233	−112.2	110	0.71

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
5800	000565-59-3	2,3-Dimethylpentane	100.206	−104	89.7	0.691
5810	000565-80-0	2,4-Dimethyl-3-pentanone	114.189	−69	125.4	
5820	000573-98-8	1,2-Dimethylnaphthalene	156.229	−1	266.5	1.01
5830	000575-43-9	1,6-Dimethyl naphthalene	156.229	−16.9	264	1
5840	000576-26-1	2,6-Dimethylphenol	122.168	45.7	201	1.13
5850	000583-57-3	1,2-Dimethylcyclohexane	112.217	0	124	0.78
5860	000583-59-5	2-Methylcyclohexanol	114.189	−9.5	163	0.92
5870	000584-02-1	3-Pentanol	88.151	−8	115.3	0.816
5880	000589-34-4	3-Methylhexane	100.206	−119	91	0.683
5890	000589-82-2	3-Pentanol	116.205	−70	156.7	0.817
5900	000590-36-3	2-Methyl-2-pentanol	102.178	−102	120	0.81
5910	000590-67-0	1-Methylcyclohexanol	114.189	25	155	0.92
5920	000591-23-1	3-Methylcyclohexanol	114.189	−1	172	0.91
5930	000591-50-4	Iodobenzene	204.11	−29	188	1.82
5940	000591-76-4	2-Methylhexane	100.21	−118.2	90	0.674
5950	000591-87-7	Allyl acetate	100.118	0	103.5	0.92
5960	000592-41-6	1-Hexene	84.162	−139.7	63.4	0.67
5970	000592-76-7	1-Heptene	98.189	−118.8	93.6	0.69
5980	000592-84-7	N-Butylformate	102.134	−91.5	106.1	0.89
5990	000593-60-2	Bromoethene	106.95	−139.54	15.8	1.47
6000	000594-82-1	2,2,3,3-Tetramethylbutane	114.233	100.7	106.4	0.82
6010	000598-75-4	3-Methyl-2-butanol	88.151	−75	111.5	0.81
6020	000616-44-4	3-Methylthiophene	98.168	−68.9	112.5	1.02
6030	000616-45-5	2-Pyrrolidinone	85.107	25	251	1.11
6040	000624-48-6	Methyl maleate	144.128	−17.5	200.5	1.15
6050	000624-92-0	Dimethyldisulfide	94.189	−84.7	109.75	1.06
6060	000627-20-3	*cis*-2-Pentene	70.136	−151.4	36.9	0.65
6070	000628-73-9	Hexanenitrile	97.161	−74	163.6	0.8
6080	000628-81-9	Butyl ethyl ether	102.178	−103	91	0.745
6090	000629-50-5	n-Tridecane	184.368	−5.3	235.4	0.753
6100	000631-36-7	Tetraethylsilane	144.335	−82.5	153	0.76
6110	000632-22-4	Tetramethylurea	116.164	−1.2	175.2	0.96
6120	000646-04-8	*trans*-2-Pentene	70.136	−140	26.3	0.64
6130	000646-06-0	1,3-Dioxolane	74.08	−95	75.6	1.06
6140	000659-70-1	Isoamyl isovalerate	172.27	−31	190.4	0.85
6150	000680-31-9	Hexamethylphosphoramide	179.204	7.2	233	1.03
6160	000688-74-4	*n*-Butyl borate	230.158	−68	233.5	0.85
6170	000821-11-4	*trans*-2-Butene-1,4-diol	88.107	25	131	1.06
6180	000827-52-1	Phenyl cyclohexane	160.261	7.3	240.1	0.94
6190	000872-05-9	1-Decene	140.271	−66.3	170.5	0.74
6200	001187-58-2	N-Methyl propionamide	87.122	−30.9	148	0.93
6210	001330-78-5	Tricresyl phosphate	416.37	−33	265	1.16
6220	001678-91-7	Ethyl cyclohexane	112.217	−111.3	130	0.79
6230	001814-88-6	1,1,1,2,2-Pentafluoropropane	134.05	−142	−17.4	
6240	002207-01-4	*cis*-1,2-Dimethylcyclohexane	112.217	−49.9	129.8	
6250	002315-68-6	Propyl benzoate	164.206	−51.6	211	
6260	002437-56-1	1-Tridecene	182.352	−20	232.8	0.77
6270	003522-94-9	2,2,5-Trimethylhexane	128.26	−105.7	124	0.7
6280	003724-65-0	Crotonic acid	86.091	71	185	1.02
6290	003744-02-3	Isomesityl oxide	98.146	−72.6	124.2	
6300	004088-60-2	*cis*-2-Buten-1-ol	72.108	−62	123	0.85
6310	005341-95-7	*Meso*-2,3-Butanediol	90.123	32	182.3	0.99
6320	005454-79-5	Cis-3-Methylcyclohexanol	114.189	−5	168	0.91
6330	005989-54-8	(-)-1-Methyl-4-(1-methylethene)	136.24	−74	175	0.849

(*continued*)

Table A1. *Continued.*

Ref No.	CAS	Name	MolWgt	MP	BP	SpecGrav
6340	006032-29-7	2-Pentanol	88.151	−73	119.3	0.82
6350	006117-80-2	*Cis*-2-Butene-1,4-diol	88.107	4	235	1.07
6360	006876-23-9	*trans*-1,2-Dimethylcyclohexane	112.217	−88	123.5	0.77
6370	006982-25-8	dl-2,3-Butandio1	90.123	7.6	176	0.993
6380	007443-52-9	*trans*-2-Methylcyclohexanol	114.189	−3.7	165	0.92
6390	007443-55-2	*trans*-3-Methylcyclohexanol	114.189	0	166	0.92
6400	007443-70-1	*cis*-2-Methylcyclohexanol	114.189	6.8	165	0.93
6410	007642-04-8	*cis*-2-Octene	112.217	−100.2	125.6	0.72
6420	007705-14-8	(+-)Dipentene	136.239	−38	174	0.84
6430	007731-28-4	*cis* 4-Methylcyclohexanol	114.189	−9.2	171	0.92
6440	007731-29-5	*trans*-4-Methylcyclohexanol	114.189	−25	171	0.91
6450	007785-53-7	d-α-Terpineol	154.254	36.9	206	0.93
6460	013389-42-9	*trans*-2-Octene	112.217	−87.7	125	0.716
6470	013952-84-6	*sec*-Butylamine	73.139	−104	63	0.72
6480	019132-06-0	d-2,3-Butanediol	90.123	−34	179	0.99
6490	024347-58-8	l-2,3-Butanediol	90.123	19	179	0.99

Table A2. Methods for the purification of solvents (Riddick et al., 1986).

General Compound Class	**Purification Method**
silanes, cumene	preparative gas chromatography
alkanes, benzene	alumina + $AgNO_3$ (to remove olefins, aromatics) and distillation
alkanes, ethyl benzene	silica gel column and distillation
cycloalkanes, alkanes	nitration to remove benzene, silica gel column, fractional distillation
alkanes	fractional melting or preparative gas chromatography
toluene	sodium treatment, then fractional distillation
xylenes	sulfonation and steam hydrolysis, then fractional distillation
tetralin	H_2SO_4 treatment, then fractional distillation
alkanols	drying followed by distillation
phenols	fractional crystallization, then fractional distillation
diethyl ether, ethers	peroxide removal by an alumina column, drying and fractional distillation
aldehydes, ketones	drying and fractional distillation
acetophenone	crystallization, drying, and fractional distillation
alkanoic acids	drying and distillation
esters	washing with water, drying, and distillation
perfluoronated compounds	fractional distillation
1-chlorobutane and other chlorinated compounds	treatment with H_2SO_4, aqueous base, water, drying, and fractional distillation
brominated alkanes	drying and fractional distillation
amines, heteroaromatic compounds, alkanolamines	fractional crystallization and distillation
nitriles	drying and distillation
nitroalkanes, nitroaromatics	fractional crystallization and distillation
amides	drying and fractional distillation
sulfur-containing compounds	fractional distillation

Table A3. Physical constants of green solvents.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
10	064741-41-9	#489-0						
20	000075-45-6a	(F-22) Anti-Static Super Freeze 1503-12	7046	25				
30	000460-73-1	1,1,1,3,3-Pentafluoropropane						
40	000680-00-2	1,1,2,2,3,3-Hexafluoropropane	7930	25	317	1.91	8.05	
50	000679-86-7	1,1,2,2,3-Pentafluoropropane	5710	25	292	2.04	4.05	
60	000079-01-6	1,1,2-Trichloroethylene	58	20	1	2.42	0.0103	3.42
70	000076-14-2	1,2-Dichlorotetrafluoroethane	1444	20	100	2.82	2.8	2.26
80	000627-92-9	1,2-Propanediol, 3-(3-methylbutoxy)-	0.0009	25	155000	0.414	6.31E-09	
90	000624-52-2	1,2-Propanediol, 3-butoxy-			0	0.015	4.75E-09	
100	000623-39-2	1,2-Propanediol, 3-methoxy-	0.6	25	1000000	–1.572	2.03E-09	
110	000460-12-8	1,3-Butadiyne	473	25	3072	1.3	0.0191	
120	000107-88-0	1,3-Butanediol	0.06	25	1000000	–1.384	2.304E-07	28.8
130	000111-32-0	1,3-Butylene glycol methyl ether			316900	–0.588	7.38E-08	
140	000542-92-7	1,3-Cyclopentadiene	400	20	4700	2.25	0.0636	
150	000504-60-9	1,3-Pentadiene	284	25	325	2.4	0.0122	
160	000123-91-1	1,4-Dioxane	37.1	25	1000000	–0.27	0.0000048	2.209
170	000591-93-5	1,4-Pentadiene	410	25	301	2.48	0.127	
180	001115-08-8	1,4-Pentadiene, 3-methyl-	280	25	115	2.94	0.169	
190	002396-65-8	1,8-Nonadiyne	3.6	25	52	3.22	0.0109	
200	000071-36-3	1-Butanol	6.83	25	74500	0.88	0.0000088 1	17.51
210	000563-46-2	1-Butene, 2-methyl-	610	25	188	2.72	0.319	
220	000558-37-2	1-Butene, 3,3-dimethyl-	382	25	95	3.04	0.359	
230	000111-70-6	1-Heptanol	1	42	2000	2.41	31.2	
240	000111-27-3	1-Hexanol	1	24	1000000	2.03	34.4	13.3
250	019430-93-4	1-Hexene, 3,3,4,4,5,5,6,6,6-nonafluoro-	2700	25	1.3	4.99	111	
260	000107-98-2	1-Methoxy-2-propanol	12.5	25	1000000	–0.49	1.81E-08	
270	000111-87-5	1-Octanol	0.075	25	540	2.97	0.0000252	10.34
280	000071-41-0	1-Pentanol	2.2	25	22000	1.56	0.000013	13.9
290	000109-67-1	1-Pentene	638	25	148	2.66	0.27	2.02
300	000691-37-2	1-Pentene, 4-methyl-	440	20	88	3.08	0.36	

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
310	000627-19-0	1-Pentyne	253	25	804	1.98	0.0283	
320	000071-23-8	1-Propanol	20.99	25	1000000	–1.52	0.00000685	20.45
330	000584-84-9	2,4-Toluenediisocyanate	1.3	20	37.6	0.21	0.0000111	
340	000110-13-4	2,5-Hexanedione	0.5	20	179100	–0.242	4.43E-08	
350	000112-34-5	2-(2-n-Butoxyethoxy)ethanol	0.0219	25	1000000	0.29	1.52E-09	
360	000078-92-2	2-Butanol	12	20	160000	0.61	0.0000102	16.56
370	000513-35-9	2-Butene, 2-methyl-	344	25	219	2.64	0.376	
380	000112-07-2	2-Butoxyethanol acetate	0.3	20	15000	1.708	0.00000638	
390	000503-17-3	2-Butyne	706	25	2246	1.46	0.0108	
400	000100-37-8	2-Diethylaminoethanol	1	20	953900	0.31	0.000313	
410	000110-80-5	2-Ethoxyethanol	5.31	25	1000000	–0.1	0.000000123	29.6
420	000111-15-9	2-Ethoxyethanol acetate	2.34	25	229000	0.65	0.00000362	7.57
430	000110-43-0	2-Heptanone	3.85	25	4300	1.98	0.000177	11.98
440	000591-78-6	2-Hexanone	11.6	25	17500	1.38	0.000116	14.56
450	000598-82-3	2-Hydroxypropanoic acid	19	38	1000000	–0.72	0.000000113	
460	000109-86-4	2-Methoxyethano1	9.5	25	1000000	–0.77	0.000000081	16.93
470	000109-83-1	2-Methylaminoethanol	0.5	20	1000000	–0.94	8.075E-10	
480	000078-83-1	2-Methylpropanol	9	20	100000	0.76	0.0000118	17.93
490	000123-96-6	2-Octanol	0.84	40	1281	2.73	0.000031	8.173
500	000107-87-9	2-Pentanone	35.4	25	59500	0.91	0.0000636	15.38
510	000109-68-2	2-Pentene	528	25	203	2.58	0.319	
520	000626-78-8	2-Propanol, 1,3-bis(3-methylbutoxy)-	0.00026	25	664	3.023	6.27E-09	
530	000623-69-8	2-Propanol, 1,3-dimethoxy-	0.67	25	1000000	–0.949	6.5E-10	
540	000111-35-3	3-Ethoxy-1-propanol			316500	–0.588	7.38E-08	
550	000563-80-4	3-Methyl-2-butanone	52.2	25	24360	0.84	0.0000873	

560	000108-11-2	4-Methyl-2-pentanol	8.2	25	16400	1.68	0.0000445	
570	000110-12-3	5-Methyl-2-hexanone	5	20	5000	1.718	0.000154	
580	000541-85-5	5-Methyl-3-heptanone	2	25	1371	2.247	0.000204	
590	064742-47-8c	Actrel 116OL cleaner	0.24	20	100			
600	064742-48-9d	Actrel 3338L cleaner	10	37				
610	064742-48-9e	Actrel 3349L cleaner	10	25	100			
620	064742-48-9c	Actrel 3360L cleaner	2	37	1000			
630	064771-72-8	Actrel 4493L cleaner	1	37	50	3.39	1.29	
640	000064-19-7	Acetic acid	15.6	20	1000000	–0.17	0.0000442	6.170
650	000108-65-6	Acetic acid, 2-methoxy-1-methylethyl ester	3.7	20	198000	0.43	0.0000036 2	
660	000628-63-7	Acetic acid, amyl ester	9.7	25	1700	2.34	0.000391	4.75
670	000108-21-4	Acetic acid, isopropyl ester	59.2	25	30900	1.28	0.000281	
680	000105-46-4	Acetic acid, sec-butyl ester	24	25	6200	1.509	0.00041	5.01
690	000067-64-1	Acetone	231	25	1000000	–0.24	0.0000397	20.56
700	000107-02-8	Acrolein	265	25	208000	–0.01	0.000122	
710	005989-27-5a	Biogenic SE 373	2	20	0	0	0	
720	000071-43-2	Benzene	95.3	25	1790	2.13	0.00555	2.27
730	002366-52-1	Butane, 1-fluoro-	838	25	832	2	0.0385	
740	000075-83-2	Butane, 2,2-dimethyl-	400	31	23.8	3.82	1.94	
750	000079-29-8	Butane, 2,3-dimethyl-	400	39	22.5	3.42	2.45	
760	000078-78-4	Butane, 2-methyl-	595	21	48	2.3	1.4	
770	000111-76-2	Butoxyethanol	0.85	25	1000000	0.83	0.0000002 08	9.30
780	000123-86-4	Butyl acetate	12.5	25	6800	2.06	0.0191	5.01
790	000109-73-9	Butylamine	91.75	25	1000000	0.97	33.8	4.88
800	000109-21-7	Butyric acid, butyl ester	1.81	25	500	2.06	0.000687	
810	000623-42-7	Butyric acid, methyl ester	40	30	9120	1.29	0.000205	5.6
820	000120-80-9	Catechol	0.01	25	440000	0.88	3.14E-09	
830	000075-45-6b	Chlorodifluoromethane	7144	20	3000	1.08	0.00572	6.11
840	000074-87-3	Chloromethane	4309	25	6480	0.91	0.00882	
850	000076-15-3	Chloropentafluoroethane	6004	20	60	2.41	8.53	1.0/g
860	000075-72-9	Chlorotrifluoromethane	27100	25	800	1.65	0.000362	2.32
870	000287-23-0	Cyclobutane	1170	25				
880	000110-82-7	Cyclohexane	96.86	25	100	3.44	0.0015	2.02
890	000108-93-0	Cyclohexanol	1	20	30000	1.23	0.000102	15

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
900	000108-94-1	Cyclohexanone	5	20	150000	0.81	0.0000511	16.10
910	000287-92-3	Cyclopentane	317.8	25	156	3	0.188	1.969
920	000142-29-0	Cyclopentene	380	25	535	2.47	0.185	
930	001191-96-4	Cyclopropane, ethyl-	302	25	231	2.61	0.192	
940	000123-42-2	Diacetone alcohol	1.71	25	1000000	–0.098	0.000000424	18.2
950	000693-65-2	Diamyl ether	0.6	25	27	4.044	0.00823	2.77
960	000142-96-1	Dibutyl ether	6.74	25	300	3.08	0.00589	3.083
970	002050-60-4	Dibutyl oxalate	0.0955	25	404	2.37	0.0000135	
980	000084-74-2	Dibutyl phthalate	0.000073	25	10	4.72	0.00000181	6.44
990	000075-71-8	Dichlorodifluoromethane	5.7	20	300	2.16	0.343	2.13
1000	000075-43-4	Dichlorofluoromethane	1688	25	9500	1.55	0.0323	5.34
1010	000111-42-2	Diethanolamine	0.0002	20	954000	–1.43	3.87E-11	
1020	000095-92-1	Diethyl oxalate	0.2	25	36000	0.56	0.00000435	1.8
1030	000111-46-6	Diethylene glycol	0.0045	25	1000000	–1.47	2.03E-09	31.6
1040	000112-73-2	Diethylene glycol dibutyl ether	0.01	20	3000	3.115	0.00000114	
1050	000112-36-7	Diethylene glycol diethyl ether	0.38	20	1000000	0.999	0.00000037	5.70
1060	000111-96-6	Diethylene glycol dimethyl ether	3.4	25	1000000	–0.48	2.28E-09	
1070	000124-17-4	Diethylene glycol monobutyl ether acetate	0.00975	25		1.772	9.91E-08	
1080	000111-90-0	Diethylene glycol monoethyl ether	0.126	25	1000000	–0.69	2.23E-10	
1090	000112-15-2	Diethylene glycol monoethyl ether acetate	0.1	20	1000000	0.714	5.62E-08	
1100	000111-77-3	Diethylene glycol monomethyl ether	0.18	25	1000000	–1.18	6.5E-10	
1110	000629-38-9	Diethylene glycol monomethyl ether acetate	0.12	20	94480	0.384	4.23E-08	
1120	000461-63-2	Difluoromethyl fluoromethyl ether						
1130	000108-83-8	Diisobutyl ketone	1.65	25	430	2.646	0.000271	
1140	000108-20-3	Diisopropyl ether	149.1	25	12000	1.488	0.219	3.88
1150	000108-18-9	Diisopropylamine	81.157	25	110000	1.158	0.0000517	

1160	000067-68-5	Dimethyl sulfoxide	0.61	25	253000	−1.35	4.96E-08	46.45
1170	000127-19-5	Dimethylacetamide	1.3	25	1000000	−0.77	5.39E-08	37.78
1180	000124-40-3	Dimethylamine	1476	25	1000000	−0.38	0.0000177	5.26
1190	000108-01-0	Dimethylethanolamine	0.42	20	10000	−0.497	1.73E-09	
1200	000138-86-3	Dipentene	20	68	13.8	4.83	0.38	2.38
1210	000101-84-8	Diphenyl ether	0.021	25	15.6	4.21	0.000118	3.87
1220	034590-94-8	Dipropylene glycol monomethyl ether	0.55	25		−0.2	4.66E-09	
1230	088917-22-0	Dipropylene glycol monomethyl ether acetate	5.17	22	13400	−0.564	7.46E-08	
1240	068526-79-4	Exxal 6	14	37	1379	2.73	0.000031	
1250	108419-43-7	Exxate 1000 solvent	0.1	20				
1260	088230-35-7	Exxate 600 solvent	1.4	20	200	2.83	0.000723	
1270	090438-79-2	Exxate 700 solvent	0.8	20				
1280	108419-32-5	Exxate 800 solvnet	0.7	20	45	3.66	0.00127	
1290	108419-33-6	Exxate 900 solvent	0.2	20	15	4.15	0.00169	
1300	064742-47-8a	Exxsol D 3135 solvent	1	20				
1310	064742-47-8b	Exxsol D 60 naphtha	1	25				
1320	000071-55-6b	Ethane, 1,1,1-trichloro-	123.7	25	1320	2.49	0.0172	7.25
1330	000354-58-5	Ethane, 1,1,1-trichloro-2,2,2-trifluoro-	360	25	2290	3.29	0.0388	
1340	000076-13-1a	Ethane, 1,1,2-trichloro-1,2,2-trifluoro-	285	20	200	3.16	0.526	
1350	000075-34-3	Ethane, 1,1-dichloro-	227	25	50300	1.79	0.00562	10
1360	001717-00-6	Ethane, 1,1-dichloro-1-fluoro-	539	22	1314	2.37	0.0241	
1370	000306-83-2	Ethane, 1,1-dichloro-2,2,2-trifluoro-	696	25	21000	2.17	0.0256	
1380	000124-73-2	Ethane, 1,2-dibromo-1,1,2,2-tetrafluoro-	434	25	32	2.96	0.162	2.34
1390	001649-08-7	Ethane, 1,2-dichloro-1,1-difluoro-	45.3	25	172	2.31	0.048	
1400	000624-72-6	Ethane, 1,2-difluoro-	621	25	2312	1.21	0.387	
1410	000076-12-0	Ethane, 1,2-difluoro-1,1,2,2-tetrachloro-	40	20	100	2.56	0.0473	
1420	013838-16-9	Ethane, 1-chloro-1,2,2-trifluoro, 2-difluoromethoxy-	227	25	5622	2.1	0.0126	
1430	026675-46-7	Ethane, 1-chloro-2,2,2-trifluoro, 1-difluoromethoxy-	311	25	4474	2.06	0.0126	
1440	003831-49-0	Ethane, 1-iodo-1,1,2,2-tetrafluoro-	221	25	55	2.36	0.114	
1450	000151-67-7	Ethane, 2-bromo-2-chloro-1,1,1-trifluoro-	302	25	3900	2.3	0.0313	
1460	000074-96-4	Ethane, bromo-	468	25	9100	1.61	0.00755	9.4
1470	000075-00-3	Ethane, chloro-	1199.2	25	4470	1.43	0.0111	9.45
1480	000354-64-3	Ethane, pentafluoroiodo-	717	10	13	2.97	1.81	
1490	020602-86-2	Ethanedioic acid, dipentyl ester	0	0	0	0	0.0000238	
1500	000064-17-5	Ethanol	44	20	1000000	−0.235	0.0000052	24.55
1510	000141-78-6	Ethyl acetate	94.5	25	80800	0.73	0.000134	6.02
1520	000075-04-7	Ethyl amine	873	20	1000000	−0.13	0.0000123	
1530	000060-29-7	Ethyl ether	537.2	25	80000	0.89	0.00123	4.2

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
1540	000109-94-4	Ethyl formate	242.8	25	118000	0.23	0.000385	7.16
1550	000105-37-3	Ethyl propionate	37.25	25	19200	1.21	0.000253	5.65
1560	000100-41-4	Ethylbenzene	7	20	100	3.15	0.00843	2.042
1570	000107-21-1	Ethylene glycol	0.06	20	1000000	−1.36	0.00000006	37.7
1580	000112-48-1	Ethylene glycol dibutyl ether	10	84	2000	3.05	0.0000733	
1590	000629-14-1	Ethylene glycol diethyl ether	9.4	20	210000	0.934	0.0000236	5.10
1600	000110-49-6	Ethylene glycol methyl ether acetate	2	20	1000000	0.121	0.00000273	8.25
1610	000622-08-2	Ethylene glycol monobenzyl ether	0.02	20	4000	0.792	3.38E-09	
1620	000122-99-6	Ethylene glycol monophenyl ether	0.03	20		1.16	1.55E-08	
1630	000075-21-8	Ethylene oxide	1109.6	20		–0.3	0.000148	13.0
1640	000060-00-4	Ethylenediaminetetraacetic acid	4.98E-13	25	500	−3.86	1.17E-23	
1650	086508-42-1e	FC-104 Fluorinert	20	25				1.86
1660	086508-42-1c	FC-40 Fluorinert	3	25				1.89
1670	086508-42-1g	FC-43 Fluorinert	1.3	20				1.90
1680	086508-42-1h	FC-5312 Fluorinert	0.1	20				1.98
1690	086508-42-1i	FC-70 Fluorinert	0.1	25				1.98
1700	125061-94-1	FC-71 Fluorinert	0.02	20	1.137E-08	9.66	215000000	
1710	086508-42-1j	FC-72 Fluorinert	232	25				1.76
1720	086508-42-1k	FC-722 Fluorad	232	20				
1730	086508-42-1l	FC-75 Fluorinert	31	25				1.86
1740	086508-42-1m	FC-77 Fluorinert	42	20				1.86
1750	086508-42-1d	FC-84 Fluorinert	79	25				1.81
1760	000050-00-0	Formaldehyde	1330	20	400000	0.35	0.00000036	
1770	000064-18-6	Formic acid	43	25	1000000	−0.54	0.00000067	58.5
1780	000110-00-9	Furan	634	26.47	10000	1.34	0.00538	2.94
1790	000098-01-1	Furfural	2.5	25	82000	0.41	0.0000134	38

1800	000098-00-0	Furfuryl alcohol	0.609	25	221000	0.28	7.86E-08	var
1810	000142-82-5	Heptane	45.7	25	3.4	4.66	2.03	1.92
1820	000999-97-3	Hexamethyldisilazane	20	20	395	2.62	0.0000869	2.27
1830	000822-06-0	Hexamethylene diisocyanate	7	25	117	1.08	0.000048	
1840	000110-54-3	Hexane	151.3	25	12.3	3.9	1.81	1.88
1850	000355-42-0	Hexane, tetradecafluoro-	218	25	0.02	6.02	24500	
1860	000123-31-9	Hydroquinone	0.00001	20	7000	0.59	3.84E-11	
1870	064742-48-9f	Isopar G solvent	10	20	100			2.0
1880	064742-48-9b	Isopar H solvent	10	20				2.015
1890	064742-48-9a	Isopar L solvent	9	20				
1900	026952-21-6	Isooctyl alcohol				2.809	0.0000388	
1910	000078-79-5	Isoprene	400	20	642	2.42	0.077	
1920	000067-63-0	Isopropyl alcohol	43.3	25	1000000	0.05	0.00000789	19.92
1930	008008-20-6	Kerosene	2.9	20	0	0	0	
1940	086508-42-1f	L-12077	60	20				
1950	006382-06-5	Lactic acid, amyl ester	0.015	25	17480	1.895	0.000113	
1960	000138-22-7	Lactic acid, butyl ester	0.4	20		1.366	0.000085	
1970	000097-64-3	Lactic acid, ethyl ester	1.2	20	472800	0.308	0.0000482	
1980	000547-64-8	Lactic acid, methyl ester	2.25	20	1000000	–0.221	0.0000363	
1990	000076-13-1c	MS-177 Freon TE Solvent	362	25				
2000	000076-13-1b	MS-178 Freon TES Solvent	287	25				
2010	000107-30-2	Methane, chloromethoxy-	192	20	0	0.32		
2020	000074-95-3	Methane, dibromo-	48	25	11930	1.7	0.000822	
2030	000075-61-6	Methane, dibromodifluoro-	620	20	139.7	1.99	0.0308	
2040	000075-09-2	Methane, dichloro-	436	25	13000	1.25	0.00325	8.93
2050	000593-53-3	Methane, fluoro-	28518	25	2400	0.51	0.017	
2060	001493-03-4	Methane, iododifluoro-						
2070	000373-53-5	Methane, iodofluoro-						
2080	000056-23-5	Methane, tetrachloro-	91	20	793.4	2.83	0.0276	2.24
2090	000067-66-3	Methane, trichloro-	194.8	25	8150	1.97	0.00367	4.81
2100	000075-69-4	Methane, trichlorofluoro-	690	20	1100	2.53	0.097	
2110	000075-75-2	Methanesulfonic acid	0.024	25	1000000	–1.224	1.26E-08	
2120	000067-56-1	Methano1	96	20	1000000	–0.77	0.00000445	32.66
2130	000100-66-3	Methoxybenzene	3.54	25	10400	2.11	0.000319	4.33

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
2140	000079-20-9	Methyl acetate	173	20	300000	0.18	0.000115	
2150	000078-93-3	Methyl ethyl ketone	71	20	280000	0.29	0.0000569	
2160	000107-31-3	Methyl formate	585.7	25	230000	0.03	0.000223	8.5
2170	000141-79-7	Methyl isobutenyl ketone	10.43	25	28900	1.045	0.0000367	15.6
2180	000108-10-1	Methyl isobutyl ketone	18.8	25	17000	1.16	0.000138	13.11
2190	000554-12-1	Methyl propionate	84	25	62370	0.671	0.000174	5.5
2200	000557-17-5	Methyl propyl ether	448	25	30500	1.21	0.000952	
2210	001634-04-4	Methyl tert-butyl ether	249	25	51000	0.94	0.000587	
2220	064475-85-0	Mineral spirits	2.3	20				
2230	000141-43-5	Monoethanolamine	0.36	20	1000000	−1.31	0.00000004	37.72
2240	000074-89-5	Monomethylamine	2680	25	1000000	−0.57	0.0000111	9.4
2250	000872-50-4a	N-Methylpyrrolidone	0.341	25	1000000	−0.38	1.56E-08	32.2
2260	000062-75-9	N-Nitrosodimethylamine	3	20		−0.57	0.000000263	
2270	064742-49-9g	Patclin #427 cold degreaser	2	20				
2280	086508-42-1b	PF-5050	610	25				
2290	086508-42-1	PF-5060	232	25	1.89E-08	10.85	73800000	
2300	000422-05-9	Pentafluoropropyl alcohol	217	25	21850	1.23	0.000148	
2310	000109-66-0	Pentane	514	25	400	3.39	1.25	1.84
2320	000678-26-2	Pentane, dodecafluoro-	655	25	1.2	4.4	2450	
2330	025322-68-3b	Polyglycol E 200	0.01	20	1000000	0	0	
2340	025322-68-3c	Polyglycol E 400			900000			
2350	025322-68-3d	Polyglycol E 600	0.01	20	1000000			
2360	025322-68-3e	Polyglycol E-1000			1000000			
2370	025322-68-3f	Polyglycol E-1450			700000			
2380	025322-68-3g	Polyglycol E-3350			900000			
2390	025322-68-3i	Polyglycol E-4500			1000000			
2400	025322-68-3h	Polyglycol E-8000			1000000			
2410	025322-68-3a	Polyglycol E-900	0	0	1000000	0	0	
2420	025322-69-4c	Polyglycol P 425						

2430	025322-69-4a	Polyglycol P-1200	0.01	20	20000			
2440	025322-69-4b	Polyglycol P-2000						
2450	000754-34-7	Propane, 1,1,1,2,2,3,3-heptafluoro-3-iodo-	244	25	1.02	3.94	9.5	
2460	000677-69-0	Propane, 1,1,1,2,3,3,3-heptafluoro-2-iodo-	244	25	1	3.94	9.5	
2470	000540-54-5	Propane, 1-chloro-	344.4	25	2383	2.04	0.0145	
2480	000075-29-6	Propane, 2-chloro-	515.3	25	3420	1.9		9.82
2490	000507-20-0	Propane, 2-chloro-2-methyl-	302	25	994	2.45	0.0192	
2500	000109-60-4	Propyl acetate	33.7	25	20000	1.24	0.000218	6.002
2510	000108-32-7	Propylene carbonate	1.2	55	175000	0.017	0.000363	64.92
2520	000057-55-6	Propylene glycol	0.133	25	1000000	−0.92	0.0000001 74	32
2530	004169-04-4	Propylene glycol monophenyl ether	0.1	25	1100	1.497	2.05E-08	
2540	000075-56-9	Propylene oxide	569	25	410000	0.03	0.000123	
2550	086508-42-1a	SF-2	80	20				
2560	018395-30-7	SIL-ACT ATS-100	5	25	13400	0.73	0.000203	
2570	000872-50-4b	SVC-150	0.05	25				
2580	064742-88-7	Solvent 140-66	0.9	25				
2590	008052-41-3	Stoddard Solvent	2	20	0	0	0	
2600	000126-33-0	Sulfolane	0.0062	25		−0.77	0.0000048 5	43.26
2610	000127-18-4	Tetrachloroethylene	18.5	25	200	3.4	0.0184	2.280
2620	000112-60-7	Tetraethylene glycol	0.0000006 1	25	1000000	−2.02	4.91E-13	
2630	000112-57-2	Tetraethylene pentamine	0.0000008	25	1000000	−1.503	3E-20	
2640	000075-73-0	Tetrafluoromethane	8830000	25	2239	1.18	4.59	1.001
2650	000109-99-9	Tetrahydrofuran	162.2	25	1000000	0.46	0.0000705	7.58
2660	000097-99-4	Tetrahydrofurfuryl alcohol	0.801	25	463400	−0.346	4.09E-09	13.61
2670	000100-72-1	Tetrahydropyran-2-methanol	0.4	20	158600	0.213	5.44E-09	
2680	000108-88-3	Toluene	28.4	25	515	2.73	0.00664	2.380
2690	000102-71-6	Triethanolamine	0.0000035 9	25	1000000	−2.48	3.38E-19	29.36
2700	000121-44-8	Triethylamine	57.1	25	55000	1.45	0.000138	2.42
2710	000112-27-6	Triethylene glycol	0.0013	25	1000000	−1.75	3.16E-11	23.69
2720	004499-99-4	Triethylene glycol diethyl ether	0	0	0	1.063	5.7E-09	
2730	000112-49-2	Triethylene glycol dimethyl ether	0.02	20	248500	0.005	3.24E-09	
2740	000075-46-7	Trifluoromethane				0.64	0.00101	1.007

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
2750	000504-63-2	Trimethylene glycol	0.0441	25	1000000	−1.693	0.0000001 74	35.0
2760	000110-88-3	Trioxane	13	25	289800	–0.43	0.0000001 97	
2770	008006-64-2	Turpentine (steam distilled)	4	20	0	0	0	
2780	008032-32-4	VM & P Naphtha	40	20	0	0	0	
2790	000071-55-6a	Vi-Chem VC-1 cleaner	100	20	40000			
2800	001330-20-7	Xylene (mixed)	6.6	20	245	3.12	0.00656	2.35
2810	010482-56-1	α-Terpineol	5	80	670	2.98	0.0000158	
2820	005989–27-5b	d-Limonene	20	68	13.8	4.83	0.38	2.37
2830	000096–48-0	gamma-Butyrolactone	0.45	25	447500	–0.64	0.0000181	39
2840	000108–38-3	*m*-Xylene	9	20	207	3.2	0.00734	2.374
2850	000142–92-7	*n*-Hexyl acetate	5	45	200	2.787	0.000723	
2860	000112–58-3	*n*-Hexyl ether	0.0461	25	100	5.102	0.0147	
2870	000095–47-6	o-Xylene	7	20	200	3.12	0.00519	2.568
2880	000106–42-3	p-Xylene	8.7	25	156	3.15	0.00766	2.27
2890	000056–81-5	Glycerol	0.003	50	1000000	−1.76	1.732E-08	42.5
2900	000060–35-5	Acetamide	1	65	410000	−1.26	1.12E-08	
2910	000062–53-3	Aniline	0.67	25	33800	0.9	0.0000020 2	6.71
2920	000068–12-2	N,N′-Dimethylformamide	3.7	25	1000000	−1.01	7.39E-08	36.7
2930	000074–83-9	Methyl bromide	1633	25	20000	1.19	0.0062	
2940	000074–88-4	Methyl iodide	400	20	10000	1.51	0.0053	7
2950	000074–97-5	Chlorobromomethane	147.2	25	16690	1.41	0.0015	
2960	000074–98-6	Propane	7111	25	62.4	2.36	0.7067	1.29
2970	000075–01-4	Vinylchloride	2660	25	2700	1.62	0.0278	6.26
2980	000075–03-6	Iodoethane	136	25	38800	2	0.0069	7.82
2990	000075–05-8	Acetonitrile	88	25	1000000	–0.34	0.0000345	35.94
3000	000075–07-0	Acetaldehyde	910	25	1000000	–0.34	0.0001	21
3010	000075–11-6	Methylene iodide	1.2	25	1240	2.3	0.0003	5.3
3020	000075–12-7	Formamide	0.08	20	1000000	−1.51	1.39E-09	111.0
3030	000075–15-0	Carbon disulfide	361	25	2100	1.94	0.0144	2.64
3040	000075–18-3	Dimethylsulfide	484.9	25	22034	0.92	0.0016	6.2

3050	000075-25-2	Bromoform	5.9	25	3180	2.4	0.0005	4.39
3060	000075-26-3	2-Bromopropane	236.3	25	2860	2.14	0.011	9.4
3070	000075-28-5	2-Methylpropane	2611	25	48.9	2.76	1.189	1
3080	000075-30-9	2-Iodopropane	43.082	25	1400	2.89	0.0069	8.19
3090	000075-31-0	Isopropylamine	574	25	1000000	0.26	0.0000451	5
3100	000075-35-4	1,1-Dichloroethene	599	25	400	2.13	0.0261	
3110	000075-37-6	1,1-Difluoroethane	4550	25	17800	0.75	0.022	
3120	000075-50-3	Trimethylamine	1454	20	480000	0.16	0.0001	
3130	000075-52-5	Nitromethane	36.6	25	111000	–0.35	0.0000286	35.87
3140	000075-64-9	*t*-Butylamine	372	25	1000000	0.4	0.0000358	
3150	000075-65-0	*t*-Butanol	42	20	1000000	0.35	0.0000144	
3160	000075-76-3	Tetramethyl silane	717.8	25	19.6	2.72	4.253	
3170	000075-79-6	Methyltrichlorosilane	167	25	1473	2.01	0.0053	
3180	000075-84-3	2,2-Dimethyl-1-propanol	16	20	35000	1.31	0.0001	
3190	000075-85-4	2-Methyl-2-butanol	10	17.2	110000	0.89	0.0000138	
3200	000075-89-8	2,2,2-Trifluoroethanol	71.271	25	168900	0.41	0.0000173	
3210	000076-01-7	Pentachloroethane	3	20	500	3.22	0.0019	
3220	000076-05-1	Trifluoroacetic acid	110	25	1000000	0.5	0.0000165	
3230	000078-40-0	Triethyl phosphate	1	39.6	500000	0.8	0.0000000	
3240	000078-75-1	1,2-Dibromopropane	7.841	25	1430	2.43	0.0015	
3250	000078-76-2	2-Bromobutane	57	25	844.8	2.58	0.0158	
3260	000078-81-9	Isobutylamine	100	19	1000000	0.73	0.0000136	
3270	000078-84-2	Isobutyraldehyde	6	20	89000	0.74	0.0002	
3280	000078-86-4	2-Chlorobutane	156.65	25	1000	2.33	0.0241	
3290	000078-87-5	1,2-Dichloropropane	40	20	3000	2.25	0.0028	
3300	000079-00-5	1,1,2-Trichloroethane	19	20	4000	1.89	0.0008	
3310	000079-09-4	Propionic acid	3	20	1000000	0.33	0.0000004	
3320	000079-10-7	Acrylic acid	3	20	1000000	0.35	0.0000001	
3330	000079-16-3	N-Methylacetamide	0.44	23	1000000	–1.05	0.0000000	
3340	000079-24-3	Nitroethane	15.6	20	50000	0.18	0.0000476	
3350	000079-27-6	1,1,2,2-Tetrabromoethane	0.02	20	700	2.55	0.0000139	
3360	000079-31-2	Isobutyric acid	1	14.7	167000	0.94	0.0000008	

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
3370	000079-34-5	1,1,2,2-Tetrachloroethane	5	20	3000	2.39	0.0004	
3380	000079-41-4	Methacrylic acid	0.7	20	90000	0.93	0.000000388	
3390	000079-46-9	2-Nitropropane	13	20	20000	0.93	0.0001	
3400	000080-56-8	α-Pinene	10	37.3	8.2	4.83	0.107	2.259
3410	000080-62-6	Methyl methacrylate	29	20	15000	1.38	0.0003	
3420	000087-62-7	2,6-Dimethylaniline	0.13	25	8240	1.84	0.00000252	
3430	000090-02-8	o-Hydroxybenzaldehyde	0.593	25	17000	1.81	0.00000176	
3440	000090-11-9	1-Bromonaphthalene	0.0097	25	9.318	4.06	0.0003	
3450	000090-12-0	1-Methylnaphthalene	0.067	25	25.8	3.87	0.0003	
3460	000090-13-1	1-Chloronaphthalene	0.029	25	17.4	3.9	0.0004	
3470	000091-16-7	1,2-Dimethoxybenzene	0.47	25	3666	1.6	0.0000189	
3480	000091-17-8	Decahydronaphthalene	5	20	0.889	4.2	0.47	
3490	000091-20-3	Naphthalene	0.085	20	31	3.3	0.0005	
3500	000091-22-5	Quinoline	0.06	25	220000	2.03	0.00000167	
3510	000091-23-6	2-Nitroanisole	0.0036	25	1690	1.73	0.000000429	
3520	000092-51-3	Dicyclohexyl	0.108	25	0.183	5.86	0.616	
3530	000093-58-3	Benzoic acid, methyl ester	0.38	25	2100	2.12	0.0000324	
3540	000093-89-0	Ethyl benzoate	0.18	20	500	2.64	0.0001	6.02
3550	000094-96-2	2-Ethyl-1,3-hexandiol	0.003	20	42000	1.6	1.37E-08	18.73
3560	000095-48-7	*o*-Cresol	0.31	25	20000	1.95	0.0000012	11.5
3570	000095-49-8	2-Chlorotoluene	3.619	20	90	3.42	0.0036	4.73
3580	000095-50-1	1,2-Dichlorobenzene	1.28	25	156	3.43	0.0019	9.93
3590	000095-51-2	2-Chloroaniline	0.2553	25	8760	1.9	0.000005386	13.4
3600	000095-52-3	*o*-Fluorotoluene	20	21.4	496.1	2.74	0.0069	4.22
3610	000095-53-4	*o*-Toluidine	0.05	25	16600	1.32	0.00000221	6.34
3620	000095-65-8	3,4-Dimethylphenol	0.0387	25	4764	2.23	0.000000683	9.02

3630	000095-68-1	2,4-Dimethylaniline	0.1539	25	6069	1.68	0.0000025	4.9
3640	000095-73-8	2,4-Dichlorotoluene	0.416	25	16.2	4.24	0.0041	
3650	000095-75-0	3,4-Dichlorotoluene	0.315	25	26	3.83	0.0026	8.970
3660	000095-87-4	2,5-Dimethylphenol	0.163	25	3543	2.33	0.0000006 83	6.36
3670	000096-14-0	3-Methylpentane	190	25	13	3.6	1.683	1.895
3680	000096-18-4	1,2,3-Trichloropropane	3.69	25	1900	2.27	0.0003	7.45
3690	000096-22-0	3-Pentanone	35	25	50000	0.99	0.0001	
3700	000096-33-3	Methyl acrylate	84	25	49400	0.8	0.0002	
3710	000096-37-7	Methylcyclopentane	138	25	42	3.37	0.363	
3720	000096-47-9	2-Methyltetrahydrofuran	73.1	25	138700	1.35	0.0001	6.97
3730	000096-49-1	1,3-Dioxolan-2-one	0.0098	25	1000000	0.12	0.0003	89.78
3740	000097-85-8	Isobutyl isobutyrate	4.33	25	1000	2.68	0.0008	
3750	000097-95-0	2-Ethyl-1-butanol	3.8	25	6300	1.75	0.0001	6.19
3760	000098-06-6	*t*-Butylbenzene	2.1	25	29.5	4.11	0.0132	2.366
3770	000098-07-7	Benzotrichloride	1.55	20	53	3.9	0.0003	6.9
3780	000098-08-8	Benzotrifluoride	38.55	25	451.5	3.01	0.0165	9.035
3790	000098-55-5	α-Terpineol	0.023	20	1980	2.98	0.0000023 6	
3800	000098-82-8	Cumene	4.5	25	65.3	3.66	0.0115	2.383
3810	000098-86-2	Acetophenone	0.37	25	6130	1.58	0.0000107	17.39
3820	000098-95-3	Nitrobenzene	0.284	25	1900	1.85	0.000024	34.78
3830	000099-87-6	*p*-Cymene	1.46	25	23.4	4.1	0.011	
3840	000099-94-5	*p*-Toluic acid	0.0001	25	400	2.27	0.0000001 2	
3850	000100-42-5	styrene	5	20	310	2.95	0.0028	
3860	000100-44-7	α-Chlorotoluene	1	20	525	2.3	0.0004	
3870	000100-47-0	Benzonitrile	1	28	2000	1.56	0.0001	25.20
3880	000100-51-6	Benzyl alcohol	0.15	25	35000	1.1	0.0000002 17	13.1
3890	000100-52-7	Benzaldehyde	1.27	25	3000	1.48	0.0000267	17.8
3900	000100-61-8	N-Methylaniline	0.453	25	5624	1.66	0.0000114	6.06
3910	000102-76-1	Triacetin	0.0025	25	58000	0.25	1.23E-08	
3920	000102-82-9	Tri N-butylamine	0.105	25	40	4.46	0.0001	
3930	000103-09-3	2-Ethylhexylacetate	0.4	20	2500	3.74	0.0015	
3940	000103-36-6	Cinnamic acid, ethyl ester	0.0125	25	178	2.99	0.0000055	
3950	000103-50-4	Dibenzyl ether	0.023	25	40	3.31	0.0000000 83	
3960	000103-73-1	Ethoxybenzene	1.53	25	1200	2.51	0.0004	4.22

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
3970	000104-51-8	N-Butylbenzene	1.1	25	11.8	4.38	0.0159	2.359
3980	000104-75-6	2-Ethylhexylamine	10	54	2500	2.82	0.0001	
3990	000104-76-7	2-Ethyl-1-hexanol	0.143	25	700	2.73	0.0000265	4.41
4000	000105-30-6	2-Methyl-1-pentanol	2.6	25	3100	1.75	0.000043	
4010	000105-34-0	Methyl cyanoacetate	0.14	25	161100	–0.47	7.27E-08	
4020	000105-45-3	Methyl acetoacetate	6	25	333000	–0.69	0.0000001 18	
4030	000105-53-3	Diethyl malonate	0.269	25	27000	0.96	0.0000021	7.87
4040	000105-54-4	Ethylbutyrate	17	25	4900	1.85	0.0004	
4050	000105-56-6	Ethyl cyanoacetate	0.039	25	259000	1.01	0.0000002 89	26.7
4060	000105-57-7	1,1-Diethoxyethane	34.1	25	50000	0.84	0.0001	3.80
4070	000105-58-8	Diethyl carbonate	10	23.8	18800	1.21	0.0001	2.820
4080	000105-60-2	Caprolactam	0.1	20	530000	–0.19	2.53E-08	
4090	000105-67-9	2,4-Dimethylphenol	0.1634	25	7870	2.3	0.000002	6.16
4100	000105-76-0	Dibutyl maleate	0.016	25	500	4.16	0.0000007 58	
4110	000106-31-0	Butyric anhydride	0.3	20	4561	1.39	0.0001	12.9
4120	000106-35-4	3-Heptanone	5.6	25	14300	1.73	0.0001	12.88
4130	000106-43-4	*p*-Chlorotoluene	5	31	1.063	3.33	0.0044	6.08
4140	000106-44-5	*p*-Cresol	0.13	25	22600	1.94	0.000001	11.07
4150	000106-46-7	1,4-DIchlorobenzene	1.76	25	87.2	3.44	0.0024	2.41
4160	000106-49-0	*p*-Toluidine	0.34	25	73500	1.39	0.0000020 2	4.98
4170	000106-69-4	1,2,6-Hexanetriol	0.001	20	1000000	–0.77	1.48E-08	
4180	000106-88-7	1,2-Butyleneoxide	180	25	95000	0.86	0.0002	
4190	000106-93-4	1,2-Dibromoethane	7.79	25	4290	1.96	0.0007	4.75
4200	000106-94-5	1-Bromopropane	138.3	25	2300	2.1	0.0073	8.09
4210	000106-97-8	*n*-Butane	1823	25	61.2	2.89	0.9497	1.002
4220	000106-98-9	1-Butene	1897	20	221.3	2.4	0.233	
4230	000107-04-0	1-Bromo-2-chloroethane	40	29.7	6864	1.92	0.0009	6.92
4240	000107-05-1	3-Chloropropylene	366.8	25	3600	1.93	0.011	8.2
4250	000107-06-2	1,2-Dichloroethane	78.9	20	8100	1.48	0.0012	10.37
4260	000107-07-3	2-Chloroethanol	7.18	25	1000000	–0.06	7.606E-07	25.8

4270	000107-08-4	1-Iodopropane	43.09	25	1070	2.57	0.009	7.00
4280	000107-10-8	Propylamine	307.9	25	1000000	0.48	0.0000148	5.08
4290	000107-11-9	Allylamine	242	25	1000000	0.03	0.00000995	
4300	000107-12-0	Propionitrile	47.63	25	103000	0.16	0.000037	28.86
4310	000107-13-1	Acrylonitrile	108.5	25	73500	0.25	0.0001	33
4320	000107-15-3	1,2-Diaminoethane	13.1	26.5	1000000	−2.04	1.73E-09	12.9
4330	000107-18-6	Allyl alcohol	28.1	25	317000	0.17	0.00000499	21.6
4340	000107-19-7	Propargyl alcohol	15.6	25	1000000	−0.38	0.00000115 1	24.5
4350	000107-41-5	2-Methyl-2,4-pentanediol	0.05	20	1000000	0.58	0.00000040 6	25.86
4360	000107-83-5	2-Methylpentane	212	25	14	3.21	1.71	1.88
4370	000107-92-6	Butyric acid	0.765	25	1000000	0.79	0.00000053 5	2.97
4380	000108-03-2	1-Nitropropane	10.23	25	15000	0.87	0.0001	23.24
4390	000108-05-4	Vinyl acetate	106	25	20000	0.73	0.0005	
4400	000108-08-7	2,4-Dimethylpentane	98	25	41	3.63	1.904	1.914
4410	000108-24-7	Acetic anhydride	5.1	25	120000	−0.58	0.0000357	20.6
4420	000108-39-4	*m*-Cresol	0.138	25	22700	1.96	0.00000086 5	12.4
4430	000108-41-8	*m*-Chlorotoluene	3.6751	25	37.98	3.28	0.0161	5.5
4440	000108-44-1	*m*-Toluidine	0.303	25	20000	1.4	0.00000284 8	5.95
4450	000108-47-4	2,4-Dimethylpyridine	3.1651	25	1000000	1.9	0.00000674	9.60
4460	000108-48-5	2,6-Lutidine	5.58	25	1000000	1.68	0.0000104	7.33
4470	000108-64-5	Ethyl isovalerate	7.9	25	2000	2.26	0.0007	4.7
4480	000108-67-8	1,3,5-Trimethylbenzene	2.48	25	48.2	3.42	0.0088	2.27
4490	000108-68-9	3,5-Dimethylphenol	0.054	25	6200	2.35	0.00000068 3	9.06
4500	000108-75-8	2,4,6-Collidine	1.9866	25	36000	1.88	0.00000881 4	
4510	000108-84-9	4-Methyl-2-pentyl acetate	4	20	1300	2.68	0.0006	
4520	000108-86-1	Bromobenzene	4.182	25	446	2.99	0.0021	5.40
4530	000108-87-2	1-Methylcyclohexane	46	25	14	3.61	0.43	2.02
4540	000108-89-4	4-Methylpyridine	5.68	25	1000000	1.22	0.000006	
4550	000108-90-7	Chlorobenzene	11.97	25	497.9	2.84	0.0038	5.62
4560	000108-91-8	Cyclohexanamine	10.1	20	1000000	1.49	0.00000133 18	4.7

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
4570	000108-95-2	Phenol	0.35	25	90000	1.46	0.0000003 33	13
4580	000108-98-5	Thiophenol	2.98	25	834	2.52	0.0003	4.38
4590	000108-99-6	3-Methylpyridine	6.05	25	1000000	1.2	0.0000077 3	
4600	000109-06-8	2-Methylpyridine	11.2	25	1000000	1.11	0.0000099 6	9.8
4610	000109-43-3	Dibutyl sebacate	0.000157	25	40	6.3	4.852E-08	4.54
4620	000109-52-4	Pentanoic acid	0.14	25	24000	1.39	0.0000004 72	2.66
4630	000109-65-9	1-Bromobutane	41.27	25	608	2.75	0.0087	7.1
4640	000109-69-3	1-Chlorobutane	101.3	25	1100	2.64	0.0167	7.39
4650	000109-74-0	Butyronitrile	19.1	25	33000	0.53	0.0001	24.83
4660	000109-78-4	Ethylene cyanohydrin	0.08	25	1000000	–1.12	7.501E-09	
4670	000109-79-5	1-Butanethiol	45.5	25	594.6	2.28	0.0091	5.20
4680	000109-87-5	Dimethoxymethane	398	25	244000	0	0.0002	2.65
4690	000109-89-7	Diethylamine	233.5	25	1000000	0.58	0.0000255	3.894
4700	000109-92-2	Ethyl vinyl ether	575	25	9000	1.04	0.0054	
4710	000109-97-7	Pyrrole	8.35	25	45000	0.75	0.000018	8.13
4720	000110-01-0	Tetrahydrothiophene	18.4	25	3730	1.79	0.0006	
4730	000110-02-1	Thiophene	79.67	25	3015	1.81	0.0029	2.705
4740	000110-19-0	*sec*-Butylacetate	17.9	25	6300	1.78	0.0005	5.29
4750	000110-53-2	1-Bromopentane	12.6	25	126.6	3.37	0.0197	6.31
4760	000110-58-7	N-Pentylamine	30.049	25	1000000	1.49	0.0000243	4.5
4770	000110-59-8	Valeronitrile	7.07	25	7746	1.12	0.0001	19.7
4780	000110-61-2	Succinonitrile	0.0077	25.14	115000	–0.99	1.68E-08	55
4790	000110-63-4	1,4-Butanediol	0.0105	25	1000000	–0.83	1.3E-09	30.2
4800	000110-71-4	Ethylene glycol dimethyl ether	48	20	1000000	–0.21	0.0000011	7.2
4810	000110-74-7	Propyl formate	82.57	25	20500	0.83	0.0004	7.72
4820	000110-83-8	Cyclohexene	88.8	25	213	2.86	0.0455	2.22
4830	000110-86-1	Pyridine	20.8	25	1000000	0.65	0.000011	12.91
4840	000110-89-4	Piperidine	32.115	25	1000000	0.84	0.0000044 5	5.8
4850	000110-91-8	Morpholine	10.08	25	1000000	–0.86	0.0000011 6	7.42
4860	000111-13-7	2-Octanone	1.35	25	1130	2.37	0.0002	10.4
4870	000111-29-5	1,5-Pentanediol	0.0039	25	1000000	0.27	0.0000003 06	

4880	000111-34-2	Butyl vinyl ether	51	25	3000	1.89	0.0022	
4890	000111-40-0	Diethylenetriamine	0.2317	25	1000000	–2.13	3.149E-07	
4900	000111-43-3	Di(N-propyl) ether	62.5	25	4900	2.03	0.0022	3.39
4910	000111-44-4	Bis(2-chloroethyl) ether	1.55	25	10200	1.29	0.000017	21.2
4920	000111-48-8	2,2′-Thiobisethanol	0.542	25	1000000	–0.63	1.85E-09	
4930	000111-55-7	Ethylene glycol diacetate	0.2	25	213000	0.4	0.000000084	
4940	000111-65-9	Octane	14.052	25	0.66	5.18	3.211	1.948
4950	000111-66-0	1-Octene	17	25	4.096	4.57	0.6266	2.08
4960	000111-84-2	n-Nonane	4.3	25	0.22	4.76	3.4	1.970
4970	000111-85-3	1-Chlorooctane	0.95	25	4.89	4.52	0.038	5.05
4980	000111-92-2	Dibutylamine	2.28	25	4700	2.83	0.0001	2.98
4990	000112-05-0	Nonanoic acid	0.001	25	284	3.42	0.00000162	
5000	000112-29-8	1-Bromodecane	0.04	25	0.197	5.6	0.109	4.44
5010	000112-40-3	Dodecane	0.12	25	0.0037	6.1	8.238	2.002
5020	000112-41-4	1-Dodecene	0.1446	25	0.1127	6.1	4.25	
5030	000112-62-9	Methyl oleate		25	0.0018	8.02	0.0144	3.2
5040	000112-80-1	Oleic acid		25	0.0115	7.73	0.0000448	2.46
5050	000115-10-6	Dimethyl ether	4450	25	353000	0.1	0.0013	5.02
5060	000115-21-9	Ethyltrichlorosilane	47.18	25	484.8	2.5	0.0071	
5070	000115-25-3	PerfluorocyclobutanE	2345	25	23.63	1.29	8.476	
5080	000117-81-7	Bis(2-ethylhexyl)phthalate	0.001	20	0.3	7.6	0.00000013	6.46
5090	000119-36-8	Methyl salicylaTE	0.11	25	7400	2.55	0.0001	9.4
5100	000119-64-2	Tetralin	0.368	25	47	3.49	0.0051	2.773
5110	000119-65-3	Isoquinoline	0.07	25	4515	2.08	0.00000068	10.7
5120	000120-51-4	Benzyl benzoate	0.0002	25	15.39	3.97	0.0000028	4.9
5130	000120-92-3	Cyclopentanone	11.4	25	9177	0.63	0.00001	1360
5140	000121-69-7	N,N-Dimethylaniline	0.7	25	1454	2.31	0.0001	4.91
5150	000123-04-6	3-(Chloromethyl)heptane	1.2	20	100	4.45	0.0023	
5160	000123-38-6	Propionaldehyde	316.8	25	306000	0.59	0.0001	18.5
5170	000123-39-7	Methylformamide	0.253	25	1000000	–0.97	1.966E-08	182.4
5180	000123-51-3	Isopentanol	2.37	25	26700	1.16	0.0000141	15.2
5190	000123-54-6	2,4-Pentanedione	8.6	22.76	166000	0.4	0.00000235	25.7
5200	000123-62-6	Propionic anhydride	0.87	25	41430	0.4	0.0001	18.3
5210	000123-72-8	Butyraldehyde	118	25	71000	0.88	0.0001	13.4
5220	000123-73-9	Trans-crotonaldehyde	38	25	150000	0.6	0.0000194	
5230	000123-75-1	Pyrrolidine	62.69	25	1000000	0.46	0.00000239	
5240	000123-92-2	Isoamyl acetate	5.6	25	2000	2.26	0.0006	4.63

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
5250	000123-95-5	N-Butyl stearate	0.00000127	20	1700	9.7	0.0382	3.11
5260	000124-07-2	Octanoic acid	0.0037	25	798	3.05	0.000000892	2.45
5270	000124-11-8	1-Nonene	5.3	25	0.0000993	5.15	0.7994	
5280	000124-12-9	Octanenitrile	0.39	25	233.7	2.75	0.0002	13.9
5290	000124-18-5	n-Decane	1.43	25	0.052	5.01	5.149	1.99
5300	000124-68-5	2-Amino-2-methyl-1-propano	1	20	1000000	–0.74	6.48E-10	
5310	000126-73-8	Tributylphosphate	0.0001	25	390	4	0.00000015	8.91
5320	000126-98-7	Methacrylonitrile	71.2	25	25400	0.68	0.0002	
5330	000127-91-3	α-Pinene	2.93	25	4.886	4.35	0.161	2.5
5340	000135-98-8	*sec*-Butylbenzene	1.752	25	17.6	4.57	0.0176	2.36
5350	000137-32-6	2-Methyl-1-butanol	3.12	25	29700	1.29	0.0000141	15.6
5360	000140-11-4	Benzyl acetate	0.177	25	3100	1.96	0.00001128	5.1
5370	000140-29-4	Phenylacetonitrile	0.9	25	100	1.56	0.00000247	18.7
5380	000140-88-5	Ethyl acrylate	38.6	25	15000	1.32	0.0004	
5390	000141-05-9	Diethyl maleate	0.105	25	14000	2.2	0.000000244	8.6
5400	000141-97-9	Acetoacetic ester	0.78	25	120000	0.25	0.00000120303	15.7
5410	000142-62-1	Hexanoic acid	0.043	25	9580	1.92	0.000000758	2
5420	000142-68-7	Tetrahydropyran	71.527	25	80200	0.95	0.0001	5.6
5430	000142-77-8	Butyl oleate			0.0001	9.49	0.0336	4.0
5440	000142-84-7	Dipropylamine	24.1	25	25000	1.67	0.0001	3.07
5450	000151-56-4	Aziridine	213	25	1000000	–0.28	0.00001207	18.3
5460	000156-59-2	*cis*-1,2-Dichloroethene	200	25	3500	1.86	0.0041	9.2
5470	000156-60-5	*trans*-1,2-Dichloroethene	340	25	6300	2.09	0.0094	2.14
5480	000311-89-7	Heptacosafluorotributylamine	0.552	25	0.000001666	9.98	54500	1.9
5490	000352-32-9	*p*-Fluorotoluene	20.969	25	680.5	2.58	0.0069	5.86
5500	000352-70-5	*m*-Fluorotoluene	21.794	25	487.1	2.75	0.0069	5.42
5510	000352-93-2	Diethylsulfide	58.4	25	8021	1.95	0.0009	5.72
5520	000355-25-9	Decafluorobutane	2007	25	1.612	4.09	667	

5530	000392-56-3	Hexafluorobenzene	80.5	25	341.5	2.55	0.0136	
5540	000420-46-2	1,1,1-Trifluoroethane	9536	25	760.9	1.74	0.77	
5550	000462-06-6	Fluorobenzene	77.2	25	1550	2.27	0.0063	5.42
5560	000463-82-1	2,2-Dimethylpropane	1285	25	33.2	3.11	2.173	1.80
5570	000464-49-3	(1R,4R)-(+)-Camphor	0.39	24.2	100	2.34	0.0001	11.35
5580	000470-82-6	1,8-Cineole	1.9	25	3500	2.5	0.0001	4.57
5590	000493-01-6	*cis*-Bicyclo(4.4.0)decane	0.786	25	6.448	4.2	0.349	2.2
5600	000493-02-7	*trans*-Bicyclo(4.4.0)decane	1.22	25	6.448	4.2	0.349	2.17
5610	000503-74-2	Isovaleric acid	0.44	25	40700	1.16	0.0000008 33	
5620	000507-19-7	2-Bromo-2-methylpropane	135.3	25	600	2.54	0.0407	10.3
5630	000512-56-1	Trimethyl phosphate	0.85	25	500000	–0.65	7.2E-09	16.4
5640	000513-36-0	Isobutyl chloride	149.593	25	925.7	2.49	0.0218	
5650	000513-38-2	1-Iodo-2-methylpropane	20	29.8	146.9	2.99	0.0129	6.5
5660	000513-85-9	2,3-Butanediol	0.9	30	1000000	–0.92	0.0000020 2	
5670	000538-93-2	Isobutylbenzene	1.93	25	10.1	4.68	0.0337	2.32
5680	000539-30-0	Benzyl ethyl ether	0.925	25	1242	2.16	0.0001	
5690	000540-84-1	2,2,4-Trimethylpentane	49.3	25	2.44	4.09	3.01	1.94
5700	000541-73-1	3-Dichlorobenzene	1.89	25	111	3.53	0.0026	5.04
5710	000542-54-1	4-Methylpentanitrile	3.69	25	3133	1.54	0.0001	15.5
5720	000542-55-2	Isobutyl formate	40.08	25	10200	1.23	0.0005	6.41
5730	000542-69-8	N-Butyl iodide	13.86	25	120	3.06	0.0167	6.3
5740	000543-49-7	2-Heptanol	1.23	25	3382	2.31	0.0001	9.2
5750	000543-59-9	1-Chloropentane	32.882	25	197.4	2.73	0.0238	
5760	000544-01-4	Diisopentyl ether	1.4	25	.200	4.25	0.0015	2.8
5770	000544-40-1	5-Thianonane	5	51	39.35	3.87	0.0043	
5780	000554-14-3	2-Methylthiophene	24.89	25	1212	2.33	0.0032	
5790	000564-02-3	2,2,3-Trimethylpentane	32.1	25	9.91	4.09	3.01	1.96
5800	000565-59-3	2,3-Dimethylpentane	68.9	25	5.25	3.63	1.73	1.94
5810	000565-80-0	2,4-Dimethyl-3-pentanone	13.42	25	5700	1.86	0.0004	
5820	000573-98-8	1,2-Dimethylnaphthalene	0.0127	25	14.85	4.31	0.0006	2.61
5830	000575-43-9	1,6-Dimethyl naphthalene	0.0146	25	0.9	4.26	0.0004	2.58
5840	000576-26-1	2,6-Dimethylphenol	0.143	25	6047	2.36	0.0000066 5	4.9
5850	000583-57-3	1,2-Dimethylcyclohexane	14.47	25	11	4.01	0.355	
5860	000583-59-5	2-Methylcyclohexanol	0.291	25	9140	1.82	0.0000065	13.3
5870	000584-02-1	3-Pentanol	8.24	25	51500	1.21	0.0000197 5	13.35
5880	000589-34-4	3-Methylhexane	61.5	25	4.95	3.71	1.64	1.93
5890	000589-82-2	3-Pentanol	0.74	22	4000	2.24	0.0000282 9	6.86

Table A3. Continued.

Ref No.	CAS	Name	VP	VP-Temp	WS	Kow	HL	Diel constant
5900	000590-36-3	2-Methyl-2-pentanol	8.6	25	32400	1.71	0.00003569	
5910	000590-67-0	1-Methylcyclohexanol	1.13	26	5582	2.09	0.0000065	
5920	000591-23-1	3-Methylcyclohexanol	0.4789	25	5990	2.05	0.0000065	12.3
5930	000591-50-4	Iodobenzene	1.009	25	340	3.25	0.0008	4.48
5940	000591-76-4	2-Methylhexane	66	25	103	3.71	3.426	1.92
5950	000591-87-7	Allyl acetate	46	30	28000	0.97	0.0001	
5960	000592-41-6	1-Hexene	186	25	69.7	3.39	0.412	2.05
5970	000592-76-7	1-Heptene	56	25	18.16	3.99	0.421	2.07
5980	000592-84-7	N-Butylformate	28.8	25	7558	1.3	0.0005	2
5990	000593-60-2	Bromoethene	1033	25	5679	1.57	0.0256	5.63
6000	000594-82-1	2,2,3,3-Tetramethylbutane	20.854	25	10.67	4.05	3.01	
6010	000598-75-4	3-Methyl-2-butanol	8.97	25	55500	1.28	0.00001748	
6020	000616-44-4	3-Methylthiophene	22.15	25	400	2.34	0.0071	
6030	000616-45-5	2-Pyrrolidinone	0.0203	25	1000000	–0.85	2.273E-09	
6040	000624-48-6	Methyl maleate	0.3	25	80000	0.22	0.00000071	
6050	000624-92-0	Dimethyldisulfide	30	25.9	3739	1.77	0.0012	9.6
6060	000627-20-3	*cis*-2-Pentene	495	25	203	2.58	0.225	
6070	000628-73-9	Hexanenitrile	2.66	25	2475	1.66	0.0001	17.26
6080	000628-81-9	Butyl ethyl ether	55.9	25	2128	2.03	0.0027	
6090	000629-50-5	n-Tridecane	0.0397	25	60	6.73	19	2.03
6100	000631-37-7	Tetraethylsilane	5	24	0.325	4.68	2.922	2.09
6110	000632-222-4	Tetramethylurea	13.9	71	1000000	0.19	8.48E-09	23.6
6120	000646-04-8	*trans*-2-Pentene	506	25	245.1	2.58	0.319	
6130	000646-06-0	1,3-Dioxolane	79	20	1000000	–0.37	0.0000245	
6140	000659-70-1	Isomyl isovalerate	1	27	44.59	3.66	0.0013	3.6
6150	000680-31-9	Hexamethylphosphoramide	0.046	25	1000000	0.28	0.00000002	29.3
6160	000688-74-4	*n*-Butyl borate	0.5262	25	214	2.52		
6170	000821-11-4	*trans*-2-Butene-1,4-diol	0.007	25	618500	–0.43	0.000000203	
6180	000827-52-1	Phenyl cyclohexane	0.04	25	5.327	4.81	0.0108	

6190	000872-05-9	1-Decene	1.67	25	0.115	5.12	2.68		
6200	001187-58-2	N-Methyl propionamide	1.149	25	189200	–0.21	3.26E-08	175.7	
6210	001330-78-5	Tricresyl phosphate	5.25E-10	25	0.6	5.11	0.000000808		
6220	001678-91-7	Ethyl cyclohexane	12.83	25	6.3	4.08	0.3		
6230	001814-88-6	1,1,1,2,2-Pentafluoropropane	3485.33	25	78.52	2.71	4.05		
6240	002207-01-4	*cis*-1,2-Dimethylcyclohexane	14.49	25	6	4.01	0.3568		
6250	002315-68-6	Propyl benzoate	0.136	25	351	3.01	0.0001		
6260	002437-56-1	1-Tridecene	0.0638	25	0.0367	6.59	2.61		
6270	003522-94-9	2,2,5-Trimethylhexane	16.56	25	1.15	4.58	2.437		
6280	003724-65-0	Crotonic acid	0.18	25	94000	0.72	0.000000428		
6290	003744-02-3	Isomesityl oxide	15.08	25	12140	1.16	0.0001		
6300	004088-60-2	*cis*-2-Buten-1-ol	60	63	166000	0.63	0.00000878		
6310	005341-95-7	*Meso*-2,3-Butanediol	0.38	25	1000000	–0.36	4.506E-08		
6320	005454-79-5	Cis-3-Methylcyclohexanol	5.6	65	5990	2.05	0.0000065	16.5	
6330	005989-54-8	(-)-1-Methyl-4-(1-methylethene)	15	64	3.153	4.83	0.38	2.37	
6340	006032-29-7	2-Pentanol	6.11	25	44600	1.19	0.0000148		
6350	006117-80-2	*Cis*-2-Butene-1,4-diol	0.0065	25	618500	–0.43	0.000000203		
6360	006876-23-9	*trans*-1,2-Dimethylcyclohexane	19.37	25	5.2	4.01	0.5425	2.04	
6370	006982-25-8	dl-2,3-Butandiol	0.1821	25	1000000	–0.36	0.00000023		
6380	007443-52-9	*trans*- 2-Methylcyclohexanol	20	72	9140	1.82	0.0000065		
6390	007443-55-2	*trans*-3-Methylcyclohexanol	5.2	61	5990	2.05	0.0000065	8.05	
6400	007443-70-1	*cis*-2-Methylcyclohexanol	16	65	9140	1.84	0.0000065		
6410	007642-04-8	*cis*-2-Octene	16	25	10.69	4.06	0.746	2.06	
6420	007705-14-8	(+-)Dipentene	20	68	3.153	4.83	0.38	2.38	
6430	007731-28-4	*cis* 4-Methylcyclohexanol	0.3277	25	10080	2.05	0.0000065		
6440	007731-29-5	*trans*-4-Methylcyclohexanol	0.3894	25	10080	1.79	0.0000065		
6450	007785-53-7	d-α-Terpineol	0.0307	25	670.4	3.33	0.0000158		
6460	013389-42-9	*trans*-2-Octene	16.44	25	10.69	4.06	0.746	2.002	
6470	013952-84-6	*sec*-Butylamine	172.6	25	112000	0.76	0.0002		
6480	019132-06-0	d-2,3-Butanediol	0.711	25	1000000	–0.92	0.00000023		
6490	024347-58-8	l-2,3-Butanediol	0.55	25	1000000	–0.36	2.3		

Table A4. The permissible exposure limit (PEL) and IDLH, the flashpoint and autoignition temperature, and the explosive limits in air of green solvents.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
10	064741-41-9	#489-0		52			FALSE	FALSE	FALSE	FALSE
20	000075-45-6a	(F-22) Anti-Static Super Freeze 1503-12			n/a	n/a	FALSE	FALSE	FALSE	FALSE
30	000460-73-1	1,1,1,3,3-Pentafluoro-propane					FALSE	FALSE	FALSE	FALSE
40	000680-00-2	1,1,2,2,3,3-Hexafluoro-propane					FALSE	FALSE	FALSE	FALSE
50	000679-86-7	1,1,2,2,3-Pentafluoro-propane			0	0	FALSE	FALSE	FALSE	FALSE
60	000079-01-6	1,1,2-Trichloroethylene	1.5	32	8	10	TRUE	FALSE	TRUE	FALSE
70	000076-14-2	1,2-Dichlorotetra-fluoroethane	1.455	n/a	n/a	n/a	FALSE	FALSE	TRUE	FALSE
80	000627-92-9	1,2-Propanediol, 3-(3-methylbutoxy)-					FALSE	FALSE	FALSE	FALSE
90	000624-52-2	1,2-Propanediol, 3-butoxy-					FALSE	FALSE	FALSE	FALSE
100	000623-39-2	1,2-Propanediol, 3-methoxy-					FALSE	FALSE	FALSE	FALSE
110	000460-12-8	1,3-Butadiyne					FALSE	FALSE	FALSE	FALSE
120	000107-88-0	1,3-Butanediol		121			FALSE	FALSE	FALSE	FALSE
130	000111-32-0	1,3-Butylene glycol methyl ether					FALSE	FALSE	FALSE	FALSE
140	000542-92-7	1,3-Cyclopentadiene		25	1.5	9.4	FALSE	FALSE	FALSE	FALSE
150	000504-60-9	1,3-Pentadiene		–34			FALSE	FALSE	FALSE	TRUE
160	000123-91-1	1,4-Dioxane		12	2	22	TRUE	FALSE	TRUE	FALSE
170	000591-93-5	1,4-Pentadiene		4			FALSE	FALSE	FALSE	FALSE
180	001115-08-8	1,4-Pentadiene, 3-methyl-		–34			FALSE	FALSE	FALSE	FALSE
190	002396-65-8	1,8-Nonadiyne		41			FALSE	FALSE	FALSE	FALSE
200	000071-36-3	1-Butanol	0.80575	28.9	1.4	11.2	FALSE	FALSE	TRUE	FALSE
210	000563-46-2	1-Butene, 2-methyl-		–34			FALSE	FALSE	FALSE	TRUE
220	000558-37-2	1-Butene, 3,3-dimethyl-		–28			FALSE	FALSE	FALSE	FALSE
230	000111-70-6	1-Heptanol	0.82	77			FALSE	FALSE	FALSE	FALSE
240	000111-27-3	1-Hexanol	0.81534	62	1.2	7.7	FALSE	FALSE	FALSE	FALSE
250	019430-93-4	1-Hexene, 3,3,4,4,5,5,6,6,6-nonafluoro-		–17			FALSE	FALSE	FALSE	FALSE
260	000107-98-2	1-Methoxy-2-propanol		32	3	12	FALSE	FALSE	FALSE	FALSE
270	000111-87-5	1-Octanol	0.82157	81			FALSE	FALSE	FALSE	FALSE
280	000071-41-0	1-Pentanol	0.8108	38			FALSE	FALSE	FALSE	FALSE
290	000109-67-1	1-Pentene		–18	1.5	8.7	FALSE	FALSE	FALSE	TRUE
300	000691-37-2	1-Pentene, 4-methyl-		–31	1.2		FALSE	FALSE	FALSE	FALSE
310	000627-19-0	1-Pentyne		–34			FALSE	FALSE	FALSE	FALSE
320	000071-23-8	1-Propanol		25	2.1	13.5	FALSE	FALSE	FALSE	FALSE
330	000584-84-9	2,4-Toluenediisocyanate	1.22	127	0.9	9.5	TRUE	TRUE	TRUE	TRUE
340	000110-13-4	2,5-Hexanedione		79			FALSE	FALSE	FALSE	FALSE
350	000112-34-5	2-(2-n-Butoxy-ethoxy)ethanol		78	0.85	24.6	FALSE	FALSE	FALSE	FALSE
360	000078-92-2	2-Butanol	0.80241	23.9	1.7	9.8	FALSE	FALSE	TRUE	FALSE
370	000513-35-9	2-Butene, 2-methyl-		0	1.6	8.7	FALSE	FALSE	FALSE	FALSE
380	000112-07-2	2-Butoxyethanol acetate	0.94	21.6	0.88	8.54	FALSE	FALSE	FALSE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
390	000503-17-3	2-Butyne		–34			FALSE	FALSE	FALSE	FALSE
400	000100-37-8	2-Diethylaminoethanol		52	6.7	11.7	FALSE	FALSE	FALSE	FALSE
410	000110-80-5	2-Ethoxyethanol		44	1.7	15.6	FALSE	FALSE	TRUE	FALSE
420	000111-15-9	2-Ethoxyethanol acetate	0.96761	51	1.7		FALSE	FALSE	FALSE	FALSE
430	000110-43-0	2-Heptanone	0.81123	39	1.1	7.9	FALSE	FALSE	FALSE	FALSE
440	000591-78-6	2-Hexanone	0.8067	25		8	FALSE	FALSE	FALSE	FALSE
450	000598-82-3	2-Hydroxypropanoic acid		110			FALSE	FALSE	FALSE	FALSE
460	000109-86-4	2-Methoxyethanol		41	2.5	14	FALSE	FALSE	TRUE	FALSE
470	000109-83-1	2-Methylaminoethanol		72	ne	ne	FALSE	FALSE	FALSE	FALSE
480	000078-83-1	2-Methylpropanol	0.7978	28	1.7	10.6	FALSE	FALSE	FALSE	FALSE
490	000123-96-6	2-Octanol	0.8171	74			FALSE	FALSE	FALSE	FALSE
500	000107-87-9	2-Pentanone	0.8015	7	1.5	8.2	FALSE	FALSE	FALSE	FALSE
510	000109-68-2	2-Pentene		–18			FALSE	FALSE	FALSE	FALSE
520	000626-78-8	2-Propanol, 1,3-bis(3-methylbutoxy)-					FALSE	FALSE	FALSE	FALSE
530	000623-69-8	2-Propanol, 1,3-dimethoxy-					FALSE	FALSE	FALSE	FALSE
540	000111-35-3	3-Ethoxy-1-propanol	0.9				FALSE	FALSE	FALSE	FALSE
550	000563-80-4	3-Methyl-2-butanone	0.81	6			FALSE	FALSE	FALSE	FALSE
560	000108-11-2	4-Methyl-2-pentanol	0.8036	41	1	5.5	FALSE	FALSE	FALSE	FALSE
570	000110-12-3	5-Methyl-2-hexanone	0.89	36	1.05	8.2	FALSE	FALSE	FALSE	FALSE
580	000541-85-5	5-Methyl-3-heptanone	0.82	58.89			FALSE	FALSE	FALSE	FALSE
590	064742-47-8c	Actrel 116OL cleaner		81	1.4	9.3	FALSE	FALSE	FALSE	FALSE
600	064742-48-9d	Actrel 3338L cleaner		40	1.2	9.6	FALSE	FALSE	FALSE	FALSE
610	064742-48-9e	Actrel 3349L cleaner		49	1.0	9.8	FALSE	FALSE	FALSE	FALSE
620	064742-48-9c	Actrel 3360L cleaner		61	1.3	8.8	FALSE	FALSE	FALSE	FALSE
630	064771-72-8	Actrel 4493L cleaner		95	1.4	8.9	FALSE	FALSE	FALSE	FALSE
640	000064-19-7	Acetic acid		42	5.4	16	FALSE	FALSE	FALSE	FALSE
650	000108-65-6	Acetic acid, 2-methoxy-1-methylethyl ester	1	42	1.3	13.1	FALSE	FALSE	FALSE	FALSE
660	000628-63-7	Acetic acid, amyl ester	0.8719	16	1.1	7.5	FALSE	FALSE	FALSE	FALSE
670	000108-21-4	Acetic acid, isopropyl ester	0.8702	2.2	1.8	8	FALSE	FALSE	FALSE	FALSE
680	000105-46-4	Acetic acid, sec-butyl ester	0.8694	17	1.7	9.8	FALSE	FALSE	FALSE	FALSE
690	000067-64-1	Acetone	0	–9	2.5	12.8	FALSE	FALSE	FALSE	FALSE
700	000107-02-8	Acrolein	0.8389	–17	2.8	31	TRUE	TRUE	TRUE	TRUE
710	005989-27-5a	Biogenic SE 373		46	0.7	6.1	FALSE	FALSE	FALSE	FALSE
720	000071-43-2	Benzene	0	–11	1.2	7.8	TRUE	FALSE	TRUE	FALSE
730	002366-52-1	Butane, 1-fluoro-					FALSE	FALSE	FALSE	FALSE
740	000075-83-2	Butane, 2,2-dimethyl-	0	–47.8	1.2	7	FALSE	FALSE	FALSE	FALSE
750	000079-29-8	Butane, 2,3-dimethyl-	0	–28.9	1.2	7	FALSE	FALSE	FALSE	FALSE
760	000078-78-4	Butane, 2-methyl-	0	–51	1.4	7.6	FALSE	FALSE	FALSE	TRUE
770	000111-76-2	Butoxyethanol		61	1.1	12.7	FALSE	FALSE	FALSE	FALSE
780	000123-86-4	Butyl acetate	0.88	22	1.7	7.6	FALSE	FALSE	FALSE	FALSE
790	000109-73-9	Butylamine		–12	1.7	9.8	FALSE	FALSE	FALSE	FALSE
800	000109-21-7	Butyric acid, butyl ester	0.9	53	n/a	n/a	FALSE	FALSE	FALSE	FALSE
810	000623-42-7	Butyric acid, methyl ester		10			FALSE	FALSE	FALSE	FALSE
820	000120-80-9	Catechol		127	1.4		TRUE	FALSE	TRUE	FALSE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
830	000075-45-6b	Chlorodifluoromethane		n/a	n/a	n/a	FALSE	FALSE	FALSE	FALSE
840	000074-87-3	Chloromethane	0.9111	<0	10.7	17.2	TRUE	FALSE	TRUE	TRUE
850	000076-15-3	Chloropentafluoroethane	1.291	n/a	n/a	n/a	FALSE	FALSE	TRUE	FALSE
860	000075-72-9	Chlorotrifluoromethane	0.9224				FALSE	FALSE	TRUE	FALSE
870	000287-23-0	Cyclobutane		<10	1.8		FALSE	FALSE	FALSE	FALSE
880	000110-82-7	Cyclohexane	0	−17	1.3	8.4	FALSE	FALSE	TRUE	FALSE
890	000108-93-0	Cyclohexanol	0.9684	68	2.4		FALSE	FALSE	TRUE	FALSE
900	000108-94-1	Cyclohexanone	0.9452	63	1.1	9.4	FALSE	FALSE	FALSE	FALSE
910	000287-92-3	Cyclopentane	0	−37	1.1	8.7	FALSE	FALSE	FALSE	FALSE
920	000142-29-0	Cyclopentene	0				FALSE	FALSE	FALSE	FALSE
930	001191-96-4	Cyclopropane, ethyl-					FALSE	FALSE	FALSE	FALSE
940	000123-42-2	Diacetone alcohol		58	1.8	6.9	FALSE	FALSE	FALSE	FALSE
950	000693-65-2	Diamyl ether	0.779	57			FALSE	FALSE	FALSE	FALSE
960	000142-96-1	Dibutyl ether	0.7641	25	1.5	7.6	FALSE	FALSE	FALSE	FALSE
970	002050-60-4	Dibutyl oxalate	0.99	104			FALSE	FALSE	FALSE	FALSE
980	000084-74-2	Dibutyl phthalate	1.0426	157	0.5		TRUE	FALSE	TRUE	FALSE
990	000075-71-8	Dichlorodifluoromethane		n/a	n/a	n/a	FALSE	FALSE	TRUE	FALSE
1000	000075-43-4	Dichlorofluoromethane	1.3662	n/a	n/a	n/a	FALSE	FALSE	TRUE	FALSE
1010	000111-42-2	Diethanolamine		137	1.6	9.8	TRUE	FALSE	TRUE	FALSE
1020	000095-92-1	Diethyl oxalate	1.08	75			FALSE	FALSE	FALSE	FALSE
1030	000111-46-6	Diethylene glycol		116	1.7	10.6	FALSE	FALSE	FALSE	FALSE
1040	000112-73-2	Diethylene glycol dibutyl ether	0.89	118			FALSE	FALSE	TRUE	FALSE
1050	000112-36-7	Diethylene glycol diethyl ether		82			FALSE	FALSE	TRUE	FALSE
1060	000111-96-6	Diethylene glycol dimethyl ether		63			FALSE	FALSE	TRUE	FALSE
1070	000124-17-4	Diethylene glycol monobutyl ether acetate	0.98	110	0.8		FALSE	FALSE	TRUE	FALSE
1080	000111-90-0	Diethylene glycol monoethyl ether		96			FALSE	FALSE	TRUE	FALSE
1090	000112-15-2	Diethylene glycol monoethyl ether acetate		107			FALSE	FALSE	TRUE	FALSE
1100	000111-77-3	Diethylene glycol monomethyl ether		93			FALSE	FALSE	TRUE	FALSE
1110	000629-38-9	Diethylene glycol monomethyl ether acetate	1.04				FALSE	FALSE	TRUE	FALSE
1120	000461-63-2	Difluoromethyl fluoromethyl ether					FALSE	FALSE	TRUE	FALSE
1130	000108-83-8	Diisobutyl ketone	0.802	49	0.81	7.1	FALSE	FALSE	FALSE	FALSE
1140	000108-20-3	Diisopropyl ether	0.71854	−27.8	1.4	7.9	FALSE	FALSE	FALSE	FALSE
1150	000108-18-9	Diisopropylamine	0.71	−6	1.1	7.1	FALSE	FALSE	FALSE	FALSE
1160	000067-68-5	Dimethyl sulfoxide		95	2.6	28.5	FALSE	FALSE	FALSE	FALSE
1170	000127-19-5	Dimethylacetamide		70	1.8	11.5	FALSE	FALSE	FALSE	FALSE
1180	000124-40-3	Dimethylamine	0.6496	20	2.8	14.4	FALSE	FALSE	TRUE	TRUE
1190	000108-01-0	Dimethylethanolamine		36			FALSE	FALSE	FALSE	FALSE
1200	000138-86-3	Dipentene	0.86	45			FALSE	FALSE	FALSE	FALSE
1210	000101-84-8	Diphenyl ether	1.06611	96	0.7	6	FALSE	FALSE	FALSE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
1220	034590-94-8	Dipropylene glycol monomethyl ether		85			FALSE	FALSE	FALSE	FALSE
1230	088917-22-0	Dipropylene glycol monomethyl ether acetate		85			FALSE	FALSE	FALSE	FALSE
1240	068526-79-4	Exxal 6	0.82	63	n/a	n/a	FALSE	FALSE	FALSE	FALSE
1250	108419-43-7	Exxate 1000 solvent		100	1.0	8.0	FALSE	FALSE	FALSE	FALSE
1260	088230-35-7	Exxate 600 solvent	0.87	57	1.0	8.0	FALSE	FALSE	FALSE	FALSE
1270	090438-79-2	Exxate 700 solvent		66	1.0	8.0	FALSE	FALSE	FALSE	FALSE
1280	108419-32-5	Exxate 800 solvent	0.87	77	1.0	8.0	FALSE	FALSE	FALSE	FALSE
1290	108419-33-6	Exxate 900 solvent	0.87	90	1.0	8.0	FALSE	FALSE	FALSE	FALSE
1300	064742-47-8a	Exxsol D 3135 solvent		38	1.4	8.1	FALSE	FALSE	FALSE	FALSE
1310	064742-47-8b	Exxsol D 60 naphtha		62	1.4	9.3	FALSE	FALSE	FALSE	FALSE
1320	000071-55-6b	Ethane, 1,1,1-trichloro-	0.15	none	n/a	n/a	FALSE	FALSE	FALSE	FALSE
1330	000354-58-5	Ethane, 1,1,1-trichloro-2,2,2-trifluoro-					FALSE	FALSE	FALSE	FALSE
1340	000076-13-1a	Ethane, 1,1,2-trichloro-1,2,2-trifluoro-	0.8	45	n/a	n/a	FALSE	FALSE	FALSE	FALSE
1350	000075-34-3	Ethane, 1,1-dichloro-		−16.7	5.4	11.4	TRUE	FALSE	TRUE	FALSE
1360	001717-00-6	Ethane, 1,1-dichloro-1-fluoro-	0.13				FALSE	FALSE	TRUE	FALSE
1370	000306-83-2	Ethane, 1,1-dichloro-2,2,2-trifluoro-	0.016				FALSE	FALSE	TRUE	FALSE
1380	000124-73-2	Ethane, 1,2-dibromo-1,1,2,2-tetrafluoro-					FALSE	FALSE	TRUE	FALSE
1390	001649-08-7	Ethane, 1,2-dichloro-1,1-difluoro-	0.047				FALSE	FALSE	TRUE	FALSE
1400	000624-72-6	Ethane, 1,2-difluoro-	0				FALSE	FALSE	FALSE	FALSE
1410	000076-12-0	Ethane, 1,2-difluoro-1,1,2,2-tetrachloro-	1	n/a	n/a	n/a	FALSE	FALSE	FALSE	FALSE
1420	013838-16-9	Ethane, 1-chloro-1,2,2-trifluoro, 2-difluoromethoxy-	0.004	n/a	n/a	n/a	FALSE	FALSE	FALSE	FALSE
1430	026675-46-7	Ethane, 1-chloro-2,2,2-trifluoro, 1-difluoromethoxy-	0.01				FALSE	FALSE	FALSE	FALSE
1440	003831-49-0	Ethane, 1-iodo-1,1,2,2-tetrafluoro-					FALSE	FALSE	FALSE	FALSE
1450	000151-67-7	Ethane, 2-bromo-2-chloro-1,1,1-trifluoro-	0.15				FALSE	FALSE	FALSE	FALSE
1460	000074-96-4	Ethane, bromo-	0.07	<15.6	6.75	8	FALSE	FALSE	FALSE	FALSE
1470	000075-00-3	Ethane, chloro-		−50	3.8	15.4	TRUE	FALSE	TRUE	TRUE
1480	000354-64-3	Ethane, pentafluoroiodo-					FALSE	FALSE	FALSE	FALSE
1490	020602-86-2	Ethanedioic acid, dipentyl ester		75			FALSE	FALSE	FALSE	FALSE
1500	000064-17-5	Ethanol		13	3.3	19	FALSE	FALSE	FALSE	FALSE
1510	000141-78-6	Ethyl acetate	0	−1	2	11.5	FALSE	FALSE	FALSE	FALSE
1520	000075-04-7	Ethyl amine	0	−17.2	3.5	14	FALSE	FALSE	FALSE	TRUE
1530	000060-29-7	Ethyl ether	0	−45	1.9	36	FALSE	FALSE	FALSE	TRUE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
1540	000109-94-4	Ethyl formate	0	–20	2.8	16	FALSE	FALSE	FALSE	FALSE
1550	000105-37-3	Ethyl propionate	0.884	12	1.9	11	FALSE	FALSE	FALSE	FALSE
1560	000100-41-4	Ethylbenzene	0.86253	18	1	6.7	TRUE	FALSE	TRUE	FALSE
1570	000107-21-1	Ethylene glycol		111	3.2	15.3	TRUE	FALSE	TRUE	FALSE
1580	000112-48-1	Ethylene glycol dibutyl ether	0.83189	85			FALSE	FALSE	TRUE	FALSE
1590	000629-14-1	Ethylene glycol diethyl ether	0.8351	27			FALSE	FALSE	TRUE	FALSE
1600	000110-49-6	Ethylene glycol methyl ether acetate		49	1.7	8.2	FALSE	FALSE	TRUE	FALSE
1610	000622-08-2	Ethylene glycol monobenzyl ether	1.07	129			FALSE	FALSE	FALSE	FALSE
1620	000122-99-6	Ethylene glycol monophenyl ether		121			FALSE	FALSE	TRUE	FALSE
1630	000075-21-8	Ethylene oxide		–29	3	100	TRUE	TRUE	TRUE	TRUE
1640	000060-00-4	Ethylenediaminetetra-acetic acid	0.721	N/A	n/a	n/a	FALSE	FALSE	FALSE	FALSE
1650	086508-42-1e	FC-104 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1660	086508-42-1c	FC-40 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1670	086508-42-1g	FC-43 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1680	086508-42-1h	FC-5312 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1690	086508-42-1i	FC-70 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1700	125061-94-1	FC-71 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1710	086508-42-1j	FC-72 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1720	086508-42-1k	FC-722 Fluorad			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1730	086508-42-1l	FC-75 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1740	086508-42-1m	FC-77 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1750	086508-42-1d	FC-84 Fluorinert			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1760	000050-00-0	Formaldehyde	0.84	83	7	73	TRUE	TRUE	TRUE	TRUE
1770	000064-18-6	Formic acid		59	18	57	FALSE	FALSE	TRUE	FALSE
1780	000110-00-9	Furan	0	–36	2.3	14.3	FALSE	TRUE	FALSE	TRUE
1790	000098-01-1	Furfural	1.1545	60	2.1	19.3	FALSE	FALSE	FALSE	FALSE
1800	000098-00-0	Furfuryl alcohol		75	1.8	16.3	FALSE	FALSE	FALSE	FALSE
1810	000142-82-5	Heptane	0	–1	1.05	6.7	FALSE	FALSE	FALSE	FALSE
1820	000999-97-3	Hexamethyldisilazane	0.77	8			FALSE	FALSE	FALSE	FALSE
1830	000822-06-0	Hexamethylene diisocyanate	1.04	140	0.9	9.5	TRUE	FALSE	TRUE	FALSE
1840	000110-54-3	Hexane	0	–26	1.1	7.5	TRUE	FALSE	TRUE	FALSE
1850	000355-42-0	Hexane, tetradecafluoro-	0				FALSE	FALSE	FALSE	FALSE
1860	000123-31-9	Hydroquinone		165			TRUE	TRUE	TRUE	FALSE
1870	064742-48-9f	Isopar G solvent		38	1	9.8	FALSE	FALSE	FALSE	FALSE
1880	064742-48-9b	Isopar H solvent		53	0.7	6.5	FALSE	FALSE	FALSE	FALSE
1890	064742-48-9a	Isopar L solvent		60	0.6	7.0	FALSE	FALSE	FALSE	FALSE
1900	026952-21-6	Isooctyl alcohol	0.82	82	0.9	5.7	FALSE	FALSE	FALSE	FALSE
1910	000078-79-5	Isoprene	0				FALSE	FALSE	FALSE	TRUE
1920	000067-63-0	Isopropyl alcohol		12	2	12.7	FALSE	FALSE	TRUE	FALSE
1930	008008-20-6	Kerosene	0.8	37	.7	5	FALSE	FALSE	FALSE	FALSE
1940	086508-42-1f	L-12077			n/a	n/a	FALSE	FALSE	FALSE	FALSE
1950	006382-06-5	Lactic acid, amyl ester	0.96	79			FALSE	FALSE	FALSE	FALSE
1960	000138-22-7	Lactic acid, butyl ester		71	1.0	7.9	FALSE	FALSE	FALSE	FALSE
1970	000097-64-3	Lactic acid, ethyl ester		47	1.55	10.6	FALSE	FALSE	FALSE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
1980	000547-64-8	Lactic acid, methyl ester		55	1.1	3.6	FALSE	FALSE	FALSE	FALSE
1990	000076-13-1c	MS-177 Freon TE solvent		45	n/a	n/a	FALSE	FALSE	FALSE	FALSE
2000	000076-13-1b	MS-178 Freon TES solvent	1.499		n/a	n/a	FALSE	FALSE	FALSE	FALSE
2010	000107-30-2	Methane, chloromethoxy-		15			TRUE	TRUE	TRUE	TRUE
2020	000074-95-3	Methane, dibromo-	0.17				FALSE	FALSE	TRUE	FALSE
2030	000075-61-6	Methane, dibromodifluoro-		n/a	n/a	n/a	FALSE	FALSE	TRUE	FALSE
2040	000075-09-2	Methane, dichloro-		n/a	13	23	TRUE	FALSE	TRUE	FALSE
2050	000593-53-3	Methane, fluoro-	0				FALSE	FALSE	TRUE	FALSE
2060	001493-03-4	Methane, iododifluoro-					FALSE	FALSE	TRUE	FALSE
2070	000373-53-5	Methane, iodofluoro-					FALSE	FALSE	TRUE	FALSE
2080	000056-23-5	Methane, tetrachloro-	1.1	N/A	N/A	N/A	TRUE	FALSE	TRUE	FALSE
2090	000067-66-3	Methane, trichloro-		n/a	n/a	n/a	TRUE	TRUE	TRUE	TRUE
2100	000075-69-4	Methane, trichlorofluoro-	1	n/a	n/a	n/a	FALSE	FALSE	TRUE	FALSE
2110	000075-75-2	Methanesulfonic acid	1.48	110			FALSE	FALSE	FALSE	FALSE
2120	000067-56-1	Methanol		12	6	36	TRUE	FALSE	TRUE	FALSE
2130	000100-66-3	Methoxybenzene	0.98932	52			FALSE	FALSE	FALSE	FALSE
2140	000079-20-9	Methyl acetate	0	−10	3.1	16	FALSE	FALSE	FALSE	FALSE
2150	000078-93-3	Methyl ethyl ketone	0	−9	1.4	11.4	TRUE	FALSE	TRUE	FALSE
2160	000107-31-3	Methyl formate	0	−19	4.5	23	FALSE	FALSE	FALSE	TRUE
2170	000141-79-7	Methyl isobutenyl ketone	0.86	37	1.4	7.2	FALSE	FALSE	FALSE	FALSE
2180	000108-10-1	Methyl isobutyl ketone	0.7963	16	1.2	8	TRUE	FALSE	TRUE	FALSE
2190	000554-12-1	Methyl propionate	0.92	−2	2.5	13	FALSE	FALSE	FALSE	FALSE
2200	000557-17-5	Methyl propyl ether	0				FALSE	FALSE	FALSE	FALSE
2210	001634-04-4	Methyl tert-butyl ether	0.76	−28	1.6	15.1	TRUE	FALSE	TRUE	FALSE
2220	064475-85-0	Mineral spirits	0.78	38			FALSE	FALSE	FALSE	FALSE
2230	000141-43-5	Monoethanolamine		85	3	23.5	FALSE	FALSE	FALSE	FALSE
2240	000074-89-5	Monomethylamine	0.6562	0	4.9	20.7	FALSE	FALSE	FALSE	TRUE
2250	000872-50-4a	N-Methylpyrrolidone		92	1.3	9.5	FALSE	FALSE	FALSE	FALSE
2260	000062-75-9	N-Nitrosodimethylamine					TRUE	TRUE	TRUE	FALSE
2270	064742-49-9g	Patclin #427 cold degreaser		40			FALSE	FALSE	FALSE	FALSE
2280	086508-42-1b	PF-5050			n/a	n/a	FALSE	FALSE	FALSE	FALSE
2290	086508-42-1	PF-5060			n/a	n/a	FALSE	FALSE	FALSE	FALSE
2300	000422-05-9	Pentafluoropropyl alcohol			n/a	n/a	FALSE	FALSE	FALSE	FALSE
2310	000109-66-0	Pentane	0	−40	1.5	7.8	FALSE	FALSE	FALSE	TRUE
2320	000678-26-2	Pentane, dodecafluoro-	0				FALSE	FALSE	FALSE	FALSE
2330	025322-68-3b	Polyglycol E 200		171			FALSE	FALSE	FALSE	FALSE
2340	025322-68-3c	Polyglycol E 400		177			FALSE	FALSE	FALSE	FALSE
2350	025322-68-3d	Polyglycol E 600		177	1.1	6.9	FALSE	FALSE	FALSE	FALSE
2360	025322-68-3e	Polyglycol E-1000	1.204	177			FALSE	FALSE	FALSE	FALSE
2370	025322-68-3f	Polyglycol E-1450	1.214	177			FALSE	FALSE	FALSE	FALSE
2380	025322-68-3g	Polyglycol E-3350	1.224	177			FALSE	FALSE	FALSE	FALSE
2390	025322-68-3i	Polyglycol E-4500	1.224	177			FALSE	FALSE	FALSE	FALSE
2400	025322-68-3h	Polyglycol E-8000	1.224	177			FALSE	FALSE	FALSE	FALSE
2410	025322-68-3a	Polyglycol E-900	1.204	232			FALSE	FALSE	FALSE	FALSE
2420	025322-69-4c	Polyglycol P 425		160			FALSE	FALSE	FALSE	FALSE
2430	025322-69-4a	Polyglycol P-1200	1.007	175			FALSE	FALSE	FALSE	FALSE
2440	025322-69-4b	Polyglycol P-2000		230			FALSE	FALSE	FALSE	FALSE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
2450	000754-34-7	Propane, 1,1,1,2,2,3,3-heptafluoro-3-iodo-					FALSE	FALSE	FALSE	FALSE
2460	000677-69-0	Propane, 1,1,1,2,3,3,3-heptafluoro-2-iodo-		115			FALSE	FALSE	FALSE	FALSE
2470	000540-54-5	Propane, 1-chloro-		18	2.6	11.1	FALSE	FALSE	FALSE	FALSE
2480	000075-29-6	Propane, 2-chloro		−32	2.8	10.7	FALSE	FALSE	FALSE	TRUE
2490	000507-20-0	Propane, 2-chloro-2-methyl-		18			FALSE	FALSE	FALSE	FALSE
2500	000109-60-4	Propyl acetate	0.99303	12.7	1.7	8	FALSE	FALSE	FALSE	FALSE
2510	000108-32-7	Propylene carbonate	1.1951	132			FALSE	FALSE	FALSE	FALSE
2520	000057-55-6	Propylene glycol		98.88	2.6	12.6	FALSE	FALSE	FALSE	FALSE
2530	004169-04-4	Propylene glycol monophenyl ether	1.063	127			FALSE	FALSE	FALSE	FALSE
2540	000075-56-9	Propylene oxide	0.8287	−35	2.3	36	TRUE	TRUE	TRUE	TRUE
2550	086508-42-1a	SF-2			n/a	n/a	FALSE	FALSE	FALSE	FALSE
2560	018395-30-7	Sil-act ats-100		95			FALSE	FALSE	FALSE	FALSE
2570	000872-50-4b	SVC-150		101			FALSE	FALSE	FALSE	FALSE
2580	064742-88-7	Solvent 140-66	0.77	41	1.0	7	FALSE	FALSE	FALSE	FALSE
2590	008052-41-3	Stoddard solvent	0.775	38	1.0		FALSE	FALSE	FALSE	FALSE
2600	000126-33-0	Sulfolane		177			FALSE	FALSE	FALSE	FALSE
2610	000127-18-4	Tetrachloroethylene	1.6		n/a	n/a	TRUE	FALSE	TRUE	FALSE
2620	000112-60-7	Tetraethylene glycol		182	1	—	FALSE	FALSE	FALSE	FALSE
2630	000112-57-2	Tetraethylene pentamine		163	0.8	4.6	FALSE	FALSE	FALSE	FALSE
2640	000075-73-0	Tetrafluoromethane					FALSE	FALSE	TRUE	FALSE
2650	000109-99-9	Tetrahydrofuran	0	−14	2	11.8	FALSE	FALSE	FALSE	FALSE
2660	000097-99-4	Tetrahydrofurfuryl alcohol		84	1.5	9.7	FALSE	FALSE	FALSE	FALSE
2670	000100-72-1	Tetrahydropyran-2-methano1		93.3			FALSE	FALSE	FALSE	FALSE
2680	000108-88-3	Toluene	0.86219	4	1.2	7.1	TRUE	FALSE	TRUE	FALSE
2690	000102-71-6	Triethanolamine		179	1.20	—	FALSE	FALSE	FALSE	FALSE
2700	000121-44-8	Triethylamine	0.72305	−6	1.2	8	TRUE	FALSE	TRUE	FALSE
2710	000112-27-6	Triethylene glycol		166	0.9	9.2	FALSE	FALSE	FALSE	FALSE
2720	004499-99-4	Triethylene glycol diethyl ether					FALSE	FALSE	TRUE	FALSE
2730	000112-49-2	Triethylene glycol dimethyl ether		111			FALSE	FALSE	TRUE	FALSE
2740	000075-46-7	Trifluoromethane	0.8781				FALSE	FALSE	TRUE	FALSE
2750	000504-63-2	Trimethylene glycol	1.05				FALSE	FALSE	FALSE	FALSE
2760	000110-88-3	Trioxane		45	3.6	29	FALSE	FALSE	FALSE	FALSE
2770	008006-64-2	Turpentine (steam distilled)	0.86	32.8	.8		FALSE	FALSE	FALSE	FALSE
2780	008032-32-4	VM & P Naphtha		−57	1	6	FALSE	FALSE	FALSE	FALSE
2790	000071-55-6a	Vi-Chem VC-1 cleaner	1.3		n/a	n/a	FALSE	FALSE	FALSE	FALSE
2800	001330-20-7	Xylene (mixed)	0.871	27	1	6	TRUE	FALSE	TRUE	FALSE
2810	010482-56-1	α-Terpineo1		90			FALSE	FALSE	FALSE	FALSE
2820	005989-27-5b	d-Limonene	0.8383	48			FALSE	FALSE	FALSE	FALSE
2830	000096-48-0	γ-Butyrolactone		98			FALSE	FALSE	FALSE	FALSE
2840	000108-38-3	*m*-Xylene	0.86009	27	1.1	7	TRUE	FALSE	TRUE	FALSE
2850	000142-92-7	*n*-Hexyl acetate		37			FALSE	FALSE	FALSE	FALSE
2860	000112-58-3	*n*-Hexyl ether	0.79	77			FALSE	FALSE	FALSE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
2870	000095-47-6	o-Xylene		32.2	0.9	6.7	TRUE	FALSE	TRUE	FALSE
2880	000106-42-3	p-Xylene		25	1.1	7	TRUE	FALSE	TRUE	FALSE
2890	000056-81-5	Glycerol		160			FALSE	FALSE	FALSE	FALSE
2900	000060-35-5	Acetamide		n/a	n/a	n/a	TRUE	FALSE	TRUE	FALSE
2910	000062-53-3	Aniline		70	1.3	11	TRUE	TRUE	TRUE	FALSE
2920	000068-12-2	N,N'-Dimethylformamide		57.8	2.2	15.2	TRUE	FALSE	TRUE	FALSE
2930	000074-83-9	Methyl bromide		n/a	10	16	TRUE	TRUE	TRUE	FALSE
2940	000074-88-4	Methyl iodide					TRUE	FALSE	TRUE	FALSE
2950	000074-97-5	Chlorobromomethane		n/a	n/a	n/a	FALSE	FALSE	FALSE	FALSE
2960	000074-98-6	Propane		−104	2.1	9.5	FALSE	FALSE	FALSE	TRUE
2970	000075-01-4	Vinylchloride		−78	3.6	33	TRUE	FALSE	TRUE	TRUE
2980	000075-03-6	Iodoethane					FALSE	FALSE	FALSE	FALSE
2990	000075-05-8	Acetonitrile		5.6	4	16	TRUE	FALSE	TRUE	FALSE
3000	000075-07-0	Acetaldehyde		−37.8	4	57	TRUE	FALSE	TRUE	TRUE
3010	000075-11-6	Methylene iodide					FALSE	FALSE	FALSE	FALSE
3020	000075-12-7	Formamide		154	n/a	n/a	FALSE	FALSE	FALSE	FALSE
3030	000075-15-0	Carbon disulfide		−30	1.3	50	TRUE	TRUE	TRUE	TRUE
3040	000075-18-3	Dimethylsulfide		−34			FALSE	FALSE	FALSE	FALSE
3050	000075-25-2	Bromoform		<79	n/a	n/a	TRUE	FALSE	TRUE	FALSE
3060	000075-26-3	2-Bromopropane					FALSE	FALSE	FALSE	FALSE
3070	000075-28-5	2-Methylpropane		−87	1.6	8.4	FALSE	FALSE	FALSE	TRUE
3080	000075-30-9	2-Iodopropane					FALSE	FALSE	FALSE	FALSE
3090	000075-31-0	Isopropylamine		−26	n/a	n/a	FALSE	FALSE	FALSE	TRUE
3100	000075-35-4	1,1-Dichloroethene		−10	6.5	15.5	TRUE	FALSE	TRUE	TRUE
3110	000075-37-6	1,1-Difluoroethane					FALSE	FALSE	FALSE	TRUE
3120	000075-50-3	Trimethylamine		−6.7	2	11.6	FALSE	FALSE	FALSE	TRUE
3130	000075-52-5	Nitromethane		35	7.3	n/a	FALSE	FALSE	FALSE	FALSE
3140	000075-64-9	*t*-Butylamine		n/a	1.7	8.9	FALSE	FALSE	FALSE	FALSE
3150	000075-65-0	*t*-Butanol		11.1	2.4	8	FALSE	FALSE	TRUE	FALSE
3160	000075-76-3	Tetramethyl silane					FALSE	FALSE	FALSE	TRUE
3170	000075-79-6	Methyltrichlorosilane					FALSE	TRUE	TRUE	TRUE
3180	000075-84-3	2,2-Dimethyl-1-propanol					FALSE	FALSE	FALSE	FALSE
3190	000075-85-4	2-Methyl-2-butanol		40.6	1.2	9	FALSE	FALSE	FALSE	FALSE
3200	000075-89-8	2,2,2-Trifluoroethanol					FALSE	FALSE	FALSE	FALSE
3210	000076-01-7	Pentachloroethane					FALSE	FALSE	TRUE	FALSE
3220	000076-05-1	Trifluoroacetic acid					FALSE	FALSE	FALSE	FALSE
3230	000078-40-0	Triethyl phosphate		115.56			FALSE	FALSE	FALSE	FALSE
3240	000078-75-1	1,2-Dibromopropane					FALSE	FALSE	FALSE	FALSE
3250	000078-76-2	2-Bromobutane		21.1			FALSE	FALSE	FALSE	FALSE
3260	000078-81-9	Isobutylamine		−9	3.4	9	FALSE	FALSE	FALSE	FALSE
3270	000078-84-2	Isobutyraldehyde		7	n/a	n/a	FALSE	FALSE	TRUE	FALSE
3280	000078-86-4	2-Chlorobutane		−10			FALSE	FALSE	FALSE	FALSE
3290	000078-87-5	1,2-Dichloropropane		15.5	3.4	14.5	TRUE	FALSE	TRUE	FALSE
3300	000079-00-5	1,1,2-Trichloroethane			6	15.5	TRUE	FALSE	TRUE	FALSE
3310	000079-09-4	Propionic acid		52.2	2.9	12.1	FALSE	FALSE	FALSE	FALSE
3320	000079-10-7	Acrylic acid		54	2.4	8	TRUE	FALSE	TRUE	FALSE
3330	000079-16-3	N-Methylacetamide					FALSE	FALSE	FALSE	FALSE
3340	000079-24-3	Nitroethane		28	3.4		FALSE	FALSE	FALSE	FALSE
3350	000079-27-6	1,1,2,2-Tetrabromoethane		n/a	n/a	n/a	FALSE	FALSE	FALSE	FALSE
3360	000079-31-2	Isobutyric acid		77			FALSE	FALSE	FALSE	FALSE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
3370	000079-34-5	1,1,2,2-Tetrachloroethane		n/a	n/a	n/a	TRUE	FALSE	TRUE	FALSE
3380	000079-41-4	Methacrylic acid		77.2			FALSE	FALSE	FALSE	FALSE
3390	000079-46-9	2-Nitropropane		23.9	2.6	11	TRUE	FALSE	TRUE	FALSE
3400	000080-56-8	α-Pinene		35			FALSE	FALSE	FALSE	FALSE
3410	000080-62-6	Methyl methacrylate		−3	1.78	8.2	TRUE	FALSE	TRUE	FALSE
3420	000087-62-7	2,6-Dimethylaniline					FALSE	FALSE	TRUE	FALSE
3430	000090-02-8	o-Hydroxybenzaldehyde					FALSE	FALSE	FALSE	FALSE
3440	000090-11-9	1-Bromonaphthalene					FALSE	FALSE	FALSE	FALSE
3450	000090-12-0	1-Methylnaphthalene					FALSE	FALSE	FALSE	FALSE
3460	000090-13-1	1-Chloronaphthalene					FALSE	FALSE	FALSE	FALSE
3470	000091-16-7	1,2-Dimethoxybenzene					FALSE	FALSE	FALSE	FALSE
3480	000091-17-8	Decahydronaphthalene		58	1.8	6.9	FALSE	FALSE	FALSE	FALSE
3490	000091-20-3	Naphthalene		79	0.9	5.9	TRUE	FALSE	TRUE	FALSE
3500	000091-22-5	Quinoline					TRUE	FALSE	TRUE	FALSE
3510	000091-23-6	2-Nitroanisole					FALSE	FALSE	FALSE	FALSE
3520	000092-51-3	Dicyclohexyl					FALSE	FALSE	FALSE	FALSE
3530	000093-58-3	Benzoic acid, methyl ester		82			FALSE	FALSE	FALSE	FALSE
3540	000093-89-0	Ethyl benzoate					FALSE	FALSE	FALSE	FALSE
3550	000094-96-2	2-Ethyl-1,3-hexandiol		126.7			FALSE	FALSE	FALSE	FALSE
3560	000095-48-7	*o*-Cresol		81	1.4		TRUE	TRUE	TRUE	FALSE
3570	000095-49-8	2-Chlorotoluene		35.6			FALSE	FALSE	FALSE	FALSE
3580	000095-50-1	1,2-Dichlorobenzene		66	2.2	9.2	FALSE	FALSE	TRUE	FALSE
3590	000095-51-2	2-Chloroaniline					FALSE	FALSE	FALSE	FALSE
3600	000095-52-3	*o*-Fluorotoluene					FALSE	FALSE	FALSE	FALSE
3610	000095-53-4	*o*-Toluidine		85	1.5		TRUE	FALSE	TRUE	FALSE
3620	000095-65-8	3,4-Dimethylphenol					FALSE	FALSE	FALSE	FALSE
3630	000095-68-1	2,4-Dimethylaniline					FALSE	FALSE	FALSE	FALSE
3640	000095-73-8	2,4-Dichlorotoluene					FALSE	FALSE	FALSE	FALSE
3650	000095-75-0	3,4-Dichlorotoluene					FALSE	FALSE	FALSE	FALSE
3660	000095-87-4	2,5-Dimethylphenol					FALSE	FALSE	FALSE	FALSE
3670	000096-14-0	3-Methylpentane		−7	1.2	7.0	FALSE	FALSE	FALSE	FALSE
3680	000096-18-4	1,2,3-Trichloropropane		71	3.2	12.6	FALSE	FALSE	TRUE	FALSE
3690	000096-22-0	3-Pentanone		13	1.6	6.4	FALSE	FALSE	FALSE	FALSE
3700	000096-33-3	Methyl acrylate		−3	2.8	25	FALSE	FALSE	TRUE	FALSE
3710	000096-37-7	Methylcyclopentane		−27			FALSE	FALSE	FALSE	FALSE
3720	000096-47-9	2-Methyltetrahydrofuran		−11			FALSE	FALSE	FALSE	FALSE
3730	000096-49-1	1,3-Dioxolan-2-one		160			FALSE	FALSE	FALSE	FALSE
3740	000097-85-8	Isobutyl isobutyrate					FALSE	FALSE	FALSE	FALSE
3750	000097-95-0	2-Ethyl-1-butanol		53			FALSE	FALSE	FALSE	FALSE
3760	000098-06-6	*t*-Butylbenzene		60			FALSE	FALSE	FALSE	FALSE
3770	000098-07-7	Benzotrichloride		97			TRUE	TRUE	TRUE	FALSE
3780	000098-08-8	Benzotrifluoride		12			FALSE	FALSE	FALSE	FALSE
3790	000098-55-5	α-Terpineol		90			FALSE	FALSE	FALSE	FALSE
3800	000098-82-8	Cumene		39	0.9	6.5	TRUE	FALSE	TRUE	FALSE
3810	000098-86-2	Acetophenone		82.2			TRUE	FALSE	TRUE	FALSE
3820	000098-95-3	Nitrobenzene		88	1.8	n/a	TRUE	TRUE	TRUE	FALSE
3830	000099-87-6	*p*-Cymene		52			FALSE	FALSE	FALSE	FALSE
3840	000099-94-5	*p*-Toluic acid					FALSE	FALSE	FALSE	FALSE
3850	000100-42-5	styrene		31	0.9	6.8	TRUE	FALSE	TRUE	FALSE
3860	000100-44-7	α-Chlorotoluene		67	1.1	n/a	TRUE	TRUE	TRUE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
3870	000100-47-0	Benzonitrile		n/a			FALSE	FALSE	FALSE	FALSE
3880	000100-51-6	Benzyl alcoho1		93			FALSE	FALSE	FALSE	FALSE
3890	000100-52-7	Benzaldehyde		64			FALSE	FALSE	FALSE	FALSE
3900	000100-61-8	N-Methylaniline		79.4			FALSE	FALSE	FALSE	FALSE
3910	000102-76-1	Triacetin		143			FALSE	FALSE	FALSE	FALSE
3920	000102-82-9	Tri N-butylamine		85			FALSE	FALSE	FALSE	FALSE
3930	000103-09-3	2-Ethylhexylacetate		88			FALSE	FALSE	FALSE	FALSE
3940	000103-36-6	Cinnamic acid, ethyl ester					FALSE	FALSE	FALSE	FALSE
3950	000103-50-4	Dibenzyl ether		135			FALSE	FALSE	FALSE	FALSE
3960	000103-73-1	Ethoxybenzene					FALSE	FALSE	FALSE	FALSE
3970	000104-51-8	N-Butylbenzene		71			FALSE	FALSE	FALSE	FALSE
3980	000104-75-6	2-Ethylhexylamine		60			FALSE	FALSE	FALSE	FALSE
3990	000104-76-7	2-Ethyl-1-hexanol		81	0.8	9.7	FALSE	FALSE	FALSE	FALSE
4000	000105-30-6	2-Methyl-1-pentanol		57			FALSE	FALSE	FALSE	FALSE
4010	000105-34-0	Methyl cyanoacetate					FALSE	FALSE	FALSE	FALSE
4020	000105-45-3	Methyl acetoacetate		77			FALSE	FALSE	FALSE	FALSE
4030	000105-53-3	Diethyl malonate		93			FALSE	FALSE	FALSE	FALSE
4040	000105-54-4	Ethylbutyrate		26			FALSE	FALSE	FALSE	FALSE
4050	000105-56-6	Ethyl cyanoacetate		110			FALSE	FALSE	FALSE	FALSE
4060	000105-57-7	1,1-Diethoxyethane		36			FALSE	FALSE	FALSE	FALSE
4070	000105-58-8	Diethyl carbonate		25			FALSE	FALSE	FALSE	FALSE
4080	000105-60-2	Caprolactam		125	1.4	8	TRUE	FALSE	FALSE	FALSE
4090	000105-67-9	2,4-Dimethylphenol					FALSE	FALSE	TRUE	FALSE
4100	000105-76-0	Dibutyl maleate		141			FALSE	FALSE	FALSE	FALSE
4110	000106-31-0	Butyric anhydride		88			FALSE	FALSE	FALSE	FALSE
4120	000106-35-4	3-Heptanone		46			FALSE	FALSE	FALSE	FALSE
4130	000106-43-4	*p*-Chlorotoluene					FALSE	FALSE	FALSE	FALSE
4140	000106-44-5	*p*-Cresol		94			TRUE	FALSE	TRUE	FALSE
4150	000106-46-7	1,4-DIchlorobenzene		65	2.5	n/a	TRUE	FALSE	TRUE	FALSE
4160	000106-49-0	*p*-Toluidine		87			FALSE	FALSE	FALSE	FALSE
4170	000106-69-4	1,2,6-Hexanetriol		193			FALSE	FALSE	FALSE	FALSE
4180	000106-88-7	1,2-Butyleneoxide		15	1.5	18.3	TRUE	FALSE	TRUE	FALSE
4190	000106-93-4	1,2-Dibromoethane		n/a	n/a	n/a	TRUE	FALSE	TRUE	FALSE
4200	000106-94-5	1-Bromopropane		79			FALSE	FALSE	FALSE	FALSE
4210	000106-97-8	*n*-Butane		–60			FALSE	FALSE	FALSE	TRUE
4220	000106-98-9	1-Butene					FALSE	FALSE	FALSE	TRUE
4230	000107-04-0	1-Bromo-2-chloroethane					FALSE	FALSE	FALSE	FALSE
4240	000107-05-1	3-Chloropropylene		–32	2.9	11.1	TRUE	FALSE	TRUE	FALSE
4250	000107-06-2	1,2-Dichloroethane		13	6.2	16	TRUE	FALSE	TRUE	FALSE
4260	000107-07-3	2-Chloroethanol		60	4.9	15.9	FALSE	TRUE	FALSE	FALSE
4270	000107-08-4	1-Iodopropane					FALSE	FALSE	FALSE	FALSE
4280	000107-10-8	Propylamine		–12			FALSE	FALSE	FALSE	FALSE
4290	000107-11-9	Allylamine		–12			FALSE	TRUE	TRUE	TRUE
4300	000107-12-0	Propionitrile		17	3.1		FALSE	TRUE	FALSE	TRUE
4310	000107-13-1	Acrylonitrile		0	3	17	TRUE	TRUE	TRUE	TRUE
4320	000107-15-3	1,2-Diaminoethane		34	2.5	12	FALSE	TRUE	FALSE	TRUE
4330	000107-18-6	Allyl alcohol		21	2.5	18	FALSE	TRUE	TRUE	TRUE
4340	000107-19-7	Propargyl alcohol		36			FALSE	FALSE	TRUE	FALSE
4350	000107-41-5	2-Methyl-2,4-pentanediol		101	1.3	15.3	FALSE	FALSE	FALSE	FALSE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
4360	000107-83-5	2-Methylpentane		−23	1.2	8	FALSE	FALSE	FALSE	FALSE
4370	000107-92-6	Butyric acid		76			FALSE	FALSE	FALSE	FALSE
4380	000108-03-2	1-Nitropropane		49	2.2	—	FALSE	FALSE	FALSE	FALSE
4390	000108-05-4	Vinyl acetate		−8	2.6	13.4	TRUE	TRUE	TRUE	TRUE
4400	000108-08-7	2,4-Dimethylpentane		−12			FALSE	FALSE	FALSE	FALSE
4410	000108-24-7	Acetic anhydride		48.9	2.7	10.3	FALSE	FALSE	FALSE	FALSE
4420	000108-39-4	*m*-Cresol		86	1.1		TRUE	FALSE	TRUE	FALSE
4430	000108-41-8	*m*-Chlorotoluene					FALSE	FALSE	FALSE	FALSE
4440	000108-44-1	*m*-Toluidine		86			FALSE	FALSE	FALSE	FALSE
4450	000108-47-4	2,4-Dimethylpyridine					FALSE	FALSE	FALSE	FALSE
4460	000108-48-5	2,6-Lutidine					FALSE	FALSE	FALSE	FALSE
4470	000108-64-5	Ethyl isovalerate					FALSE	FALSE	FALSE	FALSE
4480	000108-67-8	1,3,5-Trimethylbenzene		50			FALSE	FALSE	FALSE	FALSE
4490	000108-68-9	3,5-Dimethylphenol					FALSE	FALSE	FALSE	FALSE
4500	000108-75-8	2,4,6-Collidine					FALSE	FALSE	FALSE	FALSE
4510	000108-84-9	4-Methyl-2-pentyl acetate		43	0.9	5.83	FALSE	FALSE	FALSE	FALSE
4520	000108-86-1	Bromobenzene		65			FALSE	FALSE	FALSE	FALSE
4530	000108-87-2	1-Methylcyclohexane		−4	1.2	6.7	FALSE	FALSE	FALSE	FALSE
4540	000108-89-4	4-Methylpyridine		57			FALSE	FALSE	FALSE	FALSE
4550	000108-90-7	Chlorobenzene		28	1.3	9.6	TRUE	FALSE	TRUE	FALSE
4560	000108-91-8	Cyclohexanamine		28	1.5	9.4	FALSE	TRUE	FALSE	TRUE
4570	000108-95-2	Phenol		79	1.8	8.6	TRUE	TRUE	TRUE	FALSE
4580	000108-98-5	Thiophenol		55.5			FALSE	TRUE	FALSE	FALSE
4590	000108-99-6	3-Methylpyridine					FALSE	FALSE	FALSE	FALSE
4600	000109-06-8	2-Methylpyridine		29			FALSE	FALSE	TRUE	FALSE
4610	000109-43-3	Dibutyl sebacate		202			FALSE	FALSE	FALSE	FALSE
4620	000109-52-4	Pentanoic acid		96			FALSE	FALSE	FALSE	FALSE
4630	000109-65-9	1-Bromobutane		18			FALSE	FALSE	FALSE	FALSE
4640	000109-69-3	1-Chlorobutane		−28			FALSE	FALSE	FALSE	FALSE
4650	000109-74-0	Butyronitrile		29	1.65		FALSE	FALSE	FALSE	FALSE
4660	000109-78-4	Ethylene cyanohydrin					FALSE	FALSE	FALSE	FALSE
4670	000109-79-5	1-Butanethiol		3			FALSE	FALSE	FALSE	FALSE
4680	000109-87-5	Dimethoxymethane		−18	2.2	13.8	FALSE	FALSE	FALSE	FALSE
4690	000109-89-7	Diethylamine		−17	1.8	10.1	FALSE	FALSE	FALSE	FALSE
4700	000109-92-2	Ethyl vinyl ether					FALSE	FALSE	FALSE	TRUE
4710	000109-97-7	Pyrrole		39			FALSE	FALSE	FALSE	FALSE
4720	000110-01-0	Tetrahydrothiophene					FALSE	FALSE	FALSE	FALSE
4730	000110-02-1	Thiophene					FALSE	FALSE	FALSE	FALSE
4740	000110-19-0	*sec*-Butylacetate		18	1.3	10.5	FALSE	FALSE	FALSE	FALSE
4750	000110-53-2	1-Bromopentane		32			FALSE	FALSE	FALSE	FALSE
4760	000110-58-7	N-Pentylamine		7			FALSE	FALSE	FALSE	FALSE
4770	000110-59-8	Valeronitrile					FALSE	FALSE	FALSE	FALSE
4780	000110-61-2	Succinonitrile		132			FALSE	FALSE	FALSE	FALSE
4790	000110-63-4	1,4-Butanediol		121			FALSE	FALSE	FALSE	FALSE
4800	000110-71-4	Ethylene glycol dimethyl ether		−6			FALSE	FALSE	TRUE	FALSE
4810	000110-74-7	Propyl formate		−3			FALSE	FALSE	FALSE	FALSE
4820	000110-83-8	Cyclohexene		−11.6	1	5	FALSE	FALSE	FALSE	FALSE
4830	000110-86-1	Pyridine		20	1.83	12.4	FALSE	FALSE	TRUE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
4840	000110-89-4	Piperidine		3			FALSE	TRUE	FALSE	TRUE
4850	000110-91-8	Morpholine		37	1.4	11.2	FALSE	FALSE	FALSE	FALSE
4860	000111-13-7	2-Octanone					FALSE	FALSE	FALSE	FALSE
4870	000111-29-5	1,5-Pentanediol		129			FALSE	FALSE	FALSE	FALSE
4880	000111-34-2	Butyl vinyl ether		−1.1			FALSE	FALSE	FALSE	FALSE
4890	000111-40-0	Diethylenetriamine		98	2	6.7	FALSE	FALSE	FALSE	FALSE
4900	000111-43-3	Di(N-propyl) ether		−20.6			FALSE	FALSE	FALSE	FALSE
4910	000111-44-4	Bis(2-chloroethyl) ether		55	2.7		TRUE	TRUE	TRUE	FALSE
4920	000111-48-8	2,2′-Thiobisethanol		160			FALSE	FALSE	FALSE	FALSE
4930	000111-55-7	Ethylene glycol diacetate		96			FALSE	FALSE	FALSE	FALSE
4940	000111-65-9	Octane		13	1	6.5	FALSE	FALSE	FALSE	FALSE
4950	000111-66-0	1-Octene		21			FALSE	FALSE	FALSE	FALSE
4960	000111-84-2	n-Nonane		31	0.8	2.9	FALSE	FALSE	FALSE	FALSE
4970	000111-85-3	1-Chlorooctane					FALSE	FALSE	FALSE	FALSE
4980	000111-92-2	Dibutylamine		51	1.1		FALSE	FALSE	FALSE	FALSE
4990	000112-05-0	Nonanoic acid					FALSE	FALSE	FALSE	FALSE
5000	000112-29-8	1-Bromodecane					FALSE	FALSE	FALSE	FALSE
5010	000112-40-3	Dodecane		73			FALSE	FALSE	FALSE	FALSE
5020	000112-41-4	1-Dodecene		79			FALSE	FALSE	FALSE	FALSE
5030	000112-62-9	Methyl oleate					FALSE	FALSE	FALSE	FALSE
5040	000112-80-1	Oleic acid		189			FALSE	FALSE	FALSE	FALSE
5050	000115-10-6	Dimethyl ether		−41			FALSE	FALSE	FALSE	TRUE
5060	000115-21-9	Ethyltrichlorosilane		18			FALSE	TRUE	FALSE	FALSE
5070	000115-25-3	Perfluorocyclobutane					FALSE	FALSE	FALSE	FALSE
5080	000117-81-7	Bis(2-ethylhexyl)phthalate		171	0.3		TRUE	FALSE	TRUE	FALSE
5090	000119-36-8	Methyl salicylate		99			FALSE	FALSE	FALSE	FALSE
5100	000119-64-2	Tetralin		78			FALSE	FALSE	FALSE	FALSE
5110	000119-65-3	Isoquinoline					FALSE	FALSE	FALSE	FALSE
5120	000120-51-4	Benzyl benzoate		148			FALSE	FALSE	FALSE	FALSE
5130	000120-92-3	Cyclopentanone		26			FALSE	FALSE	FALSE	FALSE
5140	000121-69-7	N,N-Dimethylaniline		62			TRUE	FALSE	TRUE	FALSE
5150	000123-04-6	3-(Chloromethyl)heptane		58			FALSE	FALSE	FALSE	FALSE
5160	000123-38-6	Propionaldehyde		<−6			TRUE	FALSE	TRUE	FALSE
5170	000123-39-7	Methylformamide					FALSE	FALSE	FALSE	FALSE
5180	000123-51-3	Isopentanol		43	1.2	9.0	FALSE	FALSE	FALSE	FALSE
5190	000123-54-6	2,4-Pentanedione					FALSE	FALSE	FALSE	FALSE
5200	000123-62-6	Propionic anhydride		69			FALSE	FALSE	FALSE	FALSE
5210	000123-72-8	Butyraldehyde		−6.7			FALSE	FALSE	TRUE	FALSE
5220	000123-73-9	Trans-crotonaldehyde		13			FALSE	TRUE	FALSE	TRUE
5230	000123-75-1	Pyrrolidine		3			FALSE	FALSE	FALSE	FALSE
5240	000123-92-2	Isoamyl acetate		33	1	7.5	FALSE	FALSE	FALSE	FALSE
5250	000123-95-5	N-Butyl stearate		191			FALSE	FALSE	FALSE	FALSE
5260	000124-07-2	Octanoic acid					FALSE	FALSE	FALSE	FALSE
5270	000124-11-8	1-Nonene					FALSE	FALSE	FALSE	FALSE
5280	000124-12-9	Octanenitrile					FALSE	FALSE	FALSE	FALSE
5290	000124-18-5	n-Decane		46			FALSE	FALSE	FALSE	FALSE
5300	000124-68-5	2-Amino-2-methyl-1-propano		68			FALSE	FALSE	FALSE	FALSE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
5310	000126-73-8	Tributylphosphate		146			FALSE	FALSE	FALSE	FALSE
5320	000126-98-7	Methacrylonitrile		13	2	6.8	FALSE	TRUE	TRUE	TRUE
5330	000127-91-3	α-Pinene		38			FALSE	FALSE	FALSE	FALSE
5340	000135-98-8	*sec*-Butylbenzene		52			FALSE	FALSE	FALSE	FALSE
5350	000137-32-6	2-Methyl-1-butanol		46			FALSE	FALSE	FALSE	FALSE
5360	000140-11-4	Benzyl acetate		102			FALSE	FALSE	FALSE	FALSE
5370	000140-29-4	Phenylacetonitrile					FALSE	TRUE	FALSE	FALSE
5380	000140-88-5	Ethyl acrylate		9	1.4	14	TRUE	FALSE	TRUE	FALSE
5390	000141-05-9	Diethyl maleate		121			FALSE	FALSE	FALSE	FALSE
5400	000141-97-9	Acetoacetic ester		84			FALSE	FALSE	FALSE	FALSE
5410	000142-62-1	Hexanoic acid		102			FALSE	FALSE	FALSE	FALSE
5420	000142-68-7	Tetrahydropyran					FALSE	FALSE	FALSE	FALSE
5430	000142-77-8	Butyl oleate		180			FALSE	FALSE	FALSE	FALSE
5440	000142-84-7	Dipropylamine		17			FALSE	FALSE	FALSE	FALSE
5450	000151-56-4	Aziridine		−11			TRUE	TRUE	TRUE	TRUE
5460	000156-59-2	*cis*-1,2-Dichloroethene		4			FALSE	FALSE	FALSE	FALSE
5470	000156-60-5	*trans*-1,2-Dichloroethene		4			FALSE	FALSE	FALSE	FALSE
5480	000311-89-7	Heptacosafluorotributylamine					FALSE	FALSE	FALSE	FALSE
5490	000352-32-9	*p*-Fluorotoluene					FALSE	FALSE	FALSE	FALSE
5500	000352-70-5	*m*-Fluorotoluene					FALSE	FALSE	FALSE	FALSE
5510	000352-93-2	Diethylsulfide					FALSE	FALSE	FALSE	FALSE
5520	000355-25-9	Decafluorobutane					FALSE	FALSE	FALSE	FALSE
5530	000392-56-3	Hexafluorobenzene					FALSE	FALSE	FALSE	FALSE
5540	000420-46-2	1,1,1-Trifluoroethane					FALSE	FALSE	FALSE	FALSE
5550	000462-06-6	Fluorobenzene					FALSE	FALSE	FALSE	FALSE
5560	000463-82-1	2,2-Dimethylpropane		−65			FALSE	FALSE	FALSE	TRUE
5570	000464-49-3	(1R,4R)-(+)-Camphor					FALSE	FALSE	FALSE	FALSE
5580	000470-82-6	1,8-Cineole		48			FALSE	FALSE	FALSE	FALSE
5590	000493-01-6	*cis*-Bicyclo(4.4.0)decane					FALSE	FALSE	FALSE	FALSE
5600	000493-02-7	*trans*-Bicyclo(4.4.0)decane					FALSE	FALSE	FALSE	FALSE
5610	000503-74-2	Isovaleric acid					FALSE	FALSE	FALSE	FALSE
5620	000507-19-7	2-Bromo-2-methylpropane					FALSE	FALSE	FALSE	FALSE
5630	000512-56-1	Trimethyl phosphate		107			FALSE	FALSE	FALSE	FALSE
5640	000513-36-0	Isobutyl chloride					FALSE	FALSE	FALSE	FALSE
5650	000513-38-2	1-Iodo-2-methylpropane					FALSE	FALSE	FALSE	FALSE
5660	000513-85-9	2,3-Butanediol		85			FALSE	FALSE	FALSE	FALSE
5670	000538-93-2	Isobutylbenzene		60			FALSE	FALSE	FALSE	FALSE
5680	000539-30-0	Benzyl ethyl ether					FALSE	FALSE	FALSE	FALSE
5690	000540-84-1	2,2,4-Trimethylpentane		−12			TRUE	FALSE	FALSE	FALSE
5700	000541-73-1	3-Dichlorobenzene		72			FALSE	FALSE	TRUE	FALSE
5710	000542-54-1	4-Methylpentanitrile					FALSE	FALSE	FALSE	FALSE
5720	000542-55-2	Isobutyl formate					FALSE	FALSE	FALSE	FALSE
5730	000542-69-8	N-Butyl iodide					FALSE	FALSE	FALSE	FALSE
5740	000543-49-7	2-Heptanol					FALSE	FALSE	FALSE	FALSE
5750	000543-59-9	1-Chloropentane					FALSE	FALSE	FALSE	FALSE
5760	000544-01-4	Diisopentyl ether					FALSE	FALSE	FALSE	FALSE
5770	000544-40-1	5-Thianonane		76			FALSE	FALSE	FALSE	FALSE
5780	000554-14-3	2-Methylthiophene					FALSE	FALSE	FALSE	FALSE
5790	000564-02-3	2,2,3-Trimethylpentane					FALSE	FALSE	FALSE	FALSE

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
5800	000565-59-3	2,3-Dimethylpentane					FALSE	FALSE	FALSE	FALSE
5810	000565-80-0	2,4-Dimethyl-3-pentanone					FALSE	FALSE	FALSE	FALSE
5820	000573-98-8	1,2-Dimethylnaphthalene					FALSE	FALSE	FALSE	FALSE
5830	000575-43-9	1,6-Dimethylnaphthalene					FALSE	FALSE	FALSE	FALSE
5840	000576-26-1	2,6-Dimethylphenol					FALSE	FALSE	TRUE	FALSE
5850	000583-57-3	1,2-Dimethylcyclohexane		13			FALSE	FALSE	FALSE	FALSE
5860	000583-59-5	2-Methylcyclohexanol		58			FALSE	FALSE	FALSE	FALSE
5870	000584-02-1	3-Pentanol		34	1.2	9.0	FALSE	FALSE	FALSE	FALSE
5880	000589-34-4	3-Methylhexane		–4			FALSE	FALSE	FALSE	FALSE
5890	000589-82-2	3-Pentanol		60			FALSE	FALSE	FALSE	FALSE
5900	000590-36-3	2-Methyl-2-pentanol		21			FALSE	FALSE	FALSE	FALSE
5910	000590-67-0	1-Methylcyclohexanol		67			FALSE	FALSE	FALSE	FALSE
5920	000591-23-1	3-Methylcyclohexanol		62			FALSE	FALSE	FALSE	FALSE
5930	000591-50-4	Iodobenzene		74			FALSE	FALSE	FALSE	FALSE
5940	000591-76-4	2-Methylhexane		–3	1	6	FALSE	FALSE	FALSE	FALSE
5950	000591-87-7	Allyl acetate		6			FALSE	FALSE	FALSE	FALSE
5960	000592-41-6	1-Hexene		–26			FALSE	FALSE	FALSE	FALSE
5970	000592-76-7	1-Heptene					FALSE	FALSE	FALSE	FALSE
5980	000592-84-7	N-Butylformate		76			FALSE	FALSE	FALSE	FALSE
5990	000593-60-2	Bromoethene					TRUE	FALSE	TRUE	FALSE
6000	000594-82-1	2,2,3,3-Tetramethylbutane		0			FALSE	FALSE	FALSE	FALSE
6010	000598-75-4	3-Methyl-2-butanol		38			FALSE	FALSE	FALSE	FALSE
6020	000616-44-4	3-Methylthiophene		11			FALSE	FALSE	FALSE	FALSE
6030	000616-45-5	2-Pyrrolidinone		129			FALSE	FALSE	FALSE	FALSE
6040	000624-48-6	Methyl maleate		113			FALSE	FALSE	FALSE	FALSE
6050	000624-92-0	Dimethyldisulfide		24			FALSE	FALSE	FALSE	FALSE
6060	000627-20-3	*cis*-2-Pentene		–45			FALSE	FALSE	FALSE	TRUE
6070	000628-73-9	Hexanenitrile					FALSE	FALSE	FALSE	FALSE
6080	000628-81-9	Butyl ethyl ether		–5			FALSE	FALSE	FALSE	FALSE
6090	000629-50-5	n-Tridecane		79			FALSE	FALSE	FALSE	FALSE
6100	000631-36-7	Tetraethylsilane		26			FALSE	FALSE	FALSE	FALSE
6110	000632-22-4	Tetramethylurea		76			FALSE	FALSE	FALSE	FALSE
6120	000646-04-8	*trans*-2-Pentene		–18			FALSE	FALSE	FALSE	TRUE
6130	000646-06-0	1,3-Dioxolane		1			FALSE	FALSE	FALSE	FALSE
6140	000659-70-1	Isoamyl isovalerate					FALSE	FALSE	FALSE	FALSE
6150	000680-31-9	Hexamethylphosphoramide		105.5			TRUE	FALSE	TRUE	FALSE
6160	000688-74-4	*n*-Butyl borate		77			FALSE	FALSE	FALSE	FALSE
6170	000821-11-4	*trans*-2-Butene-1,4-diol					FALSE	FALSE	FALSE	FALSE
6180	000827-52-1	Phenyl cyclohexane		99			FALSE	FALSE	FALSE	FALSE
6190	000872-05-9	1-Decene		47			FALSE	FALSE	FALSE	FALSE
6200	001187-58-2	N-Methyl propionamide		102			FALSE	FALSE	FALSE	FALSE
6210	001330-78-5	Tricresyl phosphate		410			FALSE	FALSE	FALSE	FALSE
6220	001678-91-7	Ethyl cyclohexane		18	0.95	6.60	FALSE	FALSE	FALSE	FALSE
6230	001814-88-6	1,1,1,2,2-Pentafluoropropane					FALSE	FALSE	FALSE	FALSE
6240	002207-01-4	*cis*-1,2-Dimethylcyclohexane					FALSE	FALSE	FALSE	FALSE
6250	002315-68-6	Propyl benzoate					FALSE	FALSE	FALSE	FALSE
6260	002437-56-1	1-Tridecene		79			FALSE	FALSE	FALSE	FALSE
6270	003522-94-9	2,2,5-Trimethylhexane		13			FALSE	FALSE	FALSE	FALSE

(*Continued*)

Table A4. Continued.

Ref No.	CAS	Name	ODP	Flash pt	LEL	UEL	HAPS	EPCRA 302	EPCRA 313	CAA 112
6280	003724-65-0	Crotonic acid		88			FALSE	FALSE	FALSE	FALSE
6290	003744-02-3	Isomesityl oxide					FALSE	FALSE	FALSE	FALSE
6300	004088-60-2	*cis*-2-Buten-1-ol					FALSE	FALSE	FALSE	FALSE
6310	005341-95-7	*Meso*-2,3-Butanediol					FALSE	FALSE	FALSE	FALSE
6320	005454-79-5	Cis-3-Methylcyclohexanol					FALSE	FALSE	FALSE	FALSE
6330	005989-54-8	(-)-1-Methyl-4-(1-methylethene)		48	0.7	6.1	FALSE	FALSE	FALSE	FALSE
6340	006032-29-7	2-Pentanol		35			FALSE	FALSE	FALSE	FALSE
6350	006117-80-2	*Cis*-2-Butene-1,4-diol		165			FALSE	FALSE	FALSE	FALSE
6360	006876-23-9	*trans*-1,2-Dimethylcyclohexane		11			FALSE	FALSE	FALSE	FALSE
6370	006982-25-8	dl-2,3-Butandiol					FALSE	FALSE	FALSE	FALSE
6380	007443-52-9	*trans*-2-Methylcyclohexanol		68			FALSE	FALSE	FALSE	FALSE
6390	007443-55-2	*trans*-3-Methylcyclohexanol					FALSE	FALSE	FALSE	FALSE
6400	007443-70-1	*cis*-2-Methylcyclohexanol					FALSE	FALSE	FALSE	FALSE
6410	007642-04-8	*cis*-2-Octene					FALSE	FALSE	FALSE	FALSE
6420	007705-14-8	(+−)Dipentene		49			FALSE	FALSE	FALSE	FALSE
6430	007731-28-4	*cis* 4-Methylcyclohexanol					FALSE	FALSE	FALSE	FALSE
6440	007731-29-5	*trans*-4-Methylcyclohexanol					FALSE	FALSE	FALSE	FALSE
6450	007785-537	d-α-Terpineol					FALSE	FALSE	FALSE	FALSE
6460	013389-42-9	*trans*-2-Octene					FALSE	FALSE	FALSE	FALSE
6470	013952-84-6	*sec*-Butylamine		−29			FALSE	FALSE	FALSE	FALSE
6480	019132-06-0	d-2,3-Butanediol					FALSE	FALSE	FALSE	FALSE
6490	024347-58-8	1-2,3-Butanediol					FALSE	FALSE	FALSE	FALSE

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