From plastics to pharmaceuticals to dry cleaning, many of life’s comforts would be impossible without the chemical industry. Few people choose to live without the benefits of modern chemistry, but often the benefits are associated with other fields, such as medicine, materials, or engineering. Chemistry is more often associated in the public mind with pollution—from dioxins in waste incinerators to accidents in chemical factories, the biggest news about chemistry seems always to be bad. Even at school and the university, it is mainly considered difficult, leading to ever-decreasing numbers of students choosing to major in chemistry in many industrialized countries.

Can chemistry improve its image by improving its environmental credentials? Many chemical industry processes have been or still are highly polluting; for example, by emitting persistent pollutants that could interfere with the hormonal messenger system in aquatic animals and in humans. Organic solvents are particularly problematic, because many are toxic and are not broken down easily in the environment. Waste is another major issue. Vast quantities of plastic packaging end up in landfills, contributing to the waste mountains that plague modern society.

Over recent decades, the chemical industry has been increasingly regulated in order to reduce harmful emissions and effluents and ensure worker safety. The industry has learned that it is often best to cooperate with environmental legislators. Now scientists are calling for an integrated approach that goes beyond regulation of individual chemicals. Green chemistry focuses instead on making whole chemical processes less wasteful and damaging to the environment.

Any such effort must involve academia, as well as industry, if conventional thinking is to overcome. Three Viewpoints in this issue detail recent progress toward “greening” chemical processes, with a particular emphasis on industrial-scale applications. First successes are likely to come from the fine-chemical sector, especially the pharmaceutical industry, which deals with smaller quantities and is generally more flexible than the commodity-chemicals sector (Poliakoff et al., p. 807). The latter has larger investments in standing plants.

Carbon dioxide is emerging as a powerful alternative to conventional solvents, combining versatility and ease of separation with environmental compatibility (DeSimone, p. 799). Other candidates include ionic solvents, which have recently been shown to be good candidates for use as electrolytes in polymer electrochemical devices. New solvent-free syntheses have also been reported. The future success of these approaches will hinge not only on their environmental credentials but also on whether they have advantages related to performance, health, and cost.

Conventional plastics build on petrochemical feedstocks and therefore rely on fossil carbon resources. Biodegradable plastics and water-soluble polymers increasingly use annually renewable resources, such as corn. Some of these products can now compete with traditional fibers and packaging materials in terms of both cost and performance. However, without an appropriate infrastructure to collect and dispose of these new, greener plastics, they will end up in dry landfills where they cannot biodegrade (Gross and Kalra, p. 803). In contrast, biodegradable water-soluble polymers are degraded rapidly in existing wastewater treatment facilities.

At present, only a small fraction of industrial production is based on green processes. As the world population continues to increase and living standards in developing countries improve, the need for sustainable use of resources and for environmentally safe processes and products will become more urgent. Only just at its beginning, green chemistry faces an uphill struggle but is claiming its first victories. The Viewpoints in this issue provide a snapshot of some of the key areas in this process.

—JULIA FAHRENKAMP-UPPENBRINK

Practical Approaches to Green Solvents

Joseph M. DeSimone

Solvents are widely used in commercial manufacturing and service industries. Despite abundant precaution, they inevitably contaminate our air, land, and water because they are difficult to contain and recycle. Researchers have therefore focused on reducing solvent use through the development of solvent-free processes and more efficient recycling protocols. However, these approaches have their limitations, necessitating a pollution prevention approach and the search for environmentally benign solvent alternatives. This report highlights opportunities for the practical implementation of such green solvents.

Solvents, and dissolution in general, have been integral to many industries for hundreds of years. In the 1400s, alchemists had already focused on solvents and the dissolution process as they searched for “menstruum universal,” the universal solvent that possessed the powers to remove all seeds of disease from the human body (1). Today, almost all manufacturing and processing industries—automotive, electronics, pulp and paper, chemical, mining, food, cleaning—depend on the extensive use of solvents or water. To satisfy this dependency, almost 15 billion kilograms of organic and halogenated solvents are produced worldwide each year (2). The solvents are used as process aids, cleaning agents, and dispersants. They inevitably end up leaching into our ecosystems. An even larger amount of water is used and contaminated in related processes.

For example, the textile industry may require almost 100 liters of water to dye a kilogram of fiber (3). The aqueous extract from such dyeing processes must be treated, but most local municipalities’ regulations in the United States allow it to be returned to its natural source (often a local stream or river) in a contaminated condition. Furthermore, many fiber materials, such as cotton, polyamides (nylon), and polyesters, absorb large amounts of water. Because the heat of vaporization of water is high, a large amount of energy is needed to dry the dyed fibers. Indeed, water-based processes are usually very energy intensive.

The dry cleaning industry is also highly dependent on solvents (4, 5). Most dry cleaners—approximately 100,000 worldwide—use perchloroethylene (perc) as the primary processing solvent. Numerous studies have shown perc to be highly toxic, affecting plant workers and consumers who use dry cleaners; landlords and financial institutions who hold title to contaminated land; and people whose homes are in close proximity to dry cleaning establishments. Everything perc comes in contact with in a dry cleaning plant must be handled as “hazardous waste,” except for the dry-cleaned clothes we wear.

Water and solvent usage is also required for the precise fabrication of device elements for state-of-the-art microprocessors (6, 7). A typical microelectronics fabrication facility processing 5,000 wafers per day will generate almost 5 million liters of organic and aqueous solvent waste per year. For example, chemical mechanical planarization (CMP), an increasingly important operation in such facilities, uses ultra-purified water and supported silica slurries to polish wafer levels for improved manufacturability. A standard CMP tool will use 40,000 liters of ultra-pure water per day.

Even the food industry is not exempt from solvent usage and emissions (8). Hexane is used to extract most of the 8 million tons of oil isolated per year from soybean seeds and for the isolation of millions of tons of oil from other seeds and grain commodities in the United States. The U.S. Environmental Protection Agency (EPA) categorizes hexane as a HAP (hazardous air pollutant). Yet according to EPA Toxic Release Inventory (TRI) statistics, more than 20 million kg of hexane are released to the atmosphere because it is used in the solvent extraction of vegetable oils.

Since the 1960s, a number of events have raised international concern about the release of toxins into the environment. Publication of Silent Spring by Rachael Carson in 1962 led to a public outcry to regulate pesticides (9). Health concerns were linked to contamination at the Love Canal in Niagara Falls, NY. The Cuyahoga River in Ohio was so polluted that it caught fire (10). Laws in the United States attempting to tackle these problems initially focused on treatment of wastes before their release or neutralization of the waste subsequent to their release. The U.S. Pollution Prevention Act in 1990 refocused national environmental policy on preventing the formation of waste at the source. An initiative focused on pollution prevention by researchers in the chemical industry, often referred to as “green chemistry,” grew out of these legislative efforts (11).

As a result of the above changes in the law and because of the growing public sentiment in support of our environment, there has been a significant focus for industry to reduce or eliminate the use of water and organic solvents during manufacturing and processing. Approaches to mitigate the release of solvents and contaminated water into our ecosystem include reduction and/or recycling; switching to “solvent-free” processes that are not dependent on the use of solvents or processes that do not generate contaminated water; and conversion of processes that use organic solvents and water to “solvent alternatives.”

Reduction and/or Recycling

Many of the industries mentioned above have made remarkable progress in implementing “closed-loop systems” that reduce solvent and/or water use and improve their ability to recycle. Industries throughout the world have been quite effective in reducing their emissions of solvents through such process improvements. This activity has been popularized by corporate stewardship programs like 3M’s “3P” program, whose premise suggests that solvent reduction and recycling is not only important for the environment, but that such “Pollution Prevention Pays” (12).

Switching to Solvent-Free Processes

Several industries have eliminated solvents from key process steps. Examples include the elimination of organic solvents and other volatile organic compounds from many paints and coatings, resulting in dry, solvent-free powder coatings (13) and 100% solid ultraviolet curable coatings (14). The use of water in emissive applications like coatings is a preferable alternative to organics. (In contrast, water used in non emissive applications, for example, as a reaction medium in chemical transformations or as a dying medium for textile fibers, inevitably gets contaminat ed and is hard to clean up without substantial costs.) Polycarbonate producers increasingly use a solvent-free, melt-phase polymerization technology (15), based on diphenylcarbonate and bisphenol-A, instead of the traditional interfacial route, based on phosgene and bisphenol-A carried out in methylene chloride and water. Many other solvent-free processes are sure to emerge as scientists and engineers

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respond to customer demands for “dry” processes. Indeed, recent research efforts have succeeded in achieving important chemical transformations using solvent-free processes including for efficient catalytic entioselective syntheses of unsaturated amines (16) and for Wittig reactions (17).

**Solvent Alternatives**

Despite such advances, many processes have been shown to require process “liquids” of some kind. This is especially true for industries that are dependent on operations involving coatings, separations, or reactions. In such situations, some solvents are preferable to others. For example, homogeneous solvent-based coatings may be replaced with water-based heterogeneous emulsions, or chlorinated organic solvents with hydrocarbon-based solvents. Water may be used instead of organic solvents for conducting chemical reactions (18, 19), toluene instead of benzene (20), cyclic siloxanes instead of tetrachloroethylene (21), or biodegradable esters instead of nonbiodegradable solvents (22). Over the last 15 years, additional, less conventional solvent alternatives have attracted much attention from academia and industry. They include supercritical water (23, 24), ionic liquids (25–27), fluororous phases (28–30) and carbon dioxide (31–35).

**Supercritical water.** Water exists in the supercritical state at temperatures above 374°C and pressures above 221 bar. Supercritical water behaves as a nonpolar solvent primarily because hydrogen bonding is lost under these extreme conditions. The dielectric constant of water decreases from 80 at ambient conditions to <5 above the critical point. Salts are not soluble in supercritical water, whereas nonpolar organics are completely soluble, as is O2, and can be rapidly and efficiently oxidized to CO2 and H2O. Supercritical water oxidation (SCWO) was first developed in the 1970s for the destruction of organic waste (36). Oxidation reactions in supercritical water have been extensively studied, especially for chemical demilitarization and the disposal of organic waste such as nerve agents and mustand gas. However, the design of a suitable reactor poses significant challenges. Under the extreme conditions required, trace amounts of halogens lead to extensive corrosion of most reactor materials. Despite extensive research efforts, corrosion problems have not been satisfactorily solved. SCWO has not been successfully commercialized and will probably never become a practical solvent alternative.

**Ionic liquids.** Ionic liquids have recently received increasing attention as an environmentally preferable solvent alternative, because they have very low vapor pressures and may be used to replace volatile organic solvents. Several authors have shown (37–39) that chloroaluminate compounds such as 1-butylpyridinium chloride/aluminum(III) chloride mixtures can exist as liquids at room temperature. Such ionic liquids are being considered as solvents for a wide range of separations and as reaction media for processes including catalysis. The author is not aware of a successful commercialization of ionic liquids as a reaction or separation medium. However, a collaboration between academia and industry, QUILL, is actively pursuing the discovery and development of ionic liquids for such applications. The researchers associated with QUILL have shown that a variety of ionic liquids are good solvents for a wide range of inorganic, organic, and polymeric molecules. Moreover, a number of organic reactions have been shown to be compatible with these designer solvents, including cationic polymerizations, electrophilic alkylations and acylations, and pericyclic reactions. Despite this progress on the scientific pursuit of reactions in ionic fluids, there is public skepticism (40) as to their characterization as preferable solvents for reasons of environmental stewardship, simply because of their low volatility.

**Fluorous phases.** Solvent extraction is widely used in organic chemistry to separate substances from mixtures, to isolate dissolved compounds from solutions, and to remove soluble impurities from mixtures. Solvents commonly used for this purpose include diethyl ether, methylene chloride, chloroform, acetone, and water. This process is usually accomplished by exploiting the immiscibility of two liquid phases, usually one aqueous and the other organic. Highly fluorinated (fluorous) compounds are referred to as the “third liquid phase,” because organics, water, and fluorous compounds are mutually immiscible (Fig. 1). This property is often a strong function of temperature, presenting an important new opportunity for separations and for solution-phase organic synthesis (41–43). Because of their ability to be used in an integrated way that allows for product isolation, analogies can be drawn between fluorous-phase synthesis and solid-
phase synthesis with supports such as polymer resins. Solid-phase synthesis has been extensively adopted for automated synthesis and combinatorial chemistry and has revolutionized chemical synthesis while reducing the need for large amounts of solvents, especially for the separation of compounds. Fluorous phases may achieve similarly widespread adaptation and enjoy increased utility, especially with the burgeoning commercial interests from companies such as Fluorous Technologies, Inc.

**Carbon dioxide.** Carbon dioxide (CO$_2$) is an attractive solvent alternative for a variety of chemical and industrial processes, especially because it is plentiful and inexpensive, and has properties that are between those of many liquids and gases. At room temperature and above its vapor pressure, CO$_2$ exists as a liquid with a density comparable to organic solvents but with excellent wetting properties and a very low viscosity. Above its critical temperature and pressure ($31^\circ$C and $73.8$ bar), CO$_2$ is in the supercritical state and has gas-like viscosities and liquid-like densities. Small changes in temperature or pressure cause dramatic changes in the density (Fig. 2), viscosity, and dielectric properties of supercritical CO$_2$, making it an unusually tunable, versatile, and selective solvent.

Processes that use CO$_2$ do not contribute directly to the greenhouse effect associated with global warming. Most CO$_2$ sold today is isolated as a by-product from primary sources, such as from the production of ethanol, ammonia, and hydrogen (44). Because of the low heat of vaporization of CO$_2$, energy costs can be substantially reduced relative to water-intensive processes, which often demand large amounts of energy associated with drying operations.

The potential of CO$_2$ as an environmentally preferable solvent is now being realized in several areas, including separation processes in the food industry, coatings in the automotive and furniture industries, polymer production and processing, and cleaning processes for the garment care (that is, dry cleaning) and microelectronics industries. For example, supercritical CO$_2$, instead of chlorinated organic solvents, is used extensively to decaffeinate coffee beans and tea (45). Union Carbide has pioneered its use as a diluent for coating processes, dramatically lowering the amount of volatile organic compounds needed in coating operations (46). DuPont has commercialized the manufacturing of certain grades of polymers based on tetrafluoroethylene (Teflon), using CO$_2$ as the solvent instead of 1,1,2-trichloro-1,2,2-trifluoroethane or water (47–49). Micell Technologies and Global Technologies have commercialized liquid CO$_2$ dry-cleaning processes that eliminate the use of perc (50). Micell Technologies has extended their process knowledge to include precision cleaning unit operations for the manufacture of integrated circuits (Fig. 3), eliminating the need for organic solvents and water (51).

Beyond simple extensions of CO$_2$ usage into additional areas, it is expected that the unique physical properties of CO$_2$ will be exploited in entirely new ways. Nowhere is this potential more exciting than in the microelectronics and biomedical industries.

Several challenges facing the electronics industry as it reduces feature sizes to the nanometer-length scale, may be overcome with CO$_2$-based processes. For example, “image collapse” is a significant problem as feature sizes on integrated circuits approach 100 nm (52). Structures derived from organic polymers with feature sizes on the order of 150 to 50 nm and aspect ratios of 3 or greater do not have the mechanical integrity to withstand the powerful and destructive forces associated with high surface tension liquids, especially water. Carbon dioxide, with its excellent wetting properties in both the liquid and supercritical states, can be used to eliminate image collapse (Fig. 4) (53).

Precision coating may also exploit the exceedingly low surface tension and low viscosity of liquid CO$_2$. Through the precise...
control of the evaporation rates of liquid CO₂ in a novel spin-coating tool, one can generate extremely uniform, thin films of photoresists on silicon wafers (Fig. 5) (54). Processes based on CO₂ are essentially “dry” processes despite the fact that, under certain conditions, gaseous CO₂ can be condensed into use as a process liquid. The extensive use of such dry processes could eliminate the need to shuttle wafers between benches for wet processes and closed-loop dry process tools. Because totally dry processes can utilize massively interfaced manufacturing tools, the replacement of water and organic solvents with CO₂ in the microelectronics industry may dramatically reduce the need for expensive, state-of-the-art clean room facilities.

In the biomedical arena, many opportunities for CO₂-based processes are emerging. Researchers at the University of Nottingham are using CO₂ to facilitate the impregnation and modification of biocompatible polymers to improve the wear properties of implants and to provide scaffolds for tissue engineering (55). Cooper and co-workers (56) have pioneered the use of high internal-phase supercritical fluid emulsions for the preparation of well-defined porous materials that have the potential to be widely used for the manufacture of controlled release devices and biological tissue scaffolds. Other researchers (57, 58) are pioneering the use of CO₂ to facilitate the production and delivery of pharmacologically active materials. In particular, Johnston and colleagues (58) have developed a process for precipitating solutes dissolved in an organic solvent by using carbon dioxide as an antisolvent. Not only is there a significant environmental advantage for using CO₂, but this process offers a means of tuning the particle size and shape of the products to generate nano- or micrometer-scale sphere and fibrils.

Carbon dioxide is also used as a solvent in catalysis (59–62). The most advanced project of this kind, at the Thomas Swan plant in the United Kingdom, uses supercritical CO₂ in the synthesis of trimethylcyclohexanone, a derivative of acetone used in styrene products (63). The plant has also been used to hydrogenate alkenes, aldehydes, nitro compounds, ketones and oximes. Reaction rates with heterogeneous catalysts were enhanced in the high-diffusivity and low-viscosity supercritical environment, and selectivity was increased. They and others (64) have shown the benefits of carrying out reactions in supercritical fluids in continuous flow reactors instead of conventional batch equipment. Continuous processes offer significant advantages over simple batch process, including allowing one to run the reactor at steady state, enabling the feed to assume a uniform composition throughout the reactor by which a uniform reaction product is achieved, and obtaining great temperature control.

Conclusion and Outlook

Environmental advantages alone probably will not enable alternative solvents to achieve widespread applicability. The continued commercialization of pollution prevention technologies must include not only environmental or “green” advantages, but also advantages related to performance, health, and cost. The cost of ownership associated with the continued use of water and organic solvents is no longer a minor issue. Finding an appropriate solvent that is environmentally preferable can be a challenge, as the design criteria need to converge to include solubility issues, inertness to the relevant chemistries, cost, safety of handling, and environmental preferable. Solvent recycling and solvent-free processes, where appropriate, will continue to gain market share. As for the implementation of solvent alternatives, industry will increasingly choose solvents on the basis of environmental demands in the future. However, the full potential of alternative solvents will only be reached if researchers exploit the advantageous properties of such alternatives beyond their intrinsic environmental advantages. Carbon dioxide has made particular inroads as a solvent alternative because of its transient “dry” nature, which enables it to transform from a liquid to a gas, its excellent wetting characteristics, its low viscosity, and its tunable nature, especially in the supercritical state. Time will tell if carbon dioxide and the other solvent alternatives will achieve widespread utilization.

References and Notes

7. National Technology Roadmap for Semiconductors (NTRS) (Semiconductor Industry Association (SIA), San Jose, CA, 1999).

Fig. 5. A silicon wafer coated with a 193-nm photoresist system using a liquid CO₂ spin coating tool operating at slightly below room temperature. [Provided by the NSF Science and Technology Center for Environmentally Responsible Solvents and Processes: (67)]
Biodegradable Polymers for the Environment
Richard A. Gross and Bhanu Kalra

Biodegradable polymers are designed to degrade upon disposal by the action of living organisms. Extraordinary progress has been made in the development of practical processes and products from polymers such as starch, cellulose, and lactic acid. The need to create alternative biodegradable water-soluble polymers for down-the-drain products such as detergents and cosmetics has taken on increasing importance. Consumers have, however, thus far attached little or no added value to the property of biodegradability, forcing industry to compete head-to-head on a cost-performance basis with existing familiar products. In addition, no suitable infrastructure for the disposal of biodegradable materials exists as yet.

Conventional polymers such as polyethylene and polypropylene persist for many years after disposal. Built for the long haul, these polymers seem inappropriate for applications in which plastics are used for short time periods and then disposed. Furthermore, plastics are often soiled by food and other biological substances, making physical recycling of these materials impractical and generally undesirable. In contrast, biodegradable polymers (BPs) disposed in bioactive environments degrade by the enzymatic action of microorganisms such as bacteria, fungi, and algae. Their polymer chains may also be broken down by nonenzymatic processes such as chemical hydrolysis. BPs are often derived from plant processing of atmospheric CO₂. Biodegradation converts them to CO₂, CH₄, water, biomass, humic matter, and other natural substances. BPs are thus naturally recycled by biological processes (Fig. 1).

The worldwide consumption of biodegradable polymers has increased from 14 million kg in 1996 to an estimated 68 million kg in 2001. Target markets for BPs include packaging materials (trash bags, wrappings, loose-fill foam, food containers, film wrapping, laminated paper), disposable nonwovens (engineered fabrics) and hygiene products (diaper back sheets, cotton swabs), consumer goods (fast-food tableware, containers, egg cartons, razor handles, toys), and agricultural tools (mulch films, planters). BP commercialization is, however, hampered by competition with commodity plastics that are inexpensive and familiar to the customer. Also, an infrastructure for the disposal of BPs in bioactive environments must be developed and will require capital investments. Without an extensive network of efficient composting and other bioconversion facilities that, in addition to compost, yield other valuable chemical intermediates, BPs and other biodispersables (food, yard-waste, nonrecycled paper) are destined to be entombed in dry landfill environments designed to retard biodegradation.

In this Viewpoint we report on progress, technical and social challenges, and environmental benefits of BPs. We describe what we view as highly promising biodegradable polymers that are either in development or already marketed (Fig. 2). For comprehensive reviews that include more detailed descriptions on research on biodegradable polymers for environmental applications, see (1–3).

Biodegradable Plastics from Starch and Cellulose
Starch is an inexpensive, annually renewable material derived from corn and other crops. The biodegradation of starch products recycles atmospheric CO₂ trapped by starch-producing plants. All starches contain amylose and amylopectin, at ratios that vary with the starch source. This variation provides a natural mechanism for regulating starch material properties.

Starch-based BPs can be produced by blending or mixing them with synthetic polymers. By varying the synthetic blend component and its miscibility with starch, the morphology and hence the properties can be regulated easily and efficiently. This approach has been successfully implemented by Novamont under the Mater-Bi trademark (Tables 1 and 2) (4). Blends containing thermoplastic starch (destructurized starch that is noncrystalline, produced by the application of heat and work) may be blended or grafted with biodegradable polyesters [such as polycaprolactone (PCL)] to increase flexibility and resistance to moisture. These materials are mainly formed into films and sheets. Blends with more than 85% starch are used for foaming and injection molding. The foams can be used as loose-fill in place of polystyrene; the starch-based loose fills have an average density of 6 to 8 kg/m³, compared with 4 kg/m³ for expanded polystyrene loose fill (5). Loose-fill materials from starch are
generally water sensitive. This is a problem if the packaging material is exposed to water, but an advantage when down-the-drain disposal is desired. By mixing thermoplastic starch with cellulose derivatives, rigid and dimensionally stable injection-molded articles result.

Chemically modified plant cellulose is used in a remarkably diverse set of applications. For example, cellulose acetate is used in many common applications, including toothbrush handles and adhesive tape backing. Until the mid-1990s, plastic-grade cellulose acetates were believed to be nonbiodegradable because of their high degree of modification (or substitution). Between two and three of the glucose repeat unit hydroxyl groups are normally acetylated. However, studies in simulated compost environments revealed that cellulose acetates with degrees of substitution of up to 2.5 are biodegradable (6). A decrease in the degree of substitution of cellulose acetate from 2.5 to 1.7 results in a large increase in the rate of their biodegradation. Eastman Chemical Company has developed fully biodegradable cellulose acetates that are promising but not yet commercially available (7, 8).

Biodegradable Plastics from Polymesters

As early as 1973, it was shown that the polyester poly[ε-caprolactone] degrades when disposed in bioactive environments such as soil (9–11). This and related polyesters are water resistant and may be melt-extruded into sheets, bottles, and various shaped articles, making these plastics as primary targets for use as BPs. Several biodegradable polyesters are now in the market or at an advanced stage of development.

Polyhydroxyalkanoates (PHAs) are produced directly from renewable resources by microbes. They can be accumulated to high levels in bacteria (~95% of the cellular dry weight), and their structures can be manipulated by genetic or physiological strategies (12, 13). The physical properties and biodegradability of PHAs can be regulated by blending with synthetic or natural polymers. The widespread synthesis of PHAs by microbes is matched by a corresponding abundance of microbes that produce PHA-degrading enzymes. PHAs with short side chains behave similarly to polypropylene, whereas PHAs with longer side chains are elastomeric.

In the late 1980s, ICI Zeneca commercialized PHAs produced by microbial fermentation under the trade name Biopol. Wella AG used the polymer to make shampoo bottles. Biopol was expensive (Table 2), but customers accepted the price as part of an all-natural high-end cosmetic product. Such consumer behavior is unusual; in most cases, consumers are not willing to pay more for a product that is natural and/or biodegradable.

In 1994, Sommerville and co-workers developed genetically altered plants that contained the necessary metabolic pathway to accumulate PHAs (14). In an attempt to bring this technology to market, Monsanto spliced the plastic-producing gene sequence into canola plants. They created a plant that was not only 14% plastic, but also could be used to produce canola oil. However, Monsanto believed that PHA-producing plants would not be commercially viable unless 20% or more of the plant was plastic. In 1998, the company abandoned further development of PHAs.

Metabolix (Cambridge, MA) continues to pursue the commercialization of PHAs both in plant crops and by fermentation processes (15). Recent efforts to express the copolymer in Escherichia coli also hold promise for reducing production cost and simplifying purification.

Poly(lactic acid) (PLA). The manufacture of polyester from lactic acid was pioneered by Carothers in 1932 (16) and further developed by Dupont (17) and Ethicon. Prohibitive production costs restricted the applicability of these...
polymers outside the medical field until the late 1980s. Since then, major breakthroughs in process technology, coupled with decreased costs of biologically produced lactic acid, have led to the commercial-scale production of BPs from lactic acid for nonmedical applications. This integration of biotechnology and chemistry is an important strategy that will be critical to improvements in many other chemical processes in future years.

Two chemical routes have been developed to convert lactic acid to high molecular weight PLA. Cargill Dow LLC uses a solvent-free continuous process and a novel distillation method (18). In contrast, Mitsui Toats (18) converts lactic acid directly to high molecular weight PLA by a solvent-based process with the azetropic (where vapor and liquid have the same composition at some point in distillation) removal of water by distillation. Lactic acid also has no polymer applications, including the conversion of lactic acid to its ethyl ester (ethyl lactate) for use as a naturally derived solvent. As new markets for lactic acid become available, the cost of PLA will decrease further (18).

PLA crystallinity, crystallization rate, transparency, and degradation rate of finished products are conveniently controlled by the copolymerization of selected L- to D-isomer ratios of lactide or lactic acid. Upon disposal, PLA degrades primarily by hydrolysis, not microbial attack. Hence, even at high humidity, it is uncommon to encounter contamination of high molecular weight PLA by fungi, mold, or other microbes. This unusual characteristic of a BP is attractive for applications in which they are in direct contact with foods for extended time periods. PLA can be converted into compost in municipal compost facilities. It can be thermally processed with minimal changes to standard machinery.

PLA is currently used in packaging (film, thermoformed containers, and short–shelf-life bottles). Cargill Dow LLC uses conventional melt-spinning processes to form fibers for clothing and other uses (19). Fabrics produced from PLA provide a silky feel, durability, and moisture-management properties (moisture is quickly wicked away from the body, keeping the wearer dry and comfortable).

Poly(ε-caprolactone), PCL, and poly(alkylene succinate)s. PCL is a thermoplastic biodegradable polyester synthesized by chemical conversion of crude oil, followed by ring-opening polymerization. PCL has good water, oil, solvent, and chlorine resistance, a low melting point, and low viscosity, and is easily processed thermally. To reduce manufacturing costs, PCL may be blended with starch—for example, to make trash bags. By blending PCL with fiber-forming polymers (such as cellulose), hydroentangled nonwovens (in which bonding of a fiber web into a sheet is accomplished by entangling the fibers by water jets), scrub-suits, incontinence products, and bandage holders have been produced (19). The rate of hydrolysis and biodegradation of PCL depends on its molecular weight and degree of crystallinity. However, many microbes in nature produce enzymes capable of complete PCL biodegradation.

In contrast to PLA, PCL from lactide, and PHAs, a series of biodegradable aliphatic polyesters have been developed on the basis of traditional polycondensation reactions. Most notable are the poly(alkylene succinate)s manufactured by Showa Denko, trademarked Bionolle. Undoubtedly, their development was inspired by the lessons learned in working with PCL. These polyesters have properties that mimic those of traditional plastics such as low-density poly(ethylene) (LDPE). Their physical properties and biodegradation kinetics depend on the choice and composition of the diol/diacid building blocks. Current uses of Bionolle are in fibers, films, bottles, and cutlery. Bionolle plastics have been found to biodegrade in compost, moist soil, fresh water, activated sludge, and sea water.

Increasing the strength of biodegradable polyesters. The strength of aliphatic polymers may be increased by substituting a fraction of the ester links by amide groups, which increase interchain hydrogen bonding and, therefore, material strength. Bayer has introduced an injection-moldable grade of poly(ester amide), BAK 2195, built from hexamethylene diamine, adipic acid, butanediol, and diethylene glycol (20). The company recently withdrew from the production and sale of this product (21). The strength of polyester BPs can also be increased by substituting some aliphatic diacid building blocks with more rigid aromatic dicarboxylic acids. Eastman Chemical Company (22) and BASF (23) have developed such aliphatic/aromatic

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<td>100</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>900</td>
<td>1700</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>600</td>
<td>180</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>1–2.5</td>
<td>120</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td>1–8</td>
<td>15–600</td>
<td>2800–3500</td>
<td>1.25</td>
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<td>10</td>
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</table>

Table 2. Installed capacity of some starch-based materials and polyesters.

<table>
<thead>
<tr>
<th>Material</th>
<th>Company</th>
<th>Installed capacity (tons/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mater-Bi starch</td>
<td>Novamont</td>
<td>20,000</td>
</tr>
<tr>
<td>Ecofoam</td>
<td>National Starch</td>
<td>20,000</td>
</tr>
<tr>
<td>Poly(hydroxy butyrate-co-hydroxy valerate)</td>
<td>Metabolix</td>
<td>?</td>
</tr>
<tr>
<td>Poly(lactic acid)</td>
<td>Cargill Dow LLC</td>
<td>140,000</td>
</tr>
<tr>
<td>Poly(ε-caprolactone)</td>
<td>Union Carbide</td>
<td>&gt;5,000</td>
</tr>
<tr>
<td>Poly(butanevdyl succinate)</td>
<td>Showa Denko</td>
<td>3,000</td>
</tr>
<tr>
<td>Poly(ester amide)</td>
<td>Bayer</td>
<td>?</td>
</tr>
<tr>
<td>Poly(ethylene terephthalate, adipate)</td>
<td>Eastman Chemical</td>
<td>15,000</td>
</tr>
<tr>
<td>Poly(ethylene terephthalate, adipate)</td>
<td>BASF</td>
<td>8,000</td>
</tr>
</tbody>
</table>

www.sciencemag.org SCIENCE VOL 297 2 AUGUST 2002
resins that retain their biodegradability. BASF projects a double-digit growth figure for its aliphatic/aromatic resin, Ecoflex (27), which is used mainly as an additive to plastics from renewable resources (for example, blended with thermoplastic starch) and as a primary component of films and laminates. Some of the physical properties of these polymers, as well as their installed capacity and the company producing them, are listed in Tables 1 and 2.

**Water-Soluble Biodegradable Polymers**

Water-soluble polymers are used as detergent builders, scale inhibitors, flocculants, thickeners, emulsifiers, and paper-sizing agents. They are found in cleaning products, foods, toothpaste, shampoo, conditioners, skin lotions, and textiles. The largest volumes of water-soluble polymers are prepared from acrylic acid, maleic anhydride, methacrylic acid, and various combinations of these monomers. With the exception of their oligomers, these polymers are not biodegradable. Conventional water-soluble polymers therefore persist in oceans, lakes, and other water depositories. Consumers do not see these polymers washed up on beaches; their effects are harder to see, making the problem more dangerous. To avoid further accumulation of recalcitrant substances in waterways, the commercial development of water-soluble BPs is urgently needed.

Water-soluble BPs may be synthesized by modifying starch and cellulose. For example, carboxymethyl cellulose (CMC) having different degrees of carboxymethyl substitution is a family of marketed water-soluble polymers. Hydroxyethyl cellulose (HEC) is used as thickeners in drilling fluids and as fluid-loss agents in cementing. For such polysaccharide-derived BPs is widely used microbial polysaccharide. Industr-

**Perspectives and Conclusions**

The development of BPs is best viewed in the wider context of the “greening” of industrial chemistry. In future years, it will be largely driven by three factors: the need to derive more carbon for chemical processes from renewable substances instead of oil reserves, to develop cleaner chemical processes, and to avoid perturbing the ecosystem.

Key opportunities exist to build BPs from annually renewable crops and agro-industrial waste-streams (29). The production of monomers and polymers with enzymes (30), microbes, or plants represents a cleaner and safer way of doing chemistry. Breakthroughs in the genetic engineering of metabolic pathways have yielded microbes that more efficiently convert inexpensive feedstocks (such as molasses, starch, and waste lipids) to BP building blocks (such as lactic acid) (18). Cloning and expression of genes in plants has created new possibilities for using photosynthesis to directly synthesize polymers in plants (14). These powerful technologies will allow the continued development of cost-effective biological routes to a wide range of chemicals, including monomers and polymers. By using genetic methods to manufacture safe chemicals in specific plant compartments, the separation of plant-derived polymers from foods during harvesting will be facilitated.

An important benefit of renewable feedstocks, as compared with petroleum, is a reduction in the emission of fossil fuel–derived CO₂. For example, on the basis of one estimate, the volume of PLA production in 2020 will be 3.6 billion kg/year. If these polymers displace an equivalent amount of fossil fuel–based polymers, then 192 trillion Btu of fossil-derived fuel will be saved per year, resulting in a reduction in the emission of CO₂ by 10 million tons.

To avoid perturbing the ecosystem, processes must be cyclic, without creating chemical or biological imbalances. BPs from annually renewable materials allow cyclic processes that can be renewed over short time intervals (less than 1 year). The chemicals taken from nature will be returned to nature without perturbing the environment. This is a large departure from current practices. At present there is little or no current value to the manufacturer who develops such an environmentally friendly product, and BPs must therefore compete head-to-head in cost and performance with existing familiar and expensive products (e.g., plastic resins such as polyethylene cost about 50 cents per pound). This is extremely difficult because new processes require intensive research and large capital expenses and must be scaled-up to be economically competitive. BPs are often designed to mimic the “feel” of existing materials. It will be important when developing and marketing BPs to identify and exploit the unique attributes of the materials.

Biodegradable polymers are only beneficial when they can actually biodegrade. Water-soluble polymers normally enter a waste-water treatment facility; the infrastructure of such facilities is readily available in all industrially advanced nations. Such facilities provide high levels of bioactivity that rapidly degrade water-soluble BPs. In contrast, the infrastructure of bioactive systems for the disposal of non–water-soluble BPs is seriously lagging. Without such an infrastructure, valuable biodispersables such as food and yard waste (25 to 30% of total municipal solid waste) are often buried in dry landfill environments (31). The logical solution is to convert biowastes to valuable compost, chemical intermediates, and energy through aerobic and anaerobic processes. A wide network of sophisticated composting and other bioconversion facilities for the reprocessing of BPs and other biowastes is essential for the future health of our ecosystem.

On the basis of economic and environmental considerations, the commercialization of BPs will continue to increase in markets where products have a relatively short-use lifetime. It is important to remember, however, that biodegradable polymers can be sufficiently sturdy to withstand standard wash-cycle treatments in textile garments. Misconceptions that biodegradable polymers cannot be stable for multiple-use articles over lifetimes of years will need to be addressed.

**References and Notes**

The chemical industry plays a key role in sustaining the world economy and underpinning future technologies, yet is under unprecedented pressure from the effects of globalization and change in many of its traditional markets. Against this background, what will be needed for the industry to embrace efforts to make it “greener”? We explore some of the issues raised by the development of “green chemistry” techniques and identify potential barriers to their implementation by industry.

Most processes that involve the use of chemicals have the potential to cause a negative impact on the environment. It is therefore essential that the risks involved be eliminated or at least reduced to an acceptable level. In its most simple form, risk can be expressed as:

\[
\text{Risk} = \text{Hazard} \times \text{Exposure} \quad (1)
\]

Traditionally, the risks posed by chemical processes have been minimized by limiting exposure by controlling so-called circumstantial factors, such as the use, handling, treatment, and disposal of chemicals. The existing legislative and regulatory framework that governs these processes focuses almost exclusively on this issue. By contrast, green chemistry (Table 1) (1–3) seeks to minimize risk by minimizing hazard. It thereby shifts control from circumstantial to intrinsic factors, such as the design or selection of chemicals with reduced toxicity and of reaction pathways that eliminate by-products or ensure that they are benign. Such design reduces the ability to manifest hazard (and therefore risk), providing inherent safety from accidents or acts of terrorism.

Legislation has been effective in improving environmental conditions, but toxic materials are still discharged in considerable amounts—7 billion pounds (3.2 × 10^9 kg) in 2000 in the United States alone (4). Regulation clearly has a major and continuing role to play in lessening the environmental impact of the chemical industry (5). Green chemistry can potentially generate an even greater environmental benefit by removing the intrinsic hazard of particular products or processes, thereby moving them outside the scope of many environmental regulations.

**Involvement of Academia and Industry**

Green chemistry is a major component of the science underlining the “responsible care” program of the chemical industry (6) and of “sustainable development” (7). Making reduced hazard an important criterion for judging the performance of a product or process provides a new challenge for traditional academic research. Academic interest in green chemistry is reinforced by the increasing requirement by funding agencies that academic research should address quality-of-life issues and should be commercially more exploitable, and by increased “outsourcing” of industrial research to universities. As a result, worldwide research aimed at cleaner processing has increased sharply (8).

Already in the 19th century, environmental regulation resulted in the cleanup of the LeBlanc soda process and other similarly polluting processes (9). More recently, the Montreal Protocol has led to the successful replacement of chlorofluorocarbons by compounds that do not affect the ozone layer appreciably. However, given society’s demand for chemical products, most of these improvements could not have taken place in the absence of viable methods for reducing the environmental impact of the processes or introducing less harmful replacement products. Today, there is an increasing awareness that sophisticated technologies and radical new processes will be needed for the full potential for environmental improvement to be realized. Major advances in understanding the relation between the molecular structure of chemical products and their toxicity mean that we can begin to design “safer” chemicals.

The term “green chemistry” was coined only 10 years ago (10). Given that the development time for a new chemical process is often more than a decade, there has been insufficient time for green chemistry principles (Table 1) to be translated systematically into industrial processes. Nevertheless, many recently developed processes and products fulfill most of these principles. For example, the waste greenhouse gas, N₂O, from the manufacture of adipic acid (a component of nylon) is being reused as the oxidant in a greener route to phenol (11). Tetrais(hydroxymethyl)phosphonium phosphate is used as a low-dose, low-toxicity control agent for...
microbial growth in industrial cooling systems (12); it breaks down rapidly in the environment without bioaccumulation. Similarly, 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one is produced as a replacement for the environmentally problematic tri-butyl tin oxide in marine antifouling applications (13); unlike the tin compound, it degrades rapidly when released into seawater.

Academic research also has a considerable lead time. Only a few genuine green chemistry projects have been running long enough to make the transition from research laboratory to commercialization. The most striking example is the work on catalytic asymmetric synthesis by Knowles, Noyori, and Sharpless (14). Although predating the birth of green chemistry, this work reflects several of its ideals (1, 15), namely, high selectivity, atom economy, elimination of many steps from conventional synthesis, and avoidance of waste.

Ambitious Goals
Green chemistry aims to introduce radical new technologies that will transform the nature of chemical use and manufacture. Transformations on this scale are rare but not unprecedented. For example, the Haber-Bosch process for ammonia manufacture turned atmospheric nitrogen into a sustainable feedstock for nitrogen production, marginalizing the use of nitrate minerals mined in remote, environmentally sensitive locations. New technologies of this type are not merely more profitable but render the existing technology virtually obsolete on economic grounds.

Novel, profitable, and environmentally benign processes are being reported across the world. Substantial funds are becoming available for green chemistry research worldwide, and environmental regulators actively promote green processing techniques. But green chemistry has barely begun to be integrated into the chemical enterprise. What further barriers need to be overcome to incorporate it systematically in industrial processes, academic research, and education?

Barriers to Implementation
Barriers to industrial innovation have been studied extensively in other technological areas. A recent European Union study on the barriers to energy efficiency (16) identified economic, behavioral, and organizational barriers, such as tax incentives, accountancy practices, and the lowly status of energy managers in some organizations.

Similar factors apply to green chemistry technology (7). In particular, current taxation strategies often punish polluters and emitters, rather than rewarding cleaner processes (17). Furthermore, there is often little incentive to improve processes beyond the limits set by existing environmental regulations, which frequently prescribe which technology should be used. Regulatory agencies have tried to make the rules more flexible, but industry still fears that any radical process changes could result in regulatory liability.

There is, however, a big difference between energy usage and green chemistry. Appropriate strategies for energy efficiency in different sectors are generally well established. The implementation of green chemistry is much more radical and complex, resembling the introduction of fuel cells to replace fossil fuels or nuclear power generation. In only a few cases has green chemistry had time to establish a best practice. Few industrial processes have been explicitly labeled “green,” and some of the most innovative examples are proprietary. Thus, it is difficult for industry to identify the economic and environmental benefits of the new technology. This barrier can be overcome by widespread dissemination of successful green chemical processes, such as the publication of case studies (17–19).

The key question is how one can judge whether new processes do indeed have a reduced environmental impact. Sheldon’s E-factor—weight of waste per unit weight of product—has been used widely by chemists, and more practical and detailed assessment schemes have been suggested recently (21, 22). Establishing the true environmental impact of a new technology requires full life-cycle assessments as well as toxicological testing of any materials involved, such as reagents or solvents; unfortunately, many of these data cannot be obtained until the process has been tried out on a commercial scale (3, 23).

Despite its simplicity, Sheldon’s E-factor is useful in highlighting the fine chemicals and pharmaceutical industries (Table 2) as the areas in which green chemistry is likely to have its most immediate impact. Fine chemical companies tend to produce a wide range of chemicals on a small scale (500 to 5000 tons per year). They therefore offer more diverse opportunities for introducing new technology than the bulk chemicals sector, and the scale-up from laboratory to plant is less daunting.

Businesses aim to maximize profitability without contravening regulation or excessively offending public opinion. Therefore, new green chemistry processes will be introduced only if they can provide a payback quickly enough to be attractive to managers and investors. A new, greener process will not be feasible unless it provides chemical advantage over current processes and is sufficiently profitable to offset the costs of shutting down

Table 1. The most widely accepted definition of green chemistry (7) is “the design, development and implementation of chemical processes and products to reduce or eliminate substances hazardous to human health and the environment.” This definition has been expanded into 12 principles listed in the table.

**Green chemistry principles**
1. It is better to prevent waste than to treat or clean up waste after it is formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials used into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances (e.g., solvents, separation agents, and so forth) should be made unnecessary wherever possible and innocuous when used.
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material or feedstock should be renewable rather than depleting wherever technically and economically practicable.
8. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11. Analytical methodologies need to be developed further to allow for real-time in-process monitoring and control before the formation of hazardous substances.
12. Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Table 2. Environmental acceptability, as measured by the E-factor. [Adapted from (20)]

<table>
<thead>
<tr>
<th>Industry</th>
<th>Product tons per year</th>
<th>Waste/product ratio by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil refining</td>
<td>$10^3$–$10^4$</td>
<td>$&lt;0.1$</td>
</tr>
<tr>
<td>Bulk chemicals</td>
<td>$10^4$–$10^5$</td>
<td>$&lt;1$</td>
</tr>
<tr>
<td>Fine chemicals</td>
<td>$10^1$–$10^4$</td>
<td>$5$–$50$</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>$10^3$–$10^4$</td>
<td>$25$–$&gt;100$</td>
</tr>
</tbody>
</table>
the existing plant. Even then, companies that invest in successful new technologies are likely to use these as a means of gaining competitive advantage and, therefore, will resist sharing the technology with their competitors.

Perhaps the largest barrier is that proven green chemistry technologies are not as readily available as are more traditional alternatives. Speed is paramount in process development for most sectors of the chemical industry, so that profitability can be maximized within the life of a patent. Existing technologies that pollute within prescribed regulatory limits may be easier to implement than new technologies that pollute much less. Green chemistry needs the engagement of a wide cross section of the scientific community to enable it to deliver within the required time frame. A concerted research drive by industry, government, and academia is needed to develop a wide range of reliable, benign methodologies that will be available when needed.

An initiative just launched in the United Kingdom, the Crystal Faraday Partnership (24), shows the way ahead. This research forum with both industrial and government funding aims to promote research, education, and dissemination in green chemistry and processing. Experience at Nottingham University (United Kingdom) has shown that a balanced combination of industrial and government funding can lead to the rapid development of new, green chemistry–based processes. In collaboration with Thomas Swan & Co. Ltd., the university has developed a series of heterogeneously catalyzed supercritical fluid reactions (25–27), the basis of a 1000 ton per year chemical manufacturing plant (28) (Fig. 1) that successfully went on stream in March 2002.

The Scientific Challenge
Meeting the criteria of providing payback within a short time frame presents a major scientific challenge. Broadly, green chemical process research can be divided into three categories: alternative feedstocks, alternative solvents, and alternative synthetic pathways, many of which involve novel catalysis.

Alternative feedstocks. One proven approach, already widely implemented in industry, is to use the waste from one process as a feedstock or reagent in the next (29). A potential difficulty is that the production of many quite disparate products becomes linked, leading to problems if demand for one of them changes dramatically. A more radical approach is to move from hazardous, resource-depleting materials such as petroleum to those from renewable or biologically derived sources. For example, bio-derived lactic acid is now being used as a feedstock for large-scale industrial polymer production (30, 31). Renewable feedstocks are often highly amenable to bioprocessing by enzymes, but represent a chemical challenge: Biomolecules such as sugars are far more oxygenated than petrochemical hydrocarbons, and may therefore require changing the chemistry from oxidation to reduction to manufacture a particular end-product.

The simplest alternative feedstock is CO2. Making chemicals from CO2 would not only conserve petroleum but also reduce CO2 emissions. However, CO2 is thermodynamically extremely stable and therefore difficult to activate chemically. Nevertheless, progress has been made in incorporating CO2 into polymers, and in reacting it with H2 to make formic acid, HCO2H (32). The key is the design of new catalysts, and techniques such as immobilization or ultrafiltration, for separating high-value catalysts from the products so that they can be recycled.

Alternative solvents. Organic solvents are a major source of waste, and their efficient control can produce a substantial improvement in the environmental impact of a process (22). The most elegant way to avoid problems with solvents is not to use them, an approach that has been widely exploited in the paints and coatings industries. Recently, Raston et al. described organic reactions that can be carried out merely by grinding the reagents together with a catalyst (33), a process that is both cleaner and quicker than the conventional reactions. The experiment may not be easy to scale up to an industrial scale, but it has nevertheless caused a paradigm shift in the synthesis of a whole class of compounds that were previously tedious or difficult to make.

Most reactions do, however, require a solvent, and a green chemical process must necessarily involve an environmentally acceptable solvent (34). Much current research focuses on two classes of alternative solvents (23): supercritical fluids (35) and ionic liquids (36). Supercritical fluids are gases that are nearly as dense as liquids (37), while ionic liquids are salts of highly asymmetrical organic ions with melting points below or close to room temperature (36). The cheapest supercritical fluid, CO2, has solvent properties similar to those of light hydrocarbons, apart from an unusually high affinity for fluorocarbons (38). Its properties can be “tuned” by changing the applied pressure, leading to unusual chemical effects not easily achieved in more conventional solvents (25, 39, 40). Applications include dry cleaning (Fig. 2). Ionic liquids are chemically diverse owing to the huge number of possible cation/anion combinations that can be synthesized. A very broad range of chemical reactions from alkylation and polymerization to biocatalysis and electroplating have already been carried out in these solvents, although as yet none has been carried out on an industrial scale (41).

Alternative synthetic pathways. Most new pathways that lead to cleaner chemistry involve catalysts. A century ago, catalysts were not widely used in the chemical industry;
today, no petrochemical company and few chemical companies would be competitive without their use. The design of selective catalysts is crucial to the future of green chemistry because improved catalysis can reduce the number of stages in a given process and hence reduce its environmental impact. For example, a novel catalytic step has almost halved the number of stages needed to manufacture the analgesic ibuprofen (21) and has also eliminated the toxic solvent CCl₄ from the process. Similarly, Pfizer has introduced a new process, designed on green chemistry principles, that greatly reduces waste in manufacturing sertraline, the active ingredient in the antidepressive drug Zoloft (42).

The design of safer chemicals will necessarily change the detailed synthesis that is needed for a particular product. Nevertheless, there is still a major need for concerted research to improve the selectivity and performance of catalysts. Spent catalysts left at the end of a reaction also contribute to chemical waste, particularly because many contain toxic heavy metals. Research into catalyst reuse and recycling is still in its infancy. These factors should favor the use of enzymes as biocatalysts, which are often highly selective and do not involve toxic metals. Despite many commercially successful biocatalytic processes [such as the manufacture of the sweetener aspartame (43)], much research remains to be done before biocatalysts can be used routinely throughout the chemical industry.

**Conclusion**

Fundamental changes in technology are adopted by the chemical industry only when they provide real advantage. The challenge to green chemists is to develop such technolo- gies on a short time scale. Increased collaboration between academia, governments, and industry will accelerate the pace of innovation in green chemistry along the supply chain from chemical innovators through scale-up to industrial end-users. Many in both industry and academia hesitate to take the plunge. Only when more universities teach green chemistry will graduates be able to apply these principles when they enter industry. For the full potential of green chemistry to be realized, young academics need role models to inspire them, and industry needs successful case studies to convince them.

**References and Notes**

8. See, for example, Green Chemistry, www.rsc.org/issue/journals/current/green/greenpub.htm.
14. The scientific value of this work was recognized by the award of the 2001 Nobel Prize for chemistry. See www.nobel.se/chemistry/laureates/2001/press.html.
17. A modest start toward providing recognition for cleaner processes has been made with national green chemistry awards, such as the U.S. Presidential Green Chemistry Challenge (www.epa.gov/greenchemistry/presgcc.htm) and the U.K. Royal Society of Chemistry Green Chemistry Awards.
18. Green Chemistry Institute, chemistry.org/greenchemistryinstitute/.
29. The concept of integrating chemical processes has been adopted by the chemical company BASF, which has coined the apparently untranslatable German word “Verbund” for their approach; see www.basf.com/static/OpenMarket/Xcelerate/Preview_cid-994075625740_pubid-974129513031_c-Article.html.
41. For a recent summary of the role of ionic liquids in green chemistry, see the Special issue on ionic liquids, K. R. Seddon, Ed., Green Chem. 4 (no. 2), (2002).
43. See, for example, the review by A. Schmid et al., Nature, 409 258 (2002).
44. We thank the members of the School of Chemistry Business Partnership Unit (Nottingham) and all others whose views have helped shape this article.