GREEN CHEMISTRY

1. Introduction

Green chemistry and green engineering describe the efforts of chemists and engineers to develop processes and products that prevent pollution and are inherently safe for humans and the environment. Implementing green chemistry and engineering will improve the quality of the environment for present and future generations. Manufacturing a chemical product requires a synthetic pathway as well as a safe and efficient chemical manufacturing strategy. Thus, both chemistry and engineering are required to achieve true source reduction.

Green chemistry is a term first proposed by Paul Anastas, formerly of the U.S. Environmental Protection Agency (EPA). Definitions of green chemistry typically include aspects of basic chemistry and applied engineering practice. For example, Anastas and Warner (1) define green chemistry as follows: “Green chemistry is the use of chemical principles and methodologies for source reduction. Green chemistry incorporates pollution prevention in the manufacture of chemicals, and promotes pollution prevention and industrial ecology.”

A slightly more succinct definition is (1,2): “The invention, design, and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances.”

Another description of green chemistry is by Sheldon (3): “Green chemistry efficiently utilizes (preferably renewable) raw materials, eliminates waste, and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products.”

The chemical engineering profession also promotes the concept of source reduction. “Green Engineering” has been defined as follows (4): “Green Engineering is the design, commercialization, and use of processes and products that are feasible and economical, while minimizing both risk to human health and the environment, and generation of pollution at the source.”

Green chemistry, by definition, addresses source reduction, which is the highest priority activity in the listings of pollution prevention priorities given by Mulholland and Dyer (5) and Allen and Rosselot (6). Green chemistry is the science and technology of preventing wastes before they are generated, and includes every consideration from feedstock origins to end of product life. The term “sustainable chemistry” is sometimes used with essentially the same meaning (2).

Subsequent sections of this article will provide additional focus to the scope of green chemistry and engineering. First, a historical context is presented. Chemical manufacturers have invested substantial capital and effort on environmental matters for at least the past 30 years. Initially, the driving forces were government and community demand to control emissions of pollutants to the air, water, and land, and to clean up contaminated sites. The U.S. EPA has long practiced a command-and-control approach, assuming that pollution is inevitable and that the main effort of industry is to control and treat pollutants. This has led to the development of many downstream or end of pipe processes for pollution treatment, abatement, and control. To understand the historical response of the chemical industry to environmental laws, it is instructive to consult legislation such as the Toxic Substances Control Act (TSCA), the Clean Air Act, the Clean Water Act, and other legislation.

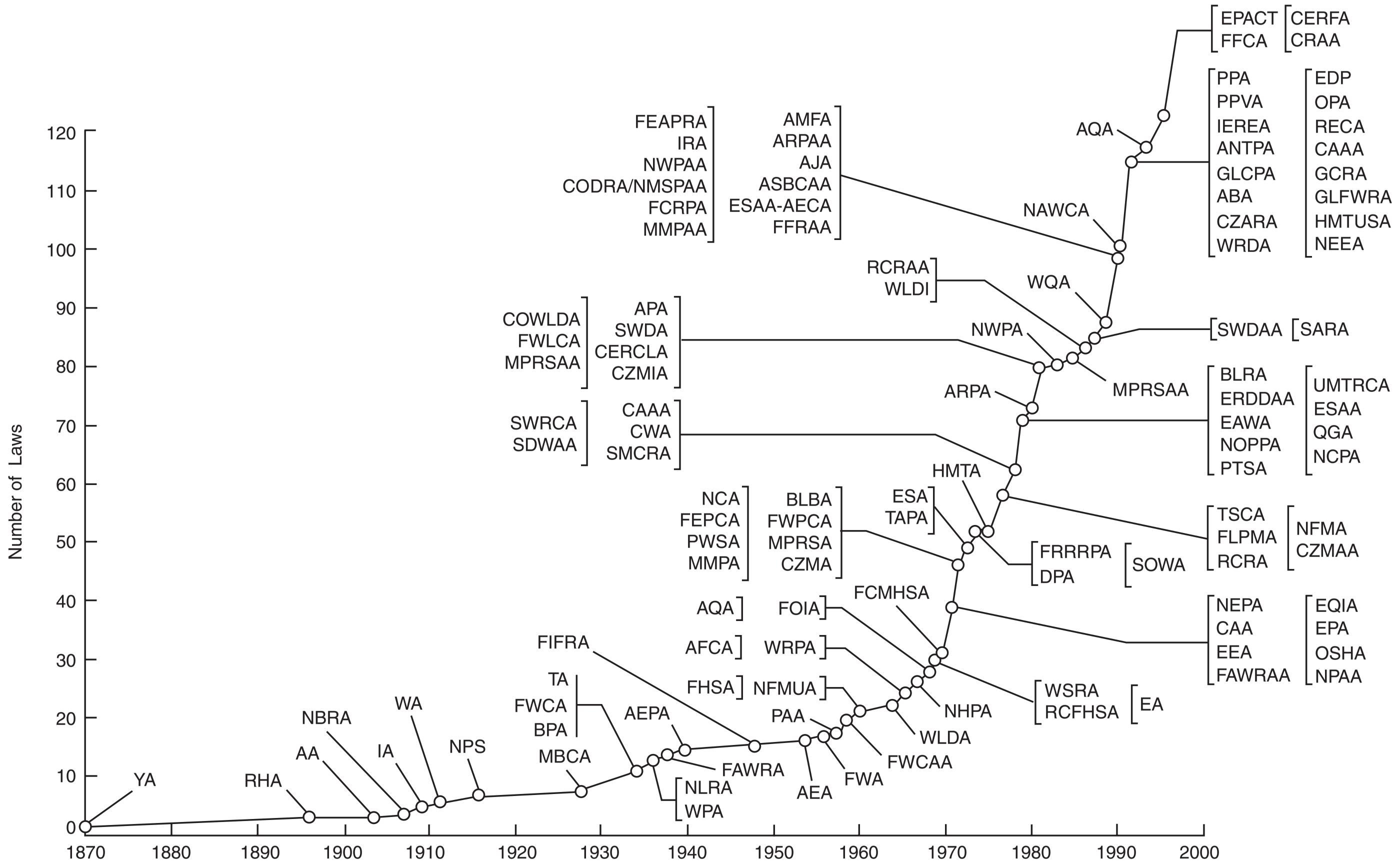

Fig. 1. Cumulative growth in federal environmental laws and amendments. (Allen/ Shonnard, *GREEN ENGINEERING: Environmentally Conscious Design of Chemical Processes*, © 2002. Electronically reproduced by permission of Pearson Education, Inc., Upper Saddle River, New Jersey).

Federal and state environmental laws provide strong incentives for green chemistry. Figure 1 (4) shows the history of federal laws and provisions in the past century. Clearly, the number of federal laws and amendments has grown enormously in the past 30 years. Figure 2 (5) compares the U.S. population with the number of federal environmental laws. Since 1960 it is clear that the number of federal environmental laws has been increasing at a rate that is much steeper than the rate of population growth. This figure does not count state environmental laws that have been enacted, nor does it reflect the large number of specific rulings that have been promulgated by EPA and the state regulatory agencies under the aegis of the various federal and state laws. Allen and Shonnard (4) and Lynch (7) review environmental law with a particular emphasis placed upon chemistry and chemical engineering.

In the past 10 years, attention has focused on the more enlightened realization that pollution should be prevented before it occurs. Green chemistry and engineering are concepts driven by the emphasis on pollution prevention (P2). The driving force for P2 in the United States is the Pollution Prevention Act of 1990. This act established pollution prevention as the preferred environmental policy of the United States, rather than end of pipe treatment, remediation, or disposal of wastes. The full spectrum of pollution prevention options ranges from true source reduction to treatment and disposal. As will be seen, green chemistry contributes to pollution prevention, but the terms are not synonymous. Allen and Rosselot (6) present the following hierarchy for pollution

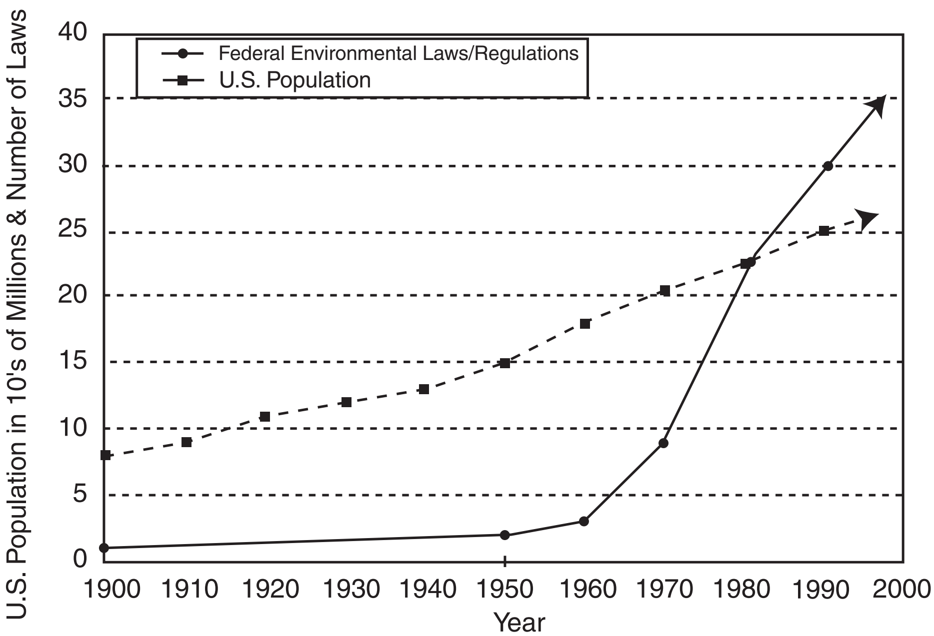

Fig. 2. Comparison between the increase in federal environmental laws and the U.S. population with time. Reproduced with permission of the American Institute of Chemical Engineering. Copyright © 1999 AIChE. All right reserved (see Ref. 5).

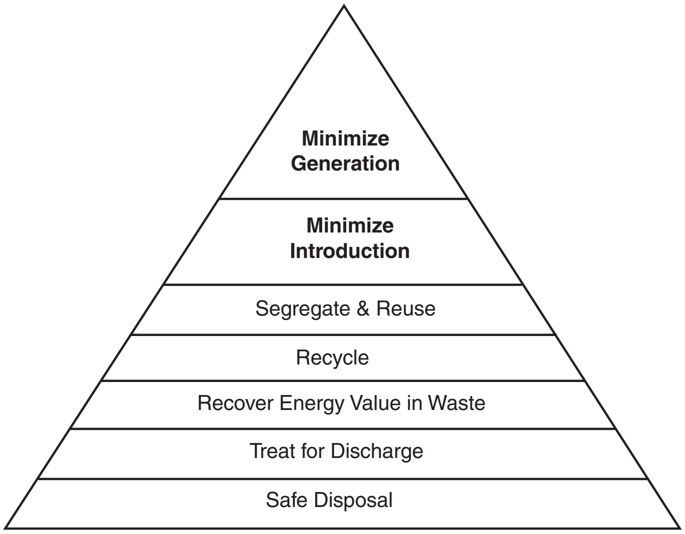

Fig. 3. Pollution prevention hierarchy used at Du Pont. Reproduced with permission of the American Institute of Chemical Engineers. Copyright © 1999 AIChE. All right reserved (see Ref. 5).

prevention and waste management, in decreasing order of preference:

1. Source reduction.
2. In process recycling.
3. On-site recycling.
4. Off-site recycling.
5. Waste treatment to render the waste less hazardous.
6. Secure disposal.
7. Direct release to the environment.

Mulholland and co-workers (5) present a similar pollution prevention hierarchy, based on practice at the Du Pont Company (Fig. 3). Green chemistry, as described below, addresses the very top level of these hierarchies. For additional information on other topics in the hierarchy (see RECYCLING, INTRODUCTION, and WASTES, INDUSTRIAL).

2. The Twelve Principles of Green Chemistry (1)

Design and implementation of completely green products and processes is an enormous challenge. Because the number of chemical synthesis pathways is enormous, there is not a systematic and failsafe method for ensuring that the chemistry being implemented is green. Indeed, it is more nearly correct to inquire if a proposed chemical manufacturing process is "greener" than other alternatives. Thus, green chemistry recognizes the importance of incremental improvements. Anastas and Warner (1) formulated a set of twelve principles that guide and define the scope of green chemistry. These principles are presented and illustrated below.

2.1. Prevention (Principle 1). It is better to prevent waste than to treat or clean up waste after it has been created. In the past, the earth and its rivers, oceans, atmosphere, and soil have been considered infinite sinks for the discharge of pollution and waste. The command and control philosophy implies that it is acceptable to generate waste, as long as the waste is safely treated and disposed or stored. Green chemistry's highest principle is that waste should not be created at all. From an economic standpoint, waste is a cost that requires paying twice: the first cost is for purchase of raw materials, and the second is for management or disposal of the waste.

2.2. Atom Economy (Principle 2). Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product. Thus, it is not sufficient even to achieve 100% yield of the desired product, if the synthesis mechanism also produces by-products; rather, it is desirable to incorporate all of the atoms of the raw materials into the products. Atom economy, as discussed by Trost (9), and atom utilization, the term coined by Sheldon (3), embody the same concept but with slightly different definitions. The atom economy is defined at the formula weight of the desired product divided by the stoichiometrically weighted formula weights of all reactants. Atom utilization is the quotient of the formula weight of the desired product with the formula weight of all products and by-products. In situations where the exact composition of all byproducts is difficult to determine, the atom economy is more practical.

Sheldon (3) also defines the E factor, which is the mass ratio of waste to desired product. E factors for bulk commodity chemicals are typically <5, and often <1. By contrast, fine chemicals and pharmaceuticals typically generate large amounts of waste per unit of product, with E factors perhaps exceeding 100. It is important to note that neither the atom efficiency nor the E factor provide any quantitative measure of the potential for human harm of the waste products.

2.3. Less Hazardous Chemical Syntheses (Principle 3). Wherever practical, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment. This principle promotes the use of less toxic reagents and intermediates, and the generation of less toxic by-products. The use of less toxic feedstocks drives the development of renewable raw materials, eg. Better catalysts and chemical reactor designs are also critical to developing less hazardous syntheses.

2.4. Design Safer Chemicals (Principle 4). Chemical products should be designed to achieve their desired function while minimizing their toxicity. This principle requires matching the desired function of chemical compound with its chemical structure. It also requires the ability to predict beforehand possible toxic effects of a given chemical substance. Thus, research and development of methods for structure–property relationship promote this principle. Industry should consider favorable environmental properties (reduced toxicity, carcinogenicity, etc) as a performance metric, as well as the traditional performance properties (vapor pressure, color, stability etc) when making the decision to develop and market a given product.

2.5. Safer Solvents and Auxiliaries (Principle 5). The use of auxiliary substances–solvents, separation agents, and other additives should be made unnecessary wherever possible and innocuous when used. Safer solvents such as water, alcohols, supercritical carbon dioxide, or biodegradable surfactant solutions, eg, are preferable to chlorinated solvents. Separation processes such as liquid extraction require mass separation agents; alternatives such as reactive separations through membrane reactors may provide a more environmentally acceptable alternative.

2.6. Design for Energy Efficiency (Principle 6). Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure. The chemical industry has reduced substantially its use of energy in manufacturing, starting with the oil embargo and energy shortages of the 1970s. Heat integration and other engineering tools are well developed in the chemical industry, and can be applied within a given process. However, it is still true that a substantial portion of energy usage in manufacturing can be attributed to the chemical industry. Thus, advances that can fundamentally alter the required energy usage with manufacturing a product are a key aspect of green chemistry (see ENERGY MANAGEMENT; RENEWABLE ENERGY RESOURCES).

2.7. Use Renewable Feedstocks (Principle 7). Raw material or feedstock should be renewable rather than depleting whenever technically and economically practical. Manufacture of chemicals from agricultural feedstocks is known as Chemurgy (see CHEMURGY). Fuels from biomass may include cultivated fuels, such as ethanol from corn, or fuels from waste biomass (see FUELS FROM BIOMASS). Natural polymers such as chitin and cellulose are receiving attention for the manufacture of engineered materials. Of particular interest is the use of CO_2 as a raw material for C_1 chemistry.

2.8. Reduce Derivatives (Principle 8). Unnecessary derivatization-use of blocking groups, protection–deprotection, and temporary modification of physical–chemical processes should be minimized or avoided if possible, because such steps require additional materials, increased solvent usage, and increased energy requirements. This principle is related to principles 2 and 5 above.

2.9. Catalysis (Principle 9). Catalytic reagents (as selective as possible) are superior to stoichiometric reagents. The use of homogeneous catalysts or heterogeneous catalysts is essential to realizing principles 2 and 3 above. Anastas and co-workers (10) referred to the use of catalysis as a "foundational pillar" of green chemistry, because catalysts can help achieve a number of green chemistry goals, including decreased material usage, increased atom efficiency, and reduced energy demands.

2.10. Design for Degradation (Principle 10). Chemical products should be designed so that at the end of their function they are broken down into innocuous degradation products that do not persist in the environment. This principle clearly intersects with the concept of Design for the Environment, a term that is defined below. "Product design" involves communication along a diverse chain of stakeholders (customers, sales representatives, engineers and materials scientists, and synthetic chemists, eg). Green chemistry therefore requires close collaboration of chemists with these other stakeholders.

2.11. Real-Time Analysis for Pollution Prevention (Principle 11). Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

Production of wastes is not always due to the synthetic chemistry; sometimes waste is produced because of poor process monitoring and control. Analytical methods frequently rely on sampling of product at the end of the production line, and may require many minutes or hours to accomplish. In such cases, by the time the product analysis is completed it is too late to adjust the process for optimum performance. Real-time process monitoring and control of temperature, pressure, feed rate, feed composition, and product composition are vital to green chemical engineering.

2.12. Inherently Safer Chemistry for Accident Prevention (Principle 12). Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires. There is some overlap of this principle with principle 5 (safer solvents and auxiliaries); eg, nontoxic supercritical carbon dioxide is an inherently nontoxic substitute for chlorinated solvents. Substitutes for lead compounds in paint and gasoline are also examples of principles 5 and 12. Principle 12, however, also applies to actions such as eliminating bulk transport and storage of hazardous intermediates in favor of on-site generation of these intermediates. While the ultimate goal of green chemistry would be to eliminate the hazardous material entirely, the possibility of a massive release of the hazardous compound is reduced or eliminated by performing on-site generation instead of relying on bulk storage. See Hazard analysis and risk assessment.

3. Concepts Related to Green Chemistry

A number of concepts and industrial initiatives are related to green chemistry. These related and sometimes competing terms may cause confusion. These related concepts are defined and described below.

3.1. Pollution Prevention. As defined by the Pollution Prevention Act of 1990, Pollution Prevention encompasses those activities listed in the Introduction (5,6). In particular, the "source reduction" aspect of pollution prevention encompasses any chemistry or chemical technology that would reduce or eliminate waste and emissions of chemicals to the environment. Activities such as waste treatment and secure disposal, as shown in Figure 3, fall outside the concept of green chemistry.

3.2. Waste Minimization. Waste minimization, and the related term waste reduction, generally refer to reduction in the amount of solid or liquid waste produced by a process (air pollution being excepted). The practice of in-process recycling, or recovery and safe treatment of solid and liquid waste, is sometimes incorporated in the concept of waste minimization. Also, material handling practices such as safe packaging, proper labeling, and management of containers can aid in waste minimization (eg, by reducing the amount of packaging to be disposed, by allowing for recycle and reuse of packaging and containers, and by preventing the accidental generation of waste due to improper labeling). Thus, the concept of waste minimization is lower on the pollution prevention hierarchy than green chemistry and green chemical engineering.

3.3. Design for the Environment. Design for the Environment (DfE) refers to the design and manufacture of products and processes in a way that has minimal impact upon the environment. For example, DfE can be applied to the manufacture of products such as automobiles or a computers, and requires that both product and process design be done with consideration for reducing or eliminating any negative environmental impacts. It is axiomatic that by the time a plant or process design is completed, 80% of the environmental impacts are fixed. DfE requires that, from the earliest stages of product and process design, minimizing environmental impacts be an explicit goal. DfE would require that the components be made of recyclable materials or from renewable resources, and that the product be designed in such a way that it could be disassembled, remanufactured, or recycled. Green chemistry intersects with the concept of design for the environment in that green chemistry will lead to the discovery and manufacture of recyclable materials, less toxic materials, or materials based upon renewable feedstocks, for example. Green chemistry provides the technology "push" and DfE the technology "pull" (11).

3.4. Industrial Ecology. As defined by Graedel and Allenby (12), industrial ecology describes the science of use and reuse of natural resources in manufacturing, rather than the traditional practice of extracting and using resources, then discarding and disposing. Industrial ecology describes the manufacturing process as an integral part of the environment. The concept is that the manufacture of goods should be a closed-loop system, analogous to the cycles that are observed in natural ecosystems.

3.5. Sustainability. Sustainability, or sustainable development, has been defined as meeting the needs of humans today, while not compromising the ability of future generations to meet their needs (13). Some regard the second half of this definition as a negative statement, and offer an equivalent definition of sustainable development: the ability to meet the needs of society today, while ensuring that future generations will also be able to meet their needs. Sustainability is perhaps the most broad and all-encompassing concept of all. Interpretation of sustainability from a corporate viewpoint has led to the concept of the so-called "triple bottom line" for industry:

1. Economic prosperity and continuity for the business and its shareholders.
2. Social well-being and equity for both employees and affected communities.
3. Environmental protection and resource conservation, both local and global.

Green chemistry is certainly an essential component of sustainability, but sustainability also encompasses the possibility of societal change (eg, the choice to use mass transportation, or the choice to conserve and not to consume). Anastas and Breen (11) indicate the relationship between green chemistry, design for the environment, industrial ecology, and sustainable development as in Figure 4.

The World Business Council for Sustainable Development (WBCSD) is a consortium first established in 1990. Based in Geneva, its business members have developed studies that demonstrate the business value of sustainable development. Business drivers include enhanced shareholder value and market positioning; increasing engagement with external stakeholders; recognition by the financial community; and increased responsibility and liability on the part of companies that use hazardous materials in their processes or products (14).

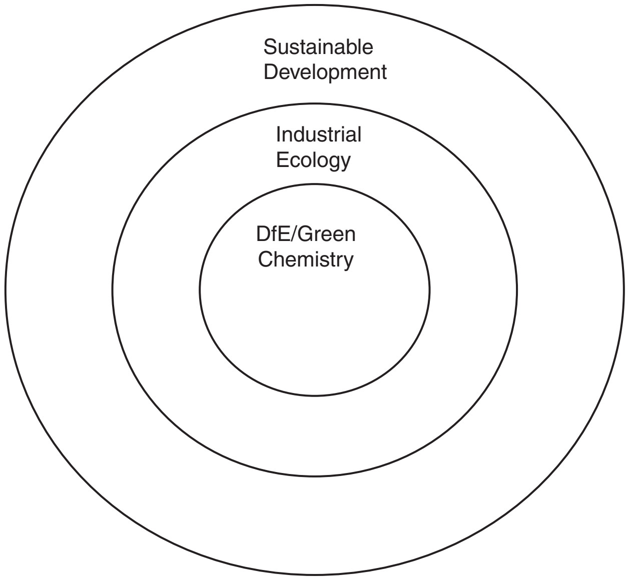

Fig. 4. Relationship between green chemistry, design for the environment, industrial ecology, and sustainability. Reprinted from the *J. Cleaner Prod.*, Vol. 5 (1–2), P. T. Anastas and J. J. Breen, "Design for the Environment and Green Chemistry: The Heart and Soul of Industrial Ecology." pp. 97–102, Copyright © 1997, with permission from Elsevier Science (see Ref. 11).

3.6. Responsible Care. The Responsible Care program is an initiative that the American Chemistry Council began in 1988 as a means of addressing the concern of the public about the manufacture and use of chemicals. Responsible Care encompasses a diversity of elements including process safety, transportation, and interaction with suppliers, distributors, and other stakeholders. With respect to the environment, the Responsible Care program describes broad obligations for members of the American Chemistry Council. These obligations include providing chemicals that can be manufactured safely and in a manner that protects the environment and the health of people.

4. Industrial Examples

The number of publications related to green chemistry and engineering has grown rapidly in the past decade. These cover the spectrum from fundamental chemistry to chemical engineering unit operations. McCann and Connelly (15) cite a number of examples of industrial and academic research in green chemistry; Matlack (16) provides an extensive bibliography and description of green chemistry, with a focus on organic industrial chemistry. The industrial examples selected below illustrate one or more of the twelve principles of green chemistry. Full assessment of economic and environmental impacts is still difficult, due to the relative immaturity of the tools needed for such assessments.

4.1. Use of Catalysts to Minimize Toxic Reagents; Inherently Safer Chemistry: Methyl Isocyanate and Agricultural Chemicals. Methyl isocyanate (MIC) is used in the manufacture of agricultural chemicals, particularly insecticides. The tragedy in Bhopal, India was caused by release of a cloud of MIC from bulk storage tanks. Prior to that incident, and especially since that incident, research on catalytic synthesis has resulted in a process that produces MIC from less hazardous materials on site, thus reducing the need to store large quantities (16). A proprietary process developed by the Du Pont Company (17) uses a heterogeneous silver catalyst to accomplish an oxidative–dehydrogenation process:

$$CH_3NH_2 + CO \rightleftharpoons CH_3NHCHO \quad (1)$$

$$CH_3NHCHO + O_2 \rightleftharpoons CH_3NCO \quad (2)$$

The patent describes a crystalline or vapor-sputtered silver catalyst on an inert support such as alumina or silica. Furthermore, to control the heat of reaction, two to four reactors in series are used to facilitate temperature control.

The new process does not obviate the need for methyl isocyanate. The main green advantage is that the process can be operated on-site in small reactors, producing MIC on demand and eliminating the need for bulk storage. Thus concerns about toxic releases, such as occurred at Bhopal, are greatly reduced.

4.2. Alternative Solvents: Supercritical Carbon Dioxide as a Media for Chemical Reactions. Supercritical fluids exist above the vapor–liquid critical point of a pure substance. Supercritical fluids are highly compressible solvents whose properties (density, viscosity, dielectric constant, etc) are sensitive functions of temperature and pressure. Thus, their solvent properties are tunable via control of processing conditions, giving rise to the prospect of controlling solubility and reaction kinetics via the solvent density. See SUPERCRITICAL FLUIDS.

Hauthal (18) and Baiker (19) reviewed recent applications, with an emphasis on the potential use of supercritical fluids as solvents for green chemistry. In particular, supercritical carbon dioxide is nontoxic, nonflammable, available from renewable resources, and is thus of great interest for green chemistry. Fundamental studies have been conducted using heterogeneous catalysts in supercritical solvents for hydrogenation, partial oxidation, alkylation, esterification, amination, and other classical reactions.

Synthesis of fluoropolymers in supercritical CO_2 has been demonstrated by DeSimone and co-workers (20). Du Pont has constructed a \$40M, 2.5 million lb/year development test facility in North Carolina to produce fluorinated ethylene propylene (FEP) and perfluoroalkoxy resin (PFA) in supercritical carbon dioxide. The CO_2 solvent eliminates the use of chlorofluorocarbon solvents used in the typical synthesis.

4.3. Inherently Safer Syntheses and Intermediates: Replacement of Chlorine via an Electrochemical Synthesis. Electrochemical processes have several key features that may be exploited to produce greener synthetic pathways. For example, reaction conditions may be near ambient temperature and pressure, and that benign solvents such as alcohols may be used. Also, the electrode catalyst is easily recovered (compared to a homogeneous catalyst) and intermediate reagents may be regenerated via indirect electrolysis.

Organic intermediates are conventionally formed via activation with chlorine. The intermediates are subsequently functionalized, giving HCl as a by-product. BASF has commercialized an electrochemical alternative that eliminates the use of chlorine and the generation of HCl, and thus has less environmental impact (21). As illustrated for the synthesis of *p*-methoxybenzaldehyde from *p*-methoxy toluene by Steckhan and co-workers (22) the conventional synthesis is as follows:

$$CH_3{-}C_6H_4{-}OCH_3 + 2\,Cl_2 \longrightarrow CHCl_2{-}C_6H_4{-}OCH_3 + 2\,HCl \qquad (3)$$

$$CHCl_2{-}C_6H_4{-}OCH_3 + H_2O \longrightarrow CHO{-}C_6H_4{-}OCH_3 + 2\,HCl \qquad (4)$$

Four moles of HCl are produced per mole of product; the HCl is dilute in aqueous solution, making recovery of chlorine difficult and energy intensive.

The BASF process uses methanol as both solvent and reagent. Sodium benzene sulfonate is the supporting electrolyte.

$$CH_3{-}C_6H_4{-}OCH_3 + 2\,CH_3OH{-}4\,e^- \longrightarrow CH(OCH_3)_2{-}C_6H_4{-}OCH_3 + 4\,H^+ \qquad (5)$$

$$CH(OCH_3)_2{-}C_6H_4{-}OCH_3 + H_2O \rightarrow CHO{-}C_6H_4{-}OCH_3 + 2\,CH_3OH \qquad (6)$$

This is a direct electrosynthesis, so the selectivity and conversion are dependent on the electrode material. Note that methanol is also a reactant, and that it is regenerated in the electrochemical process, resulting in 100% atom efficiency. Chlorine and HCl are completely eliminated in this process. This process is commercialized at BASF AG, Ludwigshafen.

Additional examples of electrochemical synthesis at the commercial scale include production of adiponitrile by cathodic hydrodimerisation of acrylonitrile (the Monsanto process), operated by BASF in the United Kingdom (23). A thorough review of the state of industrial electroorganic synthesis is given by Degner (21).

4.4. Atom-Efficiency: Synthesis of Ibuprofen. Ibuprofen [2-(4′-isobutylphenyl) propionic acid] is a popular nonsteroidal drug that is used to reduce inflammation. Originally, it was manufactured by the Boots Company of England according to a process embodied by a patent (24). The traditional synthesis, illustrated in Figure 5 (15), resulted in a loss of 60% by weight of the atoms fed to the synthesis process; these become unwanted by-products. In other words, the atom efficiency was only 40%. Also of concern is the use of $AlCl_3$ as the catalyst in the Boots synthesis, which generates large amounts of aluminum trichloride hydrate that is landfilled. Thirty five-million pounds of waste were generated each year from the production of ibuprofen between 1960 and the mid-1980s.

In the mid-1980s, Hoechst Celanese merged with the Boots Company in a joint venture known as BHC to improve the production of ibuprofen. BHC Company has developed a greener synthesis process of ibuprofen that incorporates most of the atoms from the reactants into the products, thereby greatly reducing the amount of unwanted by-products (25,26). The green BHC synthesis is also shown in Figure 5. Like the original synthesis, the first step is the reaction of

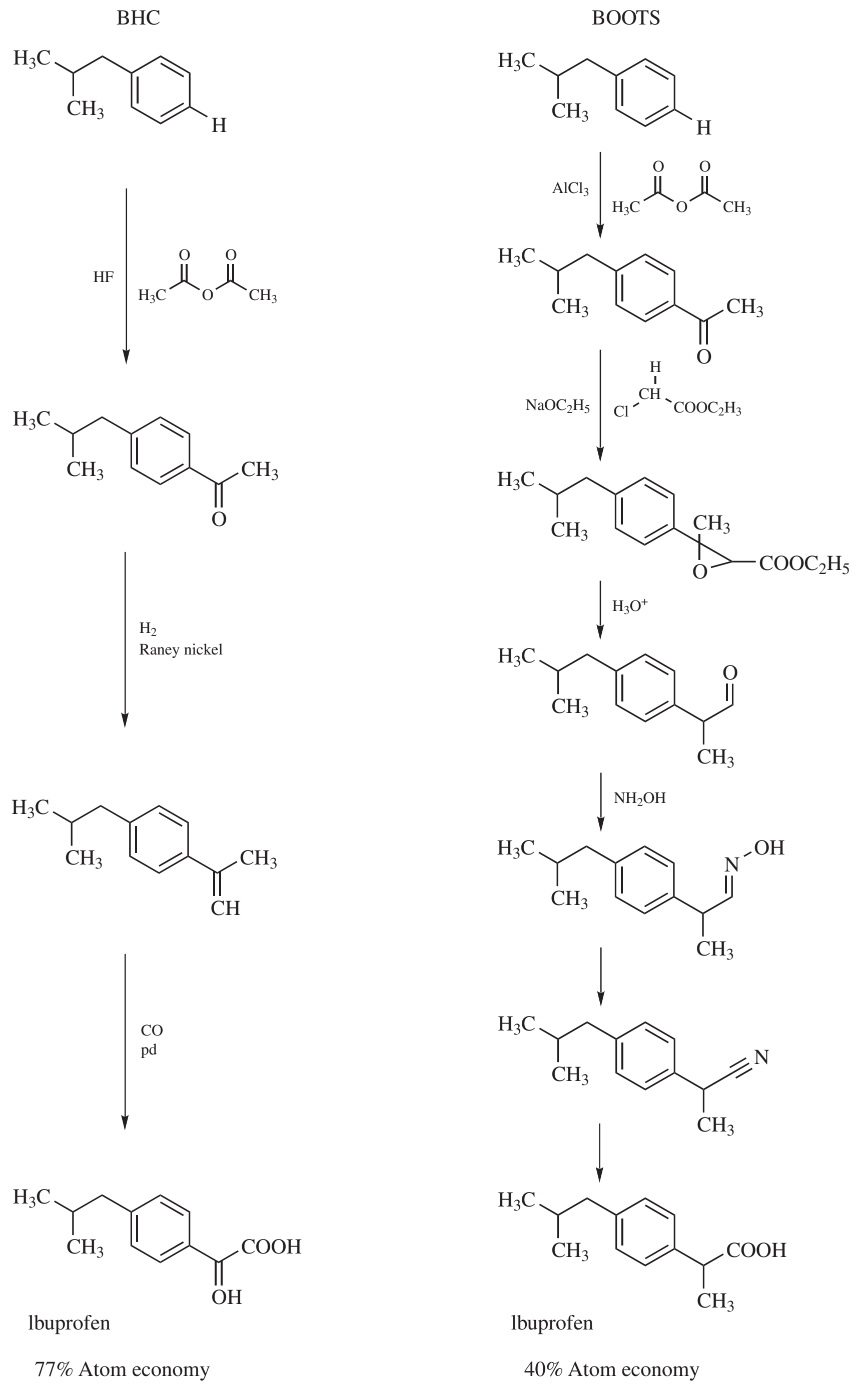

Fig. 5. Original and greener synthesis of ibuprofen. Used with permission from "Real-World Cases in Green Chemistry." Copyright © 2000 American Chemical Society.

isobutyl benzene with acetic anhydride, an acetylating agent. The reaction takes place in the presence of liquid hydrofluoric acid (HF), and a U.S. patent (26) describes a two-phase, countercurrent reactor–extractor system for optimizing the reaction residence time and recovery of the intermediate product, 4′-isobutyl acetophenone (4-IBAP). Step 2 of the green synthesis is hydrogenation of 4-IBAP using Raney nickel, and Step 3 is carbonylation to ibuprofen using CO and a palladium catalyst. Step 3 is the subject of U.S. patent (25).

This new method results in at least 77% atom economy (atoms incorporated into product), which is a significant increase from the 40% stated above. The atom economy of this green method approaches 99% if allowance is made for the recovery of acetic acid. Furthermore, the process allows for recovery of the three catalysts (HF in step 1, Raney nickel in step 2, and Pd). Therefore, this green process prevents millions of pounds of waste from being generated each year from the production of ibuprofen. The process was commercialized in Bishop, Tex. in 1992.

It should be noted that ibuprofen was originally a prescription only drug, and that the original synthesis was fixed as part of the Food and Drug Administration (FDA) approval process. As a safety measure, FDA restricts changes and modifications to drug manufacturing processes once the original process receives FDA approval. Development of the newer and greener synthetic process was thus not possible until the new patents were issued and new approvals obtained. This is an example of how a regulatory mechanism developed to insure consistency in the manufacturing approach (and therefore safety of the product) may hinder the implementation of green technology.

4.5. Design Safer Chemicals: Environmentally Safe Isothiazolone Marine Antifoulant. Increased hydrodynamic drag on a ship due to the buildup of marine organisms (barnacles, algae, and plants) on the hull causes several problems for the shipping industry, including an increase in dry docking and cleaning time, as well as increased fuel consumption that results in an increase of air pollution and depletion of nonrenewable fossil fuel. These problems can cost the shipping industry over $5.7 billion per year (15). The increased air pollution due to higher fuel consumption poses more stress on the environment and contributes to global warming (from CO_2) and higher levels of acid rain (from NO_2). Antifouling agents are used on the hull of the ship to prevent the buildup of marine organisms. Traditionally, tributyltin oxide (TBTO) compounds have been used in paints and hull coatings. While these compounds are effective antifouling agents, they are highly toxic, persist for long periods of time in the environment, and bioaccumulate in non-target organisms.

Sea-Nine 211 is an isothiazolone antifouling agent developed by Rohm and Haas in 1995 (15). It is less toxic, less persistent, and less likely to bioaccumulate in nontarget organisms as compared to tributyltin compounds. The half-life of isothiazolone is only 1 h in sediment and <24 h in seawater, compared to the 6–9 month half-life of tributyltin in sediments and 5-month half-life in seawater. Isothiazolone tends to bind to sediment, and is therefore less readily ingested by nontarget organisms. Sea-Nine comprises a family of isothiazalones. Sea-Nine 211 is 4,5-dichloro-2-*n*-octyl-4-isothiazalon-3-one. Jacobson and Willingham (27) review the properties and performance of Sea-Nine 211. Computer modeling using the Exposure Analysis Modeling System predicted a maximum concentration after leaching of only 10 ppt, well below maximum allowable limits.

4.6. Biodegradable Products: Thermal Polyaspartate Polymers. Millions of pounds of anionic polymers are used by industries each year, mainly as scale inhibitors to reduce the buildup of insoluble salts and dispersing agents. One of the most common polymers is polyacrylate (PAC). The production of PAC requires the use of >600 million lb of acrylic acid yearly. One problem with PAC is that it does not readily biodegrade, and therefore, must be removed from wastewater and the insoluble sludge must then be landfilled.

The Donlar Corporation (15) developed a process to produce a thermal polyaspartate (TPA). TPA is biodegradable, and therefore produces no waste that must be landfilled. TPA is being marketed as a scale inhibitor and antidispersing agent. Furthermore, TPA is used in agricultural applications to enhance nutrient uptake. TPA will also potentially replace the toxic amine corrosion inhibitors that are currently being used in oil production. The synthesis of TPA is a green process, in that it uses virtually no solvents and produces water as the only by-product.

4.7. Renewable Resources: Use of Renewable Fats and Oils. Hill (28) describes the use of oleochemicals as practiced by Cognis. Raw materials come from plants (coconut and oil palms; rapeseed; soybeans; sunflowers) and animals (tallow; lard). In 1998, ~14 million tonnes of oleochemical feedstocks were available. A variety of products are made from these raw materials. The surfactant cocomonoglyceride sulfate, used in cosmetic products, is obtained by transesterification of coconut oil. The market for dicarboxylic acids from oleochemicals, for use as polymer additives, is estimated at 100,000 tonn/year. Fatty acid esters are also used to produce lubricants. In 1997, 40,000 tonnes of biodegradable lubricants were consumed in Germany. See also CHEMURGY.

5. Financial Analysis of Green Chemistry

Implementing green chemistry and engineering technologies requires substantial fundamental research on synthesis, reactor design, catalysis, and improved unit operations. Such activities fall within the traditional realm of chemical and chemical engineering research, both in industry and academia. However, to meet the triple bottom line described in the section on Industrial Ecology, additional financial or economic analysis and risk assessment are required. Certain financial benefits of green chemistry (ie, reduced use of raw materials or energy, reduced disposal costs) may be quantified using traditional economic and financial metrics. Other, more long-term benefits, such as reduced risk, reduction in future liability, and reduced damage to the environment, are more difficult to quantify and the financial tools needed to quantify these benefits are still in development. Life Cycle Analysis (or Assessment, LCA), toxicology, and long-term risk assessment are among the tools being developed that may assist in evaluating the benefits of green chemistry projects. Allen and Shonnard (4) give a more extensive discussion in Chapter 2 of their book.

5.1. Life Cycle Analysis. Life cycle analysis (or life cycle assessment, LCA) is a method for developing quantitative predictions of the environmental impacts of a given chemical process. It is intended to aid in the evaluation of alternative manufacturing scenarios, thus, LCA is most useful in choosing between process options. For a process to be "green" (or more precisely, to determine which chemical manufacturing option is the "greenest"), LCA is a necessity. Herrchen and Klein (29) review life cycle assessment and its usefulness in assessing green chemical technology options. To perform a life cycle analysis, the material and energy flows of a process should be considered beginning from the point where raw materials are extracted from the environment, through transportation, processing, product manufacturing, distribution, and use, and finally ending at the point where the product is disposed, recycled, or remanufactured. LCA considers the environmental impacts of every aspect of manufacturing, including formation of by-products and use of solvents and auxiliaries. Although still in the development stages, LCA is a tool that has been in development and evaluation for over a decade. LCA alone, however, is inadequate to assess the economic and social impact of a given green technology. Additional factors must be considered; in particular, toxicology and assessment of risk associated with a product and the chemical process used in its manufacture are extremely important.

5.2. Toxicology and Environmental Risk Assessment. Risk and hazard assessment deal with both the safety of the plant and chemical process, as well as the likelihood that a given chemical or a chemical product will produce adverse effects in the environment. Toxicology is the specific science of deducing adverse affects within humans. Risk may be defined as the probability that an individual will suffer from exposure to a given chemical. Chemical risk is a function of the nature of the hazard as well as the level or intensity of the exposure. The fourth principle of Green Chemistry is to design inherently safer chemicals. Toxicology and risk assessment allow prediction and quantification of a variety of human and environmental risks based on the structure and properties of a compound. Toxicology and risk assessment are therefore critical to implement this principle. See TOXICOLOGY; HAZARD ANALYSIS AND RISK ASSESSMENT.

5.3. Total Cost Assessment (TCA). Total cost assessment is a method of accounting and assigning all costs of production to the unit or entity within the organization that generates those costs. Traditional engineering economics considers capital and operating costs, depreciation, etc, but TCA requires that additional cost and benefit categories be quantified. The Center for Waste Reduction Technologies of the American Institute of Chemical Engineers (30, www.aiche.org/cwrt) provides a guide to TCA, and a spreadsheet tool for performing TCA is available. The additional costs and benefits include so-called "hidden" manufacturing and overhead costs, liability costs, and "intangible" costs and benefits both internal and external. Hidden costs include cost of off-site waste management, permitting, manifesting, and sampling that are typically charged to corporate overhead accounts. Liability costs for future, unknown litigation must be considered to account for the possibility that an event will occur. Intangible costs and benefits may include improved worker morale associated with better or safer working conditions and improved corporate image.

Full justification and implementation of green chemistry projects will require a combination of traditional economic analysis, LCA, TCA, and risk assessment. This task may be difficult at the present time. As an example, Hertwig and co-workers (31) present a prototype software system that incorporates TCA and risk assessment to optimize the configuration of a plant complex producing sulfuric and phosphoric acids. The software also includes methods of assessing heat integration for energy efficiency.

6. Green Chemistry Education

The scope of green chemistry and engineering encompasses most if not all of the traditional educational and research disciplines (organic and inorganic chemistry, catalysis, chemical separations, thermodynamics and energy utilization, eg). The scope also includes financial analysis, safety, health, hazard and risk assessment, as well as the intersection of these with public policy. This makes green chemistry education a considerable challenge. Nevertheless, progress is being made. The U.S. EPA, in cooperation with the ACS, has an active program of workshops and textbook development for green chemistry and engineering. This EPA effort falls within the Office of Pollution Prevention and Toxics.

Several textbooks and handbooks have begun to appear; these are designed to supplement existing traditional courses, and to support new college level courses as well. Recent texts are cited in the bibliography, and include the following.

- *Introduction to Green Chemistry* (16). This book contains a wealth of examples and references to the literature on alternative synthetic pathways, alternative solvents, and many topics related to the 12 principles of green chemistry. While it does not contain problems like a traditional textbook, it does provide the green chemistry perspective on organic and inorganic chemistry.
- *Green Engineering: Environmentally Conscious Design of Chemical Processes* (4). This book is designed for advanced chemical engineering students. It includes material on life cycle assessment, risk assessment, estimating toxicological effects of individual chemicals, and analysis of process flowsheets to identify environmental impacts.
- *Handbook of Green Chemistry and Technology* (32). This book, available April 2002, provides a review and compilation of case studies on recent research and implementation of green chemical technology.
- *Pollution Prevention through Process Integration* (33). This focuses on analysis of mass exchange networks and heat exchange networks for process design and integration.
- *Pollution Prevention for Chemical Processes* (6). This book was one of the early efforts to incorporate pollution prevention into the undergraduate curriculum for chemical engineers. While it has some elements of the text by Allen and Shonnard (2002), the Allen and Rosselot text also has material directed at the more traditional aspects of the pollution prevention hierarchy.
- *Pollution Prevention: Methodology, Technology, and Practices* (5). This book illustrates the approach to pollution prevention distilled from experience at a major chemical manufacturer, du Pont. The book is

strongly oriented to industrial cases studies, techniques, and methods of valuation of products. The examples and case studies are strongly oriented toward the lower elements of the pollution prevention hierarchy (Fig. 3, which was developed by these authors) and thus the amount of the book that is truly green chemistry and green engineering, as defined in this article, is somewhat small. Nevertheless it provides information about a spectrum of pollution prevention activities, including information about costs and savings. This is not a traditional textbook, but would be an excellent supplement for an advanced course in chemical engineering process design and economics.

Other educational programs, case studies, and green chemistry and engineering materials are appearing on-line. Many of these can be accessed through the EPA Green Chemistry web site (www.epa.gov/opptintr/greenchemistry) or the Green Engineering web site (www.epa.gov/opptintr/greenengineering), under the Office of Pollution Prevention and Toxics. The ACS provides access to its green chemistry educational materials through the ACS web site (http://chemistry.org/education). Other educational materials and resources are referenced by organizations described in the concluding section of this article, including the Green Chemistry Institute and the Zero Waste Alliance.

7. Summary and Prospects

The greening of a chemical product or process may be accomplished through a number of means, including improved synthetic procedures, better catalysts, novel process design, use of renewable raw materials, discovery of less toxic products, use of environmentally benign solvents, or design of recyclable materials. Thus, the concept of green chemistry can be invoked in any aspect of fundamental or applied chemistry and chemical engineering, as well as toxicology and risk assessment.

In reality, it is difficult to declare a product or process as being completely “green”; in practice, a comparison must be made to determine if a choice of product–process is “greener” than other alternatives. Therefore, financial and social metrics must also be brought to bear alongside fundamental scientific data in all efforts to make greener chemical products and processes. Many of these metrics deal with long time frames and may not appear consistent with short economic and financial time horizons.

Achieving the goals of green chemistry requires cooperation among numerous stakeholders. For technology development, green chemistry requires an interdisciplinary approach including chemists, biochemists, biologists, engineers, statisticians, and health care professionals. Implementation of projects requires a cooperation of private industry and policy makers from local, state, and federal government. An example of industry-government cooperation is the U.S. EPA/du Pont program to minimize wastes at the Chambers Works plant (5,34). EPA and du Pont teamed to identify pollution prevention opportunities at this site. The goal for du Pont was to reduce or prevent pollution in several processes at this site, which resulted in savings and earnings of nearly

$15M/year. The goal for EPA was to develop and refine methodologies for identifying and evaluating pollution prevention technologies that would be applicable to other industries.

Other collaborations, both voluntary and mandatory, will support the adoption of green chemical technology. The International Union of Pure and Applied Chemistry (IUPAC; www.iupac.org) strategic plan incorporates a number of goals related to green chemistry (2), and IUPAC has sponsored a report on synthetic pathways for green chemistry. The Organization for Economic Cooperation and Development (OECD) and IUPAC cosponsored a workshop on Sustainable Chemistry in 1998.

The Green Chemistry Institute (GCI, see http://www.acs.org/) is a nonprofit organization that promotes green chemistry through conferences, symposia, education, outreach, and support of research. Organized in 1997 as an independent body comprising members from academia, national laboratories, and industry, the GCI recently formed an alliance with the American Chemical Society. GCI and ACS sponsor Green Chemistry Institute affiliate chapters with a number of universities around the world.

Another example of the connection between green chemistry and sustainability is the Zero Waste Alliance (ZWA) (www.zerowaste.org), located in Portland, Oregon. The stated purpose of ZWA is to support other organizations, improve profitability, competitiveness, and environmental performance. ZWA is organized around expertise at the University of Oregon and Portland State University, but it has developed a collection of volunteers and experts from the United States National Laboratories, universities, and consultants. The web page of the ZWA provides additional references and resources for green chemistry and supporting tools such as life cycle analysis and total cost accounting.

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