

ARTICLES

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Received February 4, 2002

ABSTRACT

Over the course of the past decade, green chemistry has demonstrated how fundamental scientific methodologies can protect human health and the environment in an economically beneficial manner. Significant progress is being made in several key research areas, such as catalysis, the design of safer chemicals and environmentally benign solvents, and the development of renewable feedstocks. Current and future chemists are being trained to design products and processes with an increased awareness for environmental impact. Outreach activities within the green chemistry community highlight the potential for chemistry to solve many of the global environmental challenges we now face. The origins and basis of green chemistry chart a course for achieving environmental and economic prosperity inherent in a sustainable world.

Introduction

Green chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances.¹ Advances in green chemistry address both obvious hazards and those associated with such global issues as climate change, energy production, availability of a safe and adequate water supply, food production, and the presence of toxic substances in the environment. Alternative blowing agents replace millions of pounds of chlorofluorocarbons (CFCs) in insulating

foams, new energy sources lessen our dependence on fossil fuels, and pesticides are designed to be more selective and less persistent than traditional organic pesticides. The challenge of sustainability will be met with new technologies that provide society with the products we depend on in an environmentally responsible manner.

The activities in green chemistry research, education, industrial implementation, awards, and outreach are all based on the fundamental definition of green chemistry as stated above. The concept of “design” in the definition is an essential element in requiring the conscious and deliberative use of a set of criteria, principles, and methodologies in the practice of green chemistry. Because green chemistry is intentionally designed, it is definitionally impossible to do green chemistry by accident. The phrase the “use or generation” implies the requirement of life-cycle considerations.² Green chemistry can be utilized anywhere in the life cycle, from feedstock origins to beyond end of useful life. The term “hazardous” is used in its broadest context including physical (e.g., explosion, flammability), toxicological (e.g., carcinogenic, mutagenic), and global (e.g., ozone depletion, climate change).

The design of environmentally benign products and processes may be guided by the 12 Principles of Green Chemistry (Figure 1).³ These principles are a categorization of the fundamental approaches taken to achieve the green chemistry goals of benign products and processes, and have been used as guidelines and design criteria by molecular scientists. Like all multiparameter systems, tradeoffs and balances will be made in striving toward optimization based on the specific circumstances of application. The current state-of-the-art in green chemistry has been reached due to advances in research, implementation, education, and outreach over the past decade.

History

In the United States, the Pollution Prevention Act of 1990⁴ established source reduction as the highest priority in solving environmental problems. Passage of this act signaled a move away from the “command and control” response to environmental issues and toward pollution prevention as a more effective strategy that focused on preventing waste from being formed in the first place. Shortly after the passage of the Pollution Prevention Act, it was recognized that a variety of disciplines needed to be involved in source reduction. This recognition extended to chemists, the designers of molecular structures and

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[†] This paper is dedicated to Dr. Roger Garrett, whose fundamental work and inspired vision provided the foundation of green chemistry.

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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 in the process 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, etc.) 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 of 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 further developed to allow for real-time, in-process monitoring and control prior to 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.

FIGURE 1. The 12 Principles of Green Chemistry.

transformations. In 1991, the Office of Pollution Prevention and Toxics in the U.S. Environmental Protection Agency launched the first research initiative of the Green Chemistry Program, the Alternative Synthetic Pathways research solicitation.⁵ Foundational work in chemistry and engineering at the National Science Foundation's program on Environmentally Benign Syntheses and Processes was launched in 1992, and formed a partnership with EPA through a Memorandum of Understanding that same year. In 1993, the EPA program officially adopted the name "U.S. Green Chemistry Program". Since its inception, the U.S. Green Chemistry Program has served as a focal point for major activities within the United States, such as the Presidential Green Chemistry Challenge Awards and the annual Green Chemistry and Engineering Conference.

In the first half of the 1990s, both Italy⁶ and the United Kingdom⁷ launched major initiatives in green chemistry. Several researchers in the U.K. established research and education programs in green chemistry. In Italy, a multiuniversity consortium (INCA) featured research on green chemistry as one of its central themes. During the last half of the decade, Japan organized the Green and Sustainable Chemistry Network (GSCN),⁸ with an emphasis on promoting research and development on green and sustainable chemistry. The first books, papers, and symposia on the subject of green chemistry were introduced in the 1990s. The inaugural edition of the journal *Green Chemistry*, sponsored by the Royal Society of Chemistry, appeared in 1999.⁹ Research groups in many countries quickly coalesced, and adoption by industry was evident but difficult to quantify.

In 1995, the U.S. Presidential Green Chemistry Challenge Award was announced as a way of recognizing accomplishments by industry, academia, and government in green chemistry. The five awards first given in 1996,

along with the numerous nominations for the award, provided a first, if understated, measure of adoption of green chemistry. Japan, Italy, the U.K., Australia, and other nations have adopted green chemistry awards for the purpose of highlighting the environmental and economic accomplishments of green chemistry.

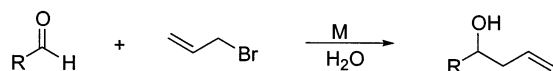
Current Status

Since its inception in 1991, green chemistry has grown into a significant internationally engaged focus area within chemistry. The importance of green chemistry was recently highlighted in a cover story in *Chemical and Engineering News*.¹⁰ Major research, education, and outreach initiatives have been established around the globe.

Research. Research programs and centers located in countries in the Americas, Europe, Asia/Pacific, and Africa are focusing efforts around the principles of green chemistry. The breadth of this research is very wide and incorporates areas such as polymers, solvents, catalysis, biobased/renewables, analytical method development, synthetic methodology development, and the design of safer chemicals. Excellent research is being conducted within each of these areas that strives to incorporate one or more of the 12 Principles of Green Chemistry.

Polymers. The nature of the hazards that can be posed by polymers in their manufacture, use, and disposal has been widely recognized in recent years, as have the green chemistry methodologies that can be used to address these hazards.¹¹ Research on renewable feedstocks and biobased transformations, structural design, and design for degradability are all promising areas.^{12–15} Carbon dioxide, for example, is a renewable feedstock that has been recovered from flue gas and, in its supercritical state, combined with pastes from fly ash to yield products such as roofing tiles and wallboard.¹⁶ Polymers derived from

Scheme 1. Metal-Mediated Reaction of an Aldehyde and Allyl Halide in Water



carbohydrate feedstocks such as soy¹⁷ and corn¹⁸ are found in consumer products like automobiles and food packaging. Microbial fermentation has been used to convert glucose to a biodegradable polymer.¹⁹

Solvents. The design of environmentally benign solvents and solventless systems has been one of the most active areas of green chemistry over the past 10 years. Solvents are highly regulated and used in large quantities. Organic solvents pose a particular concern to the chemical industry because of the sheer volume used in synthesis, processing, and separations. Many are classified as volatile organic compounds (VOCs) or hazardous air pollutants (HAPs) and are flammable, toxic, or carcinogenic.

Breakthroughs in the use of supercritical fluids such as carbon dioxide have met with success in the research laboratory as well as commercially. Supercritical fluids offer a number of benefits, such as the potential to combine reaction and separation processes and the ability to tune the solvent through variations in temperature and pressure. In the supercritical fluids area, CO₂ has received the most attention^{20–26} because its critical temperature and pressure ($T_c = 31.1\text{ }^\circ\text{C}$, $P_c = 74\text{ bar}$) are more accessible than those of other solvents (water, for example, has $T_c = 374\text{ }^\circ\text{C}$ and $P_c = 221\text{ bar}$). CO₂ offers numerous advantages as a benign solvent: it is nontoxic, nonflammable, and inexpensive, and can be separated from the product by simple depressurization. Applications of supercritical CO₂ are found in the dry cleaning industry, where CO₂ replaces perchloroethylene as a solvent;^{27,28} in semiconductor manufacturing, where the low surface tension of supercritical CO₂ avoids the damage caused by water in conventional processing;²⁹ and in chemical processing.³⁰

The use of supercritical CO₂ as a reaction medium in organic synthesis provides an excellent example of the evolution from fundamental academic research into a commercial process. In collaboration with Thomas Swan & Co. Ltd,³¹ researchers at the University of Nottingham³² developed synthetic methodologies in supercritical CO₂ that are being employed in a new supercritical fluid plant in the U.K., with a capacity up to 1000 tons per year. Conventional solvents are replaced with supercritical fluids in such key technologies as hydrogenation, Friedel–Crafts alkylations and acylations, hydroformylations, and etherification.

The use of water as a solvent in ways previously not realized has been an active area of research in green

chemistry (Scheme 1).^{33,34} A number of classic organic reactions, traditionally run in organic solvents, can be carried out in water with the proper design of catalysts and reaction conditions. Even variants of the Grignard reaction, notoriously sensitive to water, can be run in an aqueous solvent using a variety of metals, such as indium³⁵ and zinc.³⁶ The use of an obviously benign and inexpensive solvent like water could yield significant green chemistry benefits if challenges of energy and separations can be met.

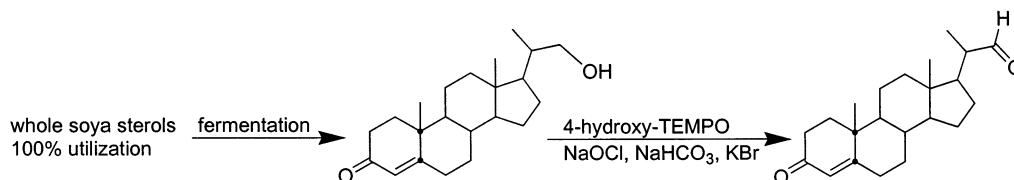
Ionic liquids, a relatively new area of solvent investigation, are attractive because of their negligible vapor pressure and their use in polar systems to generate new chemistries.^{37–40} A plethora of ionic liquids can be produced by varying the cations and anions, permitting the synthesis of ionic liquids tailored for specific applications. While questions of intrinsic hazard must still be answered for this class of solvents, the potential for the design of next generation ionic liquids holds significant promise for improved environmental benefits.

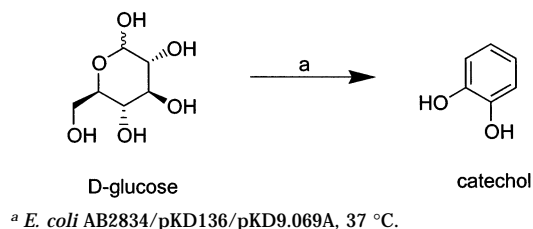
Fluorous solvent systems have demonstrated particular advantages in synthetic systems.^{41–43} Fluorous systems are particularly appealing in fluorous biphasic catalysis in which the homogeneous catalyst and the product reside in separate phases, thereby eliminating the need for energy-intensive separations. In addition to efficiency, fluorous biphasic systems may reduce accident potential by eliminating the possibility of runaway exothermic reactions.

Catalysis. The area of catalysis is sometimes referred to as a “foundational pillar” of green chemistry.⁴⁴ Catalytic reactions^{45–51} often reduce energy requirements and decrease separations due to increased selectivity; they may permit the use of renewable feedstocks or minimize the quantities of reagents needed. There is little doubt that the 2001 Nobel Prize-winning work of Sharpless, Noyori, and Knowles met many green chemistry goals.⁵² Their research on catalytic asymmetric synthesis has been crucial in producing single enantiomer compounds, particularly for the pharmaceutical industry.

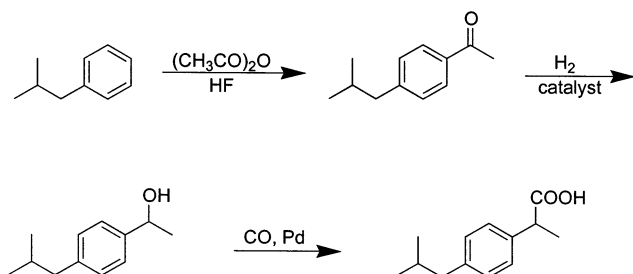
Catalysis often permits the use of less toxic reagents, as in the case of oxidations using hydrogen peroxide in place of traditional heavy metal catalysts.⁵³ Renewable resources, such as soya sterols⁵⁴ (Scheme 2) and glucose,⁵⁵ serve as feedstocks when catalytic methods are employed. Recently, water has been split into oxygen and hydrogen using a photocatalyst that absorbs light in the visible range.⁵⁶ While still at the research stage, this technology has the potential to provide an efficient source of hydrogen for use in fuel cells. Hydrogen fuel cells in cars would greatly reduce air pollution, as the oxidation product

Scheme 2. Synthesis of Bisoraldehyde from a Renewable Feedstock



Scheme 3. Synthesis of Catechol from Glucose Using Genetically Modified *E. coli*

Scheme 4. Atom-Efficient Synthesis of Ibuprofen



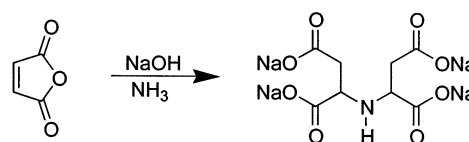
(water) is environmentally benign.⁵⁷ The application of catalysis to dematerialization, reduced toxicity systems, benign and renewable energy systems, and efficiency makes it a central focus area for green chemistry research.

Biobased/Renewables. The utilization of benign, renewable feedstocks is a needed component of addressing the global depletion of resources. More than 98% of all organic chemicals are derived from petroleum.⁵⁸ Achieving a sustainable chemical industry dictates switching from depleting finite sources to renewable feedstocks.

Research in this area has focused on both the macro and molecular levels. The carbohydrate economy provides a rich source of feedstocks for synthesizing commodity⁵⁹ and specialty chemicals. For example, agricultural wastes have been converted into useful chemical intermediates such as levulinic acid,⁶⁰ alcohols, ketones, and carboxylic acids.⁶¹ Shells from crabs and other sea life serve as a valuable and plentiful source of chitin, which can be processed into chitosan, a biopolymer with a wide range of potential applications that are being currently explored for use in the oil-drilling industry.⁶² At the molecular level, genetic engineering produces valuable chemical products via nontraditional pathways. Glucose yields catechol and adipic acid⁶³ (Scheme 3) using genetically engineered *Escherichia coli*. Recombinant *Saccharomyces* yeasts convert both glucose and xylose, present in cellulosic biomass, into ethanol.⁶⁴ Carbon dioxide is also a renewable feedstock that has been incorporated into polymers.⁶⁵

Synthetic methodologies are being designed in both academia and industry that are more environmentally benign and more atom efficient.^{66–68} New synthetic protocols have eliminated waste streams, improved worker safety, and increased yield in pharmaceutical processes (Scheme 4).^{69–71} Polymer synthesis has been redesigned to eliminate the use of highly toxic reagents and organic solvents.⁷² The utilization of biomimetic approaches,^{73,74} cascading reactions,^{75,76} and molecular self-assembly^{77,78}

Scheme 5. Synthesis of Sodium Iminodisuccinate, a Biodegradable Chelating Agent



represents some of the new chemistries being developed with green chemistry goals incorporated at the design stage.

Analytical Methods. Analytical chemistry played a central role in the environmental movement by detecting, measuring, and monitoring environmental contaminants. As we move toward prevention and avoidance technology, analytical methods are being incorporated directly into processes in real time in an effort to minimize or eliminate the generation of waste before it is formed.^{79,80} Continuous process monitoring assists in optimizing the use of feedstocks and reagents while minimizing the formation of hazardous substances and unwanted byproducts. In addition, analytical methodologies have, themselves, historically used and generated hazardous substances and are being redesigned with green chemistry goals in mind by using benign mobile and stationary phases and placing greater emphasis on in situ analysis.

Design of Safer Chemicals. Design for reduced hazard is a green chemistry principle that is being achieved in classes of chemicals ranging from pesticides to surfactants, from polymers to dyes.^{81–83} The principles of mechanistic toxicology allow for molecular design for reduced toxicity. Pesticides have been designed that are more selective and less persistent⁸⁴ than many traditional organic pesticides. Surfactants (Scheme 5)⁸⁵ and polymers^{18,86} have been developed to degrade in the environment at the end of their useful lifetime. Dyes without heavy metals⁸⁷ are finding applications in the textile industry. Understanding the physicochemical properties that underlie even global hazards allows for manipulation to reduce those hazards. The systematic development and application of design rules for reduced hazard is one of the most important challenges facing green chemistry.

Education. In the development of green chemistry, it has been realized that the next generation of scientists need to be trained in the methodologies, techniques, and principles that are central to green chemistry. Leadership from professional societies, notably the American Chemical Society and the Royal Society of Chemistry, in collaboration with the educational community, has resulted in a nascent yet impressive collection of educational materials and programs that continues to grow. Recently, the German and Japanese Chemical Societies have assumed leadership roles in promoting green chemistry education within their own countries. Educational initiatives in green chemistry include textbooks, case studies, laboratory experiments, student organizations, summer schools, faculty training, secondary teacher training, resource tools, educational symposia, and professional workshops.^{3,88–93} Within the past few years, the first



FIGURE 2. Countries with GCI chapters: Argentina/Brazil/Mexico, Australia, Canada, Estonia, Hungary, Italy, India, Japan, Nepal, New Zealand, Northern Ireland, People's Republic of China, Senegal (West Africa Chapter), South Africa, Spain, Sweden, Taiwan, United Kingdom.

undergraduate program in green chemistry,⁹⁴ the first Masters in green chemistry,^{95,96} and the first green chemistry Ph.D.⁹⁷ have been established. Courses for professional chemists are being organized through scientific societies as well as within specific companies. Educational training to developing nations has been identified as an area of engagement for IUPAC.⁹⁸ Green chemistry may also prove to be an effective tool for recruitment and retention of students to the molecular sciences in light of the concern that many students have for environmental issues.

Outreach. Since, fundamentally, green chemistry is a change in perspective and thinking in the way that chemical design is approached, an important element to achieve that change is the effective communication of green chemistry. This is being done through a variety of approaches including the establishment of networks and institutes, journals and books, conferences and symposia, awards and recognition, and national and multinational government engagement.

Networks and Institutes. The Green Chemistry Institute (GCI), begun in the mid-1990s, has grown to include chapters in 20 nations (Figure 2).⁹⁹ GCI's mission "to promote green chemistry research, education, and outreach" serves as a catalyst for a wide range of green chemistry activities internationally. The Green Chemistry Network in the U.K.,⁷ the Green and Sustainable Chemistry Network in Japan,⁸ and INCA in Italy⁶ serve similar purposes while also engaging in industrial and educational programs.

Journals. The journal *Green Chemistry*⁹ was launched by the Royal Society of Chemistry with a central focus of communicating peer-reviewed research and other advances in green chemistry to the scientific community. Journals including *Clean Products and Processes*, the *Journal of Cleaner Production*, and the *Journal of Industrial Ecology* all have significant coverage of green chemistry. Long established journals such as *Environmental Science & Technology* and *The Journal of Chemical Education* have devoted sections to green chemistry. Within the mainstream chemical literature, however, only a small fraction of the research relevant to green chemistry is identified as such.

Conferences and Symposia. Green chemistry symposia are incorporated throughout the programs of the major chemical societies and demonstrate the pervasiveness of green chemistry within technical areas. Conferences highlighting green chemistry, such as the Annual Green Chemistry and Engineering Conference in Washington, DC, the Annual Green Chemistry in China Conference, and the biennial Green Chemistry Gordon Research Conference, are held on a regular basis. Other conferences have been topical, such as IUPAC's Chemrawn XIV in June 2001 and the Conference on Green Chemistry Measures and Metrics in Germany, also in 2001. An international symposium on "Green Solvents for Catalysis" will be held in Bruchsal, Germany, in October 2002.

Awards and Recognition. Awards and recognition programs serve to highlight the success of green chemistry. The U.S. Presidential Green Chemistry Challenge Award,

currently in its sixth year, has received nominations from hundreds of companies. The winners of this award exemplify the impressive gains achieved in protecting human health and the environment through the implementation of green chemistry technologies. In June 2001, U.S. President George W. Bush called on "leaders in industry and education to pursue the principles of green chemistry to achieve environmental and economic prosperity".¹⁰⁰ The green chemistry awards in Italy, Australia, Japan, and the U.K. provide excellent examples of how cutting-edge research and industrial implementation of green chemistry are having a real-world impact.

Government Engagement. Multinational engagement, both governmental and nongovernmental, has increased. The Organization for Economic Cooperation and Development (OECD) launched an initiative in sustainable chemistry in 1998, and the United Nations Industrial Development Organization has more recently focused on green chemistry in conferences in Trieste, Italy, and Buenos Aires, Argentina. IUPAC has been actively engaged through a multidivisional green chemistry initiative as well as through the Chemrawn Committee's World Conference on Green Chemistry that attracted participation from 31 countries around the world.

Future Challenges

The future challenges facing green chemistry are as diverse as the scientific imagination and address the broadest issues of sustainability. Because of this breadth, it should be no surprise that a number of these challenges are being pursued for reasons ranging from economic to scientific.

Research Challenges. The challenges to research in achieving green chemistry principles are numerous, and a detailed discussion of each is not possible. However, a listing of some of the challenges provides an illustration of current issues and may stimulate thinking on other challenges that should be included:

- Transformations utilizing energy rather than material.
- Efficient splitting of water by visible light.
- Solvent systems that effect efficient heat and mass transfer while catalyzing reactions and intrinsically aiding in product separation.
- Development of a synthetic methodologies "toolbox" that is both atom economical and benign to human health and the environment.
- Plastics and polymers designed for innocuous degradation through the use of additives-free design.
- Materials design for recycle/reuse decisions based on embedded entropy.
- Development of "preventative toxicology" where increasing knowledge of biological and environmental mechanisms of action are continuously incorporated into the design of chemical products.
- Less energy-intensive manufacture of photovoltaic cells that are more efficient.
- Development of noncombustion, non-material-intensive energy sources.

- Value-added consumptive/fixation uses for CO₂ and other greenhouse gases at high volume.
- Transformations preserving sensitive functionality without the use of protecting groups.
- Development of surfaces and materials that are durable and do not require coatings and cleaners.

Implementation Challenges. The discovery of more environmentally benign technologies at the research stage does not guarantee that they will be adopted on an industrial scale. A number of barriers hinder the adoption of newer technologies that prevent pollution. Adoption of environmentally benign processes may be facilitated by the following:

- Flexibility in regulations.
- Tax incentives for implementing cleaner technologies.
- Research programs to facilitate technology transfer among academic institutions, government, and industry.
- Patent life extensions for cleaner process optimization.

Education Challenges. Students at all levels can be introduced to the philosophy and practice of green chemistry. Educators need appropriate tools, training, and materials to effectively integrate green chemistry into their teaching and research. Important steps to be taken to advance green chemistry within the curriculum include the following:

- Systematic recognition of hazard/toxicity as a physical/chemical property of molecular structure that can be designed and manipulated.
- Development and utilization of practical laboratory experiments to illustrate green chemistry principles.
- Balanced equations in organic textbooks and replacement of "yield" with "atom economy".
- Introduction of the basic concepts of chemical toxicology and the molecular basis of hazard.
- Incorporation of green chemistry topics on professional certification exams.
- Teacher reference materials for incorporating green chemistry into existing courses.
- Education of legislators on the benefits of green chemistry.

Conclusion

The growth of green chemistry over the course of the past decade needs to increase at an accelerated pace if molecular science is to meet the challenges of sustainability. It has been said that the revolution of one day becomes the new orthodoxy of the next. When the 12 Principles of Green Chemistry are simply incorporated as an integral part of everyday chemistry, there will no longer be a need for the focusing, highlighting, and moniker of green chemistry. And when that day comes, the challenges that chemistry will meet cannot be imagined.

Note: Many outstanding examples of green chemistry may be found in the literature. This reference list is not meant to be comprehensive, but includes a representative selection of green chemistry technologies.

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AR010065M