

## Synthetic pathways and processes in green chemistry. Introductory overview\*

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<sup>‡</sup>To whose memory this paper is dedicated. Joe Breen was a leading pioneer of green chemistry. Following his retirement from EPA, Office of Pollution Prevention and Toxics, where he worked on asbestos, dioxins, and pollution prevention, Joe became Executive Director of the Green Chemistry Institute, a not-for-profit organization promoting environmentally benign syntheses and processing. His premature death on 19 July 1999 created a void in the Working Party team, but encouraged all of us to continue our mission, having in mind his passion for this work and his exquisite friendship.

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## **GREEN CHEMISTRY IN THE INTERNATIONAL CONTEXT**

It has come to be recognized in recent years, that the science of chemistry is central to addressing the problems facing the environment. Through the utilization of the various subdisciplines of chemistry and the molecular sciences, there is an increasing appreciation that the emerging area of green chemistry\* is needed in the design and attainment of sustainable development. A central driving force in this increasing awareness is that green chemistry accomplishes both economic and environmental goals simultaneously through the use of sound, fundamental scientific principles.

Recently, a basic strategy has been proposed for implementing the relationships between industry and academia, and hence, funding of the research that constitutes the engine of economic advancement; it is what many schools of economics call the “triple bottom line” philosophy, meaning that an enterprise will be economically sustainable if the objectives of environmental protection, societal benefit, and market advantage are all satisfied [1]. Triple bottom line is a strong idea for evaluating the success of environmental technologies. It is clear that the best environmentally friendly technology or discovery will not impact on the market if it is not economically advantageous; in the same way, the market that ignores environmental needs and human involvement will not prosper. This is the challenge for the future of the chemical industry, its development being strongly linked to the extent to which environmental and human needs can be reconciled with new ideas in fundamental research.

On the other hand, it should be easy to foresee that the success of environmentally friendly reactions, products, and processes will improve competitiveness within the chemical industry. If companies are able to meet the needs of society, people will influence their own governments to foster those industries attempting such environmental initiatives. Of course, fundamental research will play a central role in achieving these worthy objectives. What we call green chemistry may in fact embody some of the most advanced perspectives and opportunities in chemical sciences.

It is for these reasons that the International Union of Pure and Applied Chemistry (IUPAC) has a central role to play in advancing and promoting the continuing emergence and impact of green chemis-

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\*The terminology “green chemistry” or “sustainable chemistry” is the subject of debate. The expressions are intended to convey the same or very similar meanings, but each has its supporters and detractors, since “green” is vividly evocative but may assume an unintended political connotation, whereas “sustainable” can be paraphrased as “chemistry for a sustainable environment”, and may be perceived as a less focused and less incisive description of the discipline. Other terms have been proposed, such as “chemistry for the environment” but this juxtaposition of keywords already embraces many diversified fields involving the environment, and does not capture the economic and social implications of sustainability. The Working Party decided to adopt the term green chemistry for the purpose of this overview. This decision does not imply official IUPAC endorsement for the choice. In fact, the IUPAC Committee on Chemistry and Industry (COCI) favors, and will continue to use sustainable chemistry to describe the discipline.

try. When we think about how IUPAC furthers chemistry throughout the world, it is useful to refer to IUPAC's Strategic Plan. This plan demonstrates the direct relevance of the mission of IUPAC to green chemistry, and explains why there is growing enthusiasm for the pursuit of this new area as an appropriate activity of a scientific Union. The IUPAC Strategic Plan outlines among other goals:

- IUPAC will serve as a scientific, international, nongovernmental body in objectively addressing global issues involving the chemical sciences. Where appropriate, IUPAC will represent the interests of chemistry in governmental and nongovernmental forums.
- IUPAC will provide tools (e.g., standardized nomenclature and methods) and forums to help advance international research in the chemical sciences.
- IUPAC will assist chemistry-related industry in its contributions to sustainable development, wealth creation, and improvement in the quality of life.
- IUPAC will facilitate the development of effective channels of communication in the international chemistry community.
- IUPAC will promote the service of chemistry to society in both developed and developing countries.
- IUPAC will utilize its global perspective to contribute toward the enhancement of education in chemistry and to advance the public understanding of chemistry and the scientific method.
- IUPAC will make special efforts to encourage the career development of young chemists.
- IUPAC will broaden the geographical base of the Union and ensure that its human capital is drawn from all segments of the world chemistry community.
- IUPAC will encourage worldwide dissemination of information about the activities of the Union.
- IUPAC will assure sound management of its resources to provide maximum value for the funds invested in the Union.

Through the vehicle of green chemistry, IUPAC can engage and is engaging the international community in issues of global importance to the environment and to industry, through education of young and established scientists, the provision of technical tools, governmental engagement, communication to the public and scientific communities, and the pursuit of sustainable development. By virtue of its status as a leading and internationally representative scientific body, IUPAC is able to collaborate closely in furthering individual national efforts as well as those of multinational entities.

An important example of such collaboration in the area of green chemistry is that of IUPAC with the Organization for the Economical Cooperation and Development (OECD) in the project on "Sustainable Chemistry", aimed at promoting increased awareness of the subject in the member countries. During a meeting of the Environment Directorate (Paris, 6 June 1999), it was proposed that United States and Italy co-lead the activity, and that implementation of five recommendations to the member countries be accorded the highest priority, namely:

- research and development
- awards and recognition for work on sustainable chemistry
- exchange of technical information related to sustainable chemistry
- guidance on activities and tools to support sustainable chemistry programs
- sustainable chemistry education

These recommendations were perceived to have socio-economic implications for worldwide implementation of sustainable chemistry. How IUPAC and, in particular, its Divisions can contribute to this effort is under discussion. IUPAC is recognized for its ability to act as the scientific counterpart to OECD for all recommendations and activities. Although the initiatives being developed by the OECD are aimed primarily at determining the role that national institutions can play in facilitating the implementation and impact of green chemistry, it is recognized that each of these initiatives also has an important scientific component. Whether it is developing criteria or providing technical assessment for awards and recognition, identifying appropriate scientific areas for educational incorporation, or providing scientific insight into the areas of need for fundamental research and development, IUPAC can

play and is beginning to play an important role as an international scientific authority on green chemistry.

Other multinational organizations including, among others, the United Nations, the European Union, and the Asian Pacific Economic Community, are now beginning to assess the role that they can play in promoting the implementation of green chemistry to meet environmental and economic goals simultaneously. As an alternative to the traditional regulatory framework often implemented as a unilateral strategy, multinational governmental organizations are discovering that green chemistry as a nonregulatory, science-based approach, provides opportunities for innovation and economic development that are compatible with sustainable development. In addition, individual nations have been extremely active in green chemistry and provide plentiful examples of the successful utilization of green chemistry technologies. There are rapidly growing activities in government, industry, and academia in the United States, Italy, the United Kingdom, the Netherlands, Spain, Germany, Japan, China, and many other countries in Europe and Asia, that testify to the importance of green chemistry to the future of the central science of chemistry around the world.

Organizations and Commissions currently involved in programs in green chemistry at the national or international level include, for example:

- U.S. Environmental Protection Agency (EPA), with the “Green Chemistry Program” which involves, among others, the National Science Foundation, the American Chemical Society, and the Green Chemistry Institute;
- European Directorate for R&D (DG Research), which included the goals of sustainable chemistry in the actions and research of the European Fifth Framework Programme;
- Interuniversity Consortium “Chemistry for the Environment”, which groups about 30 Italian universities interested in environmentally benign chemistry and funds their research groups;
- UK Royal Society of Chemistry, which promotes the concept of green chemistry through a “UK Green Chemistry Network” and the scientific journal *Green Chemistry*;
- UNIDO-ICS (International Centre for Science and High Technology of the United Nations Industrial Development Organization) which is developing a global program on sustainable chemistry focusing on catalysis and cleaner technologies with particular attention to developing and emerging countries (the program is also connected with UNIDO network of centers for cleaner production); and
- Monash University, which is the first organization in Australia to undertake a green chemistry program.

## THE CONCEPT OF GREEN CHEMISTRY

### Definition of green chemistry

The term green chemistry, as adopted by the Working Party, is defined as:

The invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances [2].

While this short definition appears straightforward, it marks a significant departure from the manner in which environmental issues have been considered or ignored in the up-front design of the molecules and molecular transformations that are at the heart of the chemical enterprise.

Looking at the definition of green chemistry, the first thing one sees is the concept of *invention* and *design*. By requiring that the *impacts* of chemical products and chemical processes are included as design criteria, the definition of green chemistry inextricably links hazard considerations to performance criteria.

Another aspect of the definition of green chemistry is found in the phrase “use and generation”. Rather than focusing only on those undesirable substances that might be inadvertently produced in a process, green chemistry also includes all substances that are part of the process. Therefore, green chemistry is a tool not only for minimizing the negative impact of those procedures aimed at optimizing efficiency, although clearly both impact minimization and process optimization are legitimate and complementary objectives of the subject. Green chemistry, however, also recognizes that there are significant consequences to the use of hazardous substances, ranging from regulatory, handling and transport, and liability issues, to name a few. To limit the definition to deal with waste only, would be to address only part of the problem. As will be seen later, green chemistry is applicable to all aspects of the product life cycle as well.

Finally, the definition of green chemistry includes the term “hazardous”. It is important to note that green chemistry is a way of dealing with risk reduction and pollution prevention by addressing the intrinsic hazards of the substances rather than those circumstances and conditions of their use that might increase their risk. Why is it important for green chemistry to adopt a hazard-based approach? To understand this, we have to revisit the concept of risk. Risk, in its most fundamental terms, is the product of hazard and exposure:

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

A substance manifesting some quantifiable hazard, together with a quantifiable exposure to that hazard, will allow us to calculate the risk associated with that substance. Virtually all common approaches to risk reduction focus on reducing exposure to hazardous substances. Regulations often require increases in control technologies and treatment technology, and in personal protective equipment such as respirators, gloves, etc., in order to reduce risk by restricting exposure.

By achieving risk reduction through hazard reduction, green chemistry addresses concerns about the cost and potential for failure of exposure controls. Regardless of the type of exposure control, ranging from engineering controls through personal protective gear, there is always going to be an up-front capital cost; to what degree this cost can be recouped will be situation-specific, but it will always be there. In contrast, there is no additional up-front capital cost necessarily associated with green chemistry. While some green chemistry options may require capital investment, others may actually lower total cost of operations from the outset. This result is frequently the case in some of the easiest ways of implementing green chemistry technologies.

Exposure controls, because they rely on either equipment or human activity to accomplish their goals, are capable of failing. Respirators can rupture, air scrubbers can break down, and so forth. When failure occurs, risk is maximized because the resultant exposure is to a constant hazard. Green chemistry, in contrast, does not rely on equipment, human activity, or circumstances of use but, instead, changes the intrinsic hazard properties of the chemical products and transformations. Consequently, green chemistry is not as vulnerable to failure, as are the traditional approaches to hazard control.

The definition of green chemistry also illustrates another important point about the use of the term “hazard”. This term is not restricted to physical hazards such as explosiveness, flammability, and corrosibility, but certainly also includes acute and chronic toxicity, carcinogenicity, and ecological toxicity. Furthermore, for the purposes of this definition, hazards must include global threats such as global warming, stratospheric ozone depletion, resource depletion and bioaccumulation, and persistent chemicals. To include this broad perspective is both philosophically and pragmatically consistent. It would certainly be unreasonable to address only some subset of hazards while ignoring or not addressing others. But more importantly, intrinsically hazardous properties constitute those issues that can be addressed through the proper design or redesign of chemistry and chemicals.

### Green chemistry: Why now?

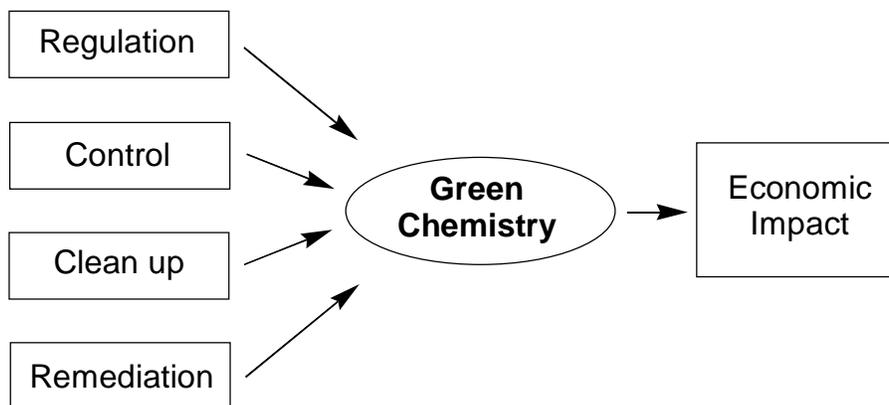
The adoption of green chemistry as one of the primary methods of pollution prevention is a fairly recent phenomenon. It is certainly reasonable to question why this fairly straightforward approach is only now taking hold. The answer is found in a combination of factors, including economic, regulatory, scientific, and even social factors. Each of these incentives has combined to make the 1990s the decade during which green chemistry was introduced and has found implementation and commercialization on a wide industrial scale.

Since the early 1960s, environmental statutes and regulations have proliferated at an exponential rate. With these regulations came cost, restrictions on the use of chemicals, and increased testing of chemical substances to determine their hazard. The increased cost and restrictions on the use of certain chemicals provided powerful incentives for industry to find replacements, substitutes, or alternatives. The toxicity testing required by many of these statutes generated new knowledge and a new awareness about the type and degree of hazard associated with many chemicals. As the collective knowledge resulting from this testing of chemicals began to grow in scientific and industrial circles, there was a corresponding growth in the public demand for more information about chemicals that are present in their communities. For example, in the United States, this culminated in the 1980s with the passage of the Emergency Planning and Community Right-to-Know Act (EPCRA), which made public relevant data on chemicals being released to the air, water, and land by industry. As a consequence, industry has been confronted by tremendous pressure, not only to reduce the release of toxic chemicals to the environment, but also to reduce the use of hazardous chemicals overall.

Lastly, the science of chemistry continues to make advances in the capacity to manipulate molecules and molecular transformations. As we learn more about the hazards of chemicals, the subject translates this knowledge into powerful tools for structure–activity relationships that correlate hazard with molecular construction. Armed with this knowledge, chemists are now able to do what they do best, which is to design and manipulate molecules, and to apply their findings to reduction of hazard. Therefore, from a scientific point of view the answer to “why now for green chemistry” is because now we can. We now have scientific tools to address our environmental concerns at the molecular level.

### The historical context of green chemistry [3]

Green chemistry concerns the development of chemical technology and processes that are designed to be incapable of causing pollution. We humans have dealt with toxicity and pollution throughout our



**Scheme 1** Environmental protection activities that require the intervention of green chemistry to minimize their impact.

entire history, but only recently have we been armed with an understanding of its sources and consequences. Scheme 1 portrays how green chemistry can diminish the need for other approaches to environmental protection. Ideally, the application of green chemistry principles and practice renders regulation, control, clean-up, and remediation unnecessary, and the resultant environmental benefit can be expressed in terms of economic impact.

During the 1990s, environmental protection forces have been enveloping the science of chemistry with ideas and examples of green chemistry, and Paul Anastas coined the term “green chemistry” to focus attention on an area of research and development that was undergoing rapid expansion and that was increasingly characterized by emergence of distinctive objectives and principles. The principles of green chemistry, as articulated by Anastas and Warner [2], can guide chemists towards fulfilling their unique and vital role in achieving sustainable development. These principles are:

- It is better to prevent waste than treat or clean up waste after is formed.
- Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
- Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
- Chemical products should be designed to preserve efficacy of function while reducing toxicity.
- The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
- 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.
- A raw material or feedstock should be renewable, rather than depleting, wherever technically and economically practicable.
- Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
- Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
- 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.
- Analytical methodologies need to be further developed to allow for real-time in-processing monitoring and control prior to the formation of hazardous substances.
- 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.

The principles can motivate chemistry at all levels: research, reduction to practice, education, national and international policy, and public perception. Stated another way, green chemistry is about the redevelopment of chemistry to protect life itself. Such promise and intent hold enormous attraction for people. Just a few examples of recent initiatives and undertakings serve to illustrate the historical growth and incalculable potential of green chemistry:

- In the United States, green chemistry was an official focus area by the EPA at the beginning of the 1990s, and there was a great deal of activity in research, symposia, and education. In 1995, the United States launched the Presidential Green Chemistry Challenge Awards, which sought to provide visibility and recognition to those companies and academic researchers with outstanding achievements in green chemistry.
- In Italy, the Interuniversity Consortium Chemistry for the Environment (INCA) was established in 1993, with the aim to join together the academic groups dealing with chemistry and the environment; one of its focus areas is pollution prevention through research for cleaner reactions, products and processes. INCA organized its first meeting in Venice “Processi Chimici Innovative Tutela dell’ Ambiente”, in February 1993.
- In August 1996, IUPAC approved the formation of the Working Party on Green Chemistry under Commission III.2, which provided the beginnings of this work. The First International Green

Chemistry Conference in Venice was held in September 1997 under the IUPAC sponsorship. The same year, the Green Chemistry Institute was founded.

- The European Commission has sustainability in its main research area, and the aims of green chemistry are present in the 4<sup>th</sup> and 5<sup>th</sup> Framework Programmes.

### **The emergence of green chemistry**

Since its initial introduction in the early 1990s, green chemistry has spread throughout all aspects of the international chemical enterprise. There has been general recognition that green chemistry affects all of the various subdisciplines of chemistry and cuts across the interests and goals of industry, academia, and government. In addition to spreading across these boundaries, the development and use of green chemistry also transcends national borders. One example is that of the International Green Chemistry Summer School held in Venice, Italy each year, and funded by the European Commission. It is managed by INCA and hosts postgraduate students from approximately twenty nations. The students are trained by an international group of authorities on green chemistry, representing a wide range of expertise.

The next CHEMRAWN conference organized by IUPAC in Boulder, Colorado, USA in June 2001 is entitled *Toward Environmentally Benign Processes and Products*, and will attract speakers and delegates, from both industrialized as well as developing nations, to deliberate on how the subject can contribute toward achieving the goals of sustainable development.

Currently, around the world there are conferences, research funding programs, national awards, and recognition and educational programs devoted to green chemistry. Institutions such as INCA, the Green Chemistry Institute (which has chapters in over a dozen countries) the Green Chemistry Network located in the UK, and the Japanese Chemical Innovation Institute are working to coordinate and disseminate green chemistry information around the globe. In recent years, a number of research institutes and centers have been established in the United States, Italy, China, Japan, Australia, Sweden, the United Kingdom, Germany, Spain, Taiwan, and other nations as well.

The chemical literature on green chemistry has been expanding through books [4], journals, and direct Internet publishing. The primary literature as well as reviews and analysis continue to grow, as an understanding of the applicability of green chemistry to industrial interests and traditional scientific challenges becomes known.

The growth of green chemistry has continued at an amazingly rapid pace in recent years, but it must be put into context. While there are numerous fine examples of how green chemistry is being used for the benefit of industry, the environment, and society, they constitute only a small fraction of the unrealized potential. The scientific tools and methodologies must be made available and used by the chemistry community for maximum benefit. The alternative of the costly and inefficient regulatory measures of the past, as a unilateral process, should no longer be an option. IUPAC is uniquely positioned to play a major role, in supporting and advancing economic and environmental benefits through scientific innovation in green chemistry.

## **THE CONTENT OF GREEN CHEMISTRY**

### **Areas of green chemistry**

Economic considerations and environmental evaluations have pushed the chemical industry to adopt new eco-friendly technologies to survive in a market that becomes more demanding every day. Green chemistry will be one of the fields in which these sometimes conflicting forces will contend. Those companies that accept such a challenge and are the first to develop new, environmentally friendly technologies are most likely to gain the market, and to enjoy the support of their governments in promoting their initiatives.

In the framework of the OECD “Risk Management Programme”, a new activity called “Sustainable Chemistry” was endorsed by the member countries (Paris, February 1998), with the aim of encouraging the development of chemical products and processes (and of recommending the related actions) which are at the same time environmentally friendly and economically viable.

The activity started with a survey of the Steering Group [USA, Italy, Japan, Germany, Belgium, Canada, Mexico, Sweden, UK, and Business and Industry Advisory Committee to the OECD (BIAC)] on programs and initiatives on green chemistry launched worldwide by governments, industries and academies.

In consideration of the results of the survey, the policy and programmatic aspects of the sustainable chemistry activity were discussed at the Venice Workshop (October 1998) in the presence of representatives of governments, industries, and academies from 22 countries and approved at the OECD meeting in Paris (6 June 1999) [5].

The areas for the development of green chemistry have been identified as follows:

**Use of alternative feedstocks:** The use of feedstocks that are both renewable rather than depleting and less toxic to human health and the environment.

**Use of innocuous reagents:** The use of reagents that are inherently less hazardous and are catalytic whenever feasible.

**Employing natural processes:** Use of biosynthesis, biocatalysis, and biotech-based chemical transformations for efficiency and selectivity.

**Use of alternative solvents:** The design and utilization of solvents that have reduced potential for detriment to the environment and serve as alternatives to currently used volatile organic solvents, chlorinated solvents, and solvents that damage the natural environment.

**Design of safer chemicals:** Use of molecular structure design—and consideration of the principles of toxicity and mechanism of action—to minimize the intrinsic toxicity of the product while maintaining its efficacy of function.

**Developing alternative reaction conditions:** The design of reaction conditions that increase the selectivity of the product and allow for dematerialization of the product separation process.

**Minimizing energy consumption:** The design of chemical transformations that reduce the required energy input in terms of both mechanical and thermal inputs and the associated environmental impacts of excessive energy usage.

This delineation of topics will be adopted in the ensuing Symposium-in-Print, since it is presently the most recognizable subdivision of the field. But, as the OECD is a socio-economic organization, this classification does not necessarily prescribe to a scientific interpretation of green chemistry. This is particularly true in the present case, where synthetic transformations and organic syntheses are the topics of our issue. The introductory overview will therefore be divided into sections according to a few key factors in synthesis, namely:

- alternative feedstocks
- benign reagents/synthetic pathways
- synthetic transformations
- solvents/reaction conditions
- products/design of safer chemicals
- minimization of energy consumption

This subdivision refers more specifically to organic synthesis and shows that the principles of green chemistry can be used for all aspects of chemical processes. The OECD subdivision will be maintained in the Symposium-in-Print, where full scientific references are given.

### Preliminary remarks

The key to waste minimization in fine chemicals manufacture is the widespread substitution of classical organic syntheses employing stoichiometric amounts of inorganic reagents with cleaner, catalytic alternatives.

Reaction efficiency, much like product selectivity, has long been a goal of synthetic design and, even prior to the enunciation of green chemistry principles, was recognized to offer environmental benefits. When the overall yield of a process is increased by 10 or 20%, less material ends up in waste streams and more is converted into product. However, yield is not entirely adequate as a measure of reaction efficiency, and needs to be considered in conjunction with the concept of "atom economy" (see below). In order to measure the "green" character of a reaction, a few simple parameters have been proposed.

The E factors (kg waste per kg product) of chemical processes increase dramatically on going downstream from bulk to fine chemicals and pharmaceuticals, mainly owing to the use of stoichiometric methods. The concept of atom efficiency is a useful tool for rapid evaluation of the amount of waste generated by alternative processes. The general theme of atom efficiency, is illustrated (see the opening review by Sheldon, this issue, pp. 1233–1246) with industrially relevant examples. These include catalysis by solid acids and bases, catalytic reductions and oxidations, catalytic C–C bond formation, asymmetric catalysis, biocatalysis, and catalysis in novel media (aqueous and fluorous biphasic systems, supercritical fluids, and ionic liquids).

The concept of atom economy has been proposed to join the concept of *reaction efficiency* based on the yields. As Trost has outlined [6], a synthetic transformation can achieve 100% yield of product and still generate a substantial amount of waste if the transformation is not "atom economical". Atom economy is the ratio of the molecular weight of the target molecule to the sum total of the molecular weights of all the substances produced in the stoichiometric equation for the reaction involved. The comparison is made on a theoretical basis (100% yield) and provides a better measure of the intrinsic efficiency of the transformation. From the green chemistry point of view, reactions that have an atom economy of 1.0 have an intrinsic synthetic elegance, and are easily recognizable since no by-products are formed at all.

These parameters do not evaluate the environmental impact of the reaction involved, and other factors must be taken into account. They are considered as the environmental quotient (EQ), which is E multiplied by an arbitrarily assigned unfriendliness quotient. Of course, the magnitude of Q is the object of debate (see the following paper of Herrchen and Klein), but on this basis it is possible to quantitatively assess the environmental impact of processes.

The second opening review deals with life-cycle assessment (LCA), a useful tool for waste management (Herrchen and Klein, this issue pp. 1247–1252). A life-cycle conceptual approach comprises the consideration of all stages along the life cycle of a chemical, as well as the consideration of environmental impacts caused by by-products and auxiliaries.

The environmental LCA is a fairly new management methodology and represents an innovative approach; it can be used either for evaluating already existing products/processes (as a criterion for eco-label release) or to design and assess new products or new processes. In the life-cycle approach, all stages along the life cycle of a chemical (i.e., raw material extraction, pre-production, production, use, recycling, and disposal) as well as environmental impacts caused by by-products and auxiliaries (such as solvents, additives, technical facilities) are considered.

A significant improvement in the evaluation of green chemical products can be approached by the complementary use of the methodologies of LCA and risk assessment. The use and combination of both methodologies can either be performed by a separate use of the instruments, depending on the scope, definition, and application of LCA, an iterative use of LCA and risk assessment, or a complete integration of both instruments.

This aspect is closely related to green chemistry, as it gives the principles that *a priori* regulate new chemical production. The lack of knowledge of the effects of several pollutants, and the scarce

availability of reliable data for industrial processes, stress the necessity of a rational and pragmatic approach.

### **Alternative feedstocks**

The synthesis and manufacture of any chemical substance begins with the selection of a starting material from which the final product will be built. In many cases the selection of a starting material can be the most significant factor in determining the impact of the synthesis on the environment. This selection not only needs to be assessed in terms of what the material's characteristics are, but also on what the upstream impacts of the origins of this starting material were, as well as what the implications for the rest of the process by the choice of this particular starting material will be. If the substance itself does not pose any hazard to human health or the environment, for example, but the retrieval and/or isolation of the substance causes significant risk to either, then this factor must be taken into account in the selection. Or, if the use of the starting material means that a particularly toxic or otherwise hazardous reagent will be required in order to carry out the requisite synthetic transformation, then this factor also needs to be considered in the selection process.

#### *Innocuous or more innocuous*

Certainly, a first-level assessment of any starting material must be whether or not the substance itself poses a hazard in the form of either toxicity, accident potential, possible ecosystem damage, or another form. This hazard can be evaluated in terms for which there are extensive data on properties ranging from dose response to flammability to ozone depleting potential. In the absence of empirical data, there are a wide range of structure–activity relationship models, which can give reasonable approximations for the properties in question.

#### *Renewable*

In addition to the direct hazard associated with a particular chemical substance, the implications of using a renewable versus a depleting feedstock need to be included in the selection of that substance as a starting material in a synthetic transformation. The feasibility and benefits of using bio-based instead of petroleum-based feedstocks, for example, is actively being researched in both academia and the chemical industry.

To ensure a high degree of product safety for consumers and the environment, renewable resources have often been shown to have advantages when compared with petrochemical raw materials and can therefore be regarded as being the preferred source of raw material.

Oleochemistry is a branch of chemistry that uses vegetable oils and fats as renewable resources. Some recent applications of derivatives of oils and fats friendly for human health and the environment, in cosmetic formulations, polymer synthesis, lubricant production, are discussed in Hill's paper (this issue pp. 1255–1264).

Together with carbohydrates and proteins, fatty oils are important renewable resources compared to fossil and mineral raw materials. Results from oleochemistry show that the use of vegetable fats and oils allows the development of competitive, powerful products, which are both consumer-friendly and environmentally friendly.

Light is another emerging feedstock in a broad sense, a safe alternative to toxic catalysts in many synthetic transformations. Beside UV light, the most renewable and environmentally ideal energy source is sunlight. In this regard, the sentence (about one century ago) of Giacomo Ciamician, one of the founders of photochemistry must be quoted [7]. His sentence looks like a Jules Verne description, but one concerning chemistry:

“On the arid lands there will spring up industrial colonies without smoke and without smokestacks; forests of glass tubes will extend over the plants and glass buildings will rise everywhere; inside of these will take place the photochemical processes that hitherto have been the guarded secret of the plants, but that will have been mastered by human industry

which will know how to make them bear even more abundant fruit than nature, for nature is not in a hurry but mankind is”.

Although it appeared (and still is) futuristic, we now know that many of these former fictions can be realized and applied. To address such enormous tasks, photocatalytic systems that are able to operate effectively and efficiently not only under UV light but also under the most environmentally ideal energy source, sunlight, must be established.

One example is given by Anpo (this issue pp. 1265–1270), who discusses the development of titanium oxide photocatalysts able to operate under conditions as mild as visible light and/or solar beam irradiation. His report involves new approaches in the design and development of second-generation titanium oxide photocatalysts operating effectively under visible light and/or solar beam irradiation and practical industrial applications of titanium oxide photocatalysts in Japan.

#### *Solve other environmental problems*

Selection of a starting material should be assessed not only for any hazards that the substance might or might not possess, but also for existing environmental problems that its use as a starting material might assist in solving. In many communities in the United States, for example, waste biomass has become a problem due to limited landfill capacity and other solid waste disposal issues. Utilization of waste biomass as a chemical feedstock in chemical manufacturing processes can alleviate if not completely eliminate such waste problems.

Biocatalysis harnesses the catalytic potential of enzymes to produce building blocks for the pharmaceutical and chemical industry. Located at the interface between fermentation processes and petroleum-based chemistry, biotransformation processes broaden the toolbox for bioconversion of organic compounds to functionalized products.

As discussed by Witholt (this issue pp. 1337–1343), a key technology to facilitate and smooth the necessary transition from petroleum-based chemistry to the use of renewable resources for the production of chemicals is represented by biocatalytic processes.

While fermentations use the carbon source for *de novo* product synthesis, biocatalytic processes employ a different strategy. Precursor molecules are fed to the biocatalyst, which transforms them to the desired compound by a limited number of functionalizing steps (usually one). Carbon and energy required for production of the biocatalyst commonly come from a different easily metabolizable carbon source such as a sugar. Here, the range of products is not limited by the metabolism of the biocatalyst: non-natural (xenobiotic) precursor molecules can be efficiently transformed because biocatalysts can transform non-natural as well as natural and renewable compounds.

The sequestering of carbon dioxide is another example of how the selection of a starting material can help solve an existing environmental problem. It is well known that carbon dioxide is among the most potent of “greenhouse gases” that have been found to contribute to global warming. Research is currently being conducted in the design of new materials that could be used in applications that sequester carbon dioxide during manufacturing processes. The utilization of carbon dioxide in manufacturing processes in a way that does not allow its escape to the environment might not solve the global warming issue but can help reduce the amount of greenhouse gases in the atmosphere.

#### **Benign reagents/synthetic pathways**

As in the selection of a starting material, the selection of a reagent must include an evaluation to identify what the hazards associated with a particular reagent are. This evaluation should include an analysis of the reagent itself, as well as an analysis of the synthetic transformation associated with the use of that reagent (i.e., to determine product selectivity, reaction efficiency, separation needs, etc.). In addition, an investigation should be undertaken to determine if more alternative reagents are available that either are themselves more environmentally benign or are able to carrying out the necessary synthetic transformation in a more environmentally benign way.

### *Innocuous or more innocuous*

As in the selection of a starting material, the selection of a reagent should start with an evaluation of the reagent itself to determine if it possesses any hazardous properties. Inherent in this analysis is the question: Is the transformation requiring the hazardous reagent necessary, or can the final target compound be obtained from an alternative pathway that uses a less hazardous reagent?

In order to answer this question alternative reagents must be identified, and any hazardous properties that the alternatives possess must be compared with the hazardous properties associated with the reagent originally selected. One example of an innocuous reagent (which is produced from nontoxic intermediates) is dimethylcarbonate [8].

### *Generates less waste*

An important consideration and benefit associated with the use of a particular reagent is whether it is responsible for the generation of more or less waste than other reagents. The amount of waste either generated or eliminated, however, cannot be the only consideration. The type of any waste generated must also be assessed. Just as all chemical products are not equal in terms of their hazard, neither are chemical waste streams. Waste streams therefore must also be assessed for any hazard properties that they possess. In this regard, it is obvious that oxidation reactions involving oxygen and hydrogen peroxide will be of outstanding priority, as they produce water as a by-product.

Green oxidation reactions require the use of nontoxic solvents (water or CO<sub>2</sub>) and mild reaction conditions. Oxidations using air as a reagent are difficult to control, being either too slow or too fast for industrial applications, and intrinsically nonselective when selectivity is very often a crucial parameter. Hydrogen peroxide is a clean reagent, with water the only by-product formed, and a very high selectivity can be obtained. However, the use of hydrogen peroxide for fine chemical production is currently limited by its poor reactivity and its ease to undergo radical decomposition. Therefore, there is a great effort to develop systems able to selectively activate oxygen and hydrogen peroxide for oxidative transformations. In this context, both homogeneous and heterogeneous catalysis play a key role. Oxidation reactions are critical to pharmaceutical, petrochemical, and agricultural industries. Several examples of how environmentally benign oxidants such as molecular oxygen, hydrogen peroxide or nitrous oxide can be activated on heterogeneous catalysts are illustrated by Hoelderich (this issue, pp. 1273–1287). Direct oxidation of isoprenol,  $\beta$ -picoline and benzene are chosen as examples for continuous gas-phase processes, and oxidation of cyclopentanone, limonene, pinene, and propylene as examples for semi continuous or batchwise processes in the liquid phase.

These examples illustrate that features known from the synthesis of bulk chemicals can successfully be applied to manufacturing intermediate and specialty chemicals by utilizing the phases associated with conventional industrial reactor systems.

Metal-peroxo systems, polyoxometallates and heteropolyanions, zeolitic and smectitic materials, and other titanium catalysts are discussed by Sanderson (this issue, pp. 1289–1304). Recent research progress in catalytic systems for potential use with hydrogen peroxide in industrial chemical synthesis is reviewed in terms of the positive features identified to date, and the obstacles yet to be surmounted in order to become more widely adopted.

It is believed that fully inorganic systems have more scope for commercialization than those containing organic ligands or supports, however robust. Critical targets are larger-pore analogs of titanium silicalite (TS-1), more exploration of smectite-based materials, effective immobilization of activated metal-peroxo systems, and improvements in design and manipulation of polyoxometallate compounds. Cooperation between branches of chemistry that have not traditionally worked closely together is advocated.

### *Selective*

Utilizing a reagent that is more selective means that more of the starting material is going to be converted into the desired product. High product selectivity does not always translate into high product yield (and less waste generated), however. Both high selectivity and high conversion must be achieved in order for

a synthetic transformation to generate little or no waste. Utilizing highly selective reagents can mean that separation, isolation, and purification of the product will be significantly less difficult. Since a substantial portion of the burden to the environment that chemical manufacturing processes incur often results from separation and purification processes, highly selective reagents are very desirable in green chemistry.

### *Catalytic*

If a catalyst is necessary, it should be used in actually “catalytic amount”. In fact, if a reagent can be utilized and yet not consumed in the process, it will require less material to continuously effect the transformation. This implies that catalysis has to be as efficient (not only effective) as possible, involving a high turnover number.

Other criteria that should be used in the selection of a reagent need to be balanced against each another in order to optimize the utility of the reagent and minimize the environmental impact.

A large number of industrial processes are based on the use of inorganic or mineral acids. While many of these processes are catalytic, some require (e.g., acylation using  $\text{AlCl}_3$ ) stoichiometric amounts of Lewis acid. Final isolation of the product necessitates neutralization steps to remove the acid, resulting in enormous quantities of hazardous waste, with the cost of disposal of this waste often outweighing the value of the product.

Misono (this issue, pp. 1305–1311) discusses the use of heteropolyacids as green catalysts for both acid-catalyzed and oxidation reactions, reporting as examples, two industrial processes which were made greener by the use of such catalysts in liquid bi-phase systems. The first is the hydration of a mixture of butenes; only isobutylene reacts selectively and supplies the starting material for the two-step oxidation to methacrylic acid (1- and 2-butenes left after reaction are utilized as raw material in the production of low-density polyethylene).

The second example is the polymerization of tetrahydrofuran, which gives poly-oxytetramethyleneglycol, used as an elastic fiber and elastomer.

Heteropolyacids can be active solid-acid catalysts, providing the unique reaction environment of a pseudoliquid (catalytically active solid solvent) and thus find many green applications in the future (see also M. J. Earle and K. R. Seddon, this issue, pp. 1391–1398).

As Clark (this issue, pp. 1313–1319) discusses, the use of heterogeneous catalysts in these processes may simplify catalyst removal, thus minimizing the amount of waste formed. Diffusion limitation of liquids within porous solids dictates that effective solid acids for liquid-phase reactions require the use of mesoporous materials  $<20\text{--}100 \text{ \AA}$ .

In particular, Clark focuses on new mesoporous solid acids which minimize diffusion limitation in liquid phase organic transformations and open up new possibilities in the preparation of solid acid catalysts for liquid-phase reactions. Solid-acid catalysts in organic synthesis are discussed in terms of properties, preparation, and a few selected applications.

### **Synthetic transformations**

The various reaction types most commonly used in synthesis can have different degrees of impact on human health and the environment. Addition reactions, for example, completely incorporate the starting materials into the final product and, therefore, do not produce waste that needs to be treated, disposed of, or otherwise dealt with. Substitution reactions, on the other hand, necessarily generate stoichiometric quantities of substances as by-products and waste. Elimination reactions do not require input of materials during the course of the reaction other than the initial input of a starting material, but they do generate stoichiometric quantities of substances that are not part of the final target molecule. As such, elimination reactions are among the least atom-economical transformations. For any synthetic transformation, it is important to evaluate the hazardous properties of all substances necessarily being generated from the transformation, just as it is important to evaluate the hazardous properties of all starting materials and

reagents that are added in a synthetic transformation.

Free-radical chemistry has shown a magnificent development over the last 30 years. In the past, radicals were generally thought to be too reactive to be controlled and unlikely to produce synthetic applications. Now, the view is that they are useful and selective intermediates. This change has arisen as a result of two significant achievements: the first change was the determination for radical reactions of a large number of kinetic constants which led to an understanding of their reaction mechanism. Secondly, the successful application of radical reaction to the total synthesis of complex molecules demonstrated that this tool was ready for innovative pathways in organic chemistry.

The photochemical approach to produce radicals is described by Albini (this issue, pp. 1321–1326), who aims at developing environment-friendly reactions, in particular radical alkylation of electrophilic alkenes via photoinduced electron transfer. This paper illustrates the scope and versatility of radical alkylation of electrophilic alkenes via photoinduced electron transfer and presents a few applications in special fields.

The peculiar versatility of photochemical reactions in forming covalent bonds is expected to lead to their rapid development in organic synthesis. As an example, the scarce medium-dependence of excited state reactions may be exploited for switching to water as the solvent; the mild reaction conditions are useful for mild cleavage of protective groups or in supramolecular chemistry, or in controlling the molecular weight of polymers formed from self-assembling units.

Clean radical reactions which use economical reagents are discussed by Murphy (this issue, pp. 1327–1334). The situation that prevents the utilization of radical reactions in synthetic transformation, is the reagent which is usually used. Tributyltin hydride currently plays a key role in radical chemistry, but it is a neurotoxic compound; as a consequence, this unacceptable reagent, if not replaced with other less toxic ones, does preclude the development of green and innovative synthetic pathways for the formation of the C–C bond.

Two methods for effecting radical reactions in an environmentally friendly way are presented: (i) The tetrathiafulvalene (TTF)-mediated radical-polar crossover reaction converts arenediazonium salts to aryl radicals, which have sufficient lifetime to cyclize onto alkenes—the resulting alkyl radicals couple with  $\text{TTF}^{\bullet+}$  to afford sulfonium salts which, in turn, undergo solvolysis to alcohols, ethers, or amides. The method provides the key step in a synthesis of ( $\pm$ )-aspidospermidine; (ii) Hypophosphite salts and hypophosphorous acid, on the other hand, form C–C bonds with reductive termination. These economical reagents give radicals efficiently from alkyl halides and allow a very easy separation of products from by-products.

### **Solvents/reaction conditions**

The use of solvents in the chemical industry and the chemical related industries is ubiquitous. With increasing regulatory pressure focusing on solvents, there is significant attention being paid to the use of green chemistry alternatives to traditional solvents.

#### *Less toxic*

Certainly, solvents have been developed with an eye toward their safety, since they are often used in such large volumes. The earliest and most obvious hazards that were recognized in solvent molecules were their ability to explode or ignite. With the greater understanding of the health and environmental effects that could be caused by a large number of solvents, new designer solvents are being scrutinized for other hazards as well.

#### *Human health*

Solvents are particularly of concern because the likelihood of significant levels of exposure is extremely high. Many solvents, by their nature, have high vapor pressure and, in combination with the volumes that are often used, can result in sufficient doses to cause harm to humans. Halogenated solvents such as carbon tetrachloride, perchloroethylene, and chloroform have been implicated as potential and/or suspect

carcinogens, while other classes of solvents have demonstrated neurotoxicological effects. However, the direct toxicity to humans is only one aspect of the total hazards that solvents possess. There are a number of environmental implications of the use of large volumes of solvents.

#### *Environment (local and global)*

An important part of our effort toward more environmentally friendly green chemistry is aimed at reducing the use of organic solvents. Usually, organic solvents are used in much larger quantities than the solutes they carry and are wasted into the environment through evaporation and leakage.

The use of chlorofluorocarbons (CFCs) and their role in stratospheric ozone depletion has created a global phase-out of the substances from virtually all uses. The use of certain volatile organic compounds (VOCs) as solvents and other uses has generated great concern about their ability to elevate atmospheric ozone levels. Other substances used as solvents have also been found to possess significant global warming potential and are thought to contribute to the overall greenhouse gas loading in the environment.

Some of the main areas of research on alternative solvents includes supercritical fluids, aqueous applications, polymerized/immobilized solvents, ionic liquids, solventless systems, and reduced hazard organic solvents.

In the last ten years, there has been incredible growth in research involving the use of carbon dioxide as an environmentally benign solvent for chemical reactions and polymerizations. It has become a widespread, growing reality, both in academia and in industry. CO<sub>2</sub> is a nontoxic, nonflammable, and inexpensive solvent. While CO<sub>2</sub> is a gas at ambient conditions, its liquid and supercritical states are easily attained by compression and heat. Both liquid and scCO<sub>2</sub> have a tuneable density (and dielectric constant) that increases with increasing pressure or decreasing temperature. Many small molecules are soluble in CO<sub>2</sub>, including high-vapor-pressure solvents such as methanol, acetone, and tetrahydrofuran, many vinyl monomers, and azo- and peroxy-initiators. Water and ionic compounds are insoluble, as are most polymers.

The two methodologies described by Howdle for dissolving ionic/polar species in scCO<sub>2</sub> lead to a widening of the range of applications for supercritical solvents. (See P. B. Webb *et al.*, this issue, pp. 1347–1355.) Fluorinated surfactants may be used to prepare water in carbon dioxide microemulsions and allow solubilization of ionic and biological species. The preparation of scCO<sub>2</sub> soluble metal precursors that can be impregnated efficiently into polymeric substrates is outlined. Further processing by heat or UV light leads to metallic particles distributed throughout a polymer substrate. The clean synthesis of such composites can be applied to the development of improved medical implants.

The synthesis and applications of two classes of polymers that are soluble in CO<sub>2</sub> at relatively mild conditions (amorphous or low-melting fluoropolymers and silicone-based polymers), are described by De Simone (this issue, pp. 1357–1363). This article highlights polymer synthesis, characterization, and applications in CO<sub>2</sub> and places the outstanding research of this leading group in the context of both green chemistry and the latest developments in CO<sub>2</sub> technology.

The increased focus on water in synthetic organic chemistry during the past few decades has resulted in a large number of reactions that can now be performed successfully in an aqueous medium. Among these reactions are allylation reactions, the aldol condensation, the Michael addition, the Mannich reaction, indium-mediated allylation [9] and Grignard-type additions, and the benzoin condensation [10].

Engberts (this issue, pp. 1365–1372) describes not only how the Diels–Alder reaction can be successfully performed in water, but also how the rate and selectivity of this important organic transformation are enhanced by the peculiar properties of this solvent. Also, possibilities for achieving further increases in rate and enantioselectivity of aqueous Diels–Alder reactions through Lewis acid and micellar catalysis are reviewed.

Kobayashi (this issue, pp. 1373–1380) developed a new class of water-stable Lewis acid catalysts for performing carbon–carbon bond-forming reactions in water instead of organic solvents. The system is composed of rare earth metal triflates, which are completely recovered and re-used after the reaction. Furthermore, Lewis acid-surfactant-combined catalysts, which can be used for reactions in water with-

out using any organic solvents, have been also developed. Finally, Lewis acid catalysis in supercritical carbon dioxide has been successfully performed. These investigations will contribute to the development of environmentally friendly Lewis acid catalysis.

A new emerging class of solvents is represented by ionic liquids, which offer alternatives to conventional molecular solvents for many synthetic transformations, with both the thermodynamics and kinetics of reactions carried out in ionic liquids being different to those in conventional molecular solvents. These solvents are often fluid at room temperature, and consist entirely of organic ionic species; they have no measurable vapor pressure, and hence can emit no VOCs. Seddon (this issue, pp. 1391–1398) reviews the current range of organic chemical reactions that can be performed in ionic liquids.

Makosza's paper (this issue, pp. 1399–1403) discusses phase-transfer catalysis as a green approach to waste minimization. This key synthetic methodology utilizes water as the solvent and is applied and applicable to a great variety of reactions in which inorganic and organic anions and also carbenes react with organic substrates. It makes use of heterogeneous two-phase systems—one phase (water) being a reservoir of reacting anions or base for generation of organic anions, whereas organic reactants and catalysts are located in the second, organic phase. The reacting anions are continuously introduced into the organic phase in the form of lipophilic ion-pairs with lipophilic cations supplied by the catalyst.

Phase-transfer catalysis can be carried out in liquid-liquid, solid-liquid, and gas-liquid conditions. The latter (gas-liquid phase-transfer catalysis, GL-PTC) is of importance in green chemistry also because it is performed under continuous-flow conditions. Transforming the batch reactions into continuous-flow processes is a challenge for chemical engineers because harmful reactions are avoided, reaction control is easier, and the volume in which the reaction takes place is greatly reduced [11].

### **Products/design of safer chemicals**

The design of safer chemicals is a process that utilizes an analysis of the chemical structure to identify what part of a molecule is providing the characteristic or property that is desired from the products and what part of the molecule is responsible for the toxicity or hazard. By knowing this information, it is possible to maintain efficacy of function while minimizing the hazard. This goal of designing safer chemicals can be achieved through several different strategies, the choice of which is largely dependent on the amount of information that exists on the particular substance.

#### *Mechanism of action*

In cases where a mechanism of action is known, there is the greatest potential to design a chemical that is safer from the perspective of toxicity or other hazard to human health and the environment. Simply stated, if the pathway toward toxicity is known, and then if any step within that pathway can be prevented from occurring, then the toxic endpoint will be avoided.

#### *Structure–activity relationships*

Although mechanisms of action may be unknown, there are often detailed correlations, by way of structure–activity relationships, that can be used to design a safer chemical. As an example, if it is known that the methyl-substituted analog of a substance has very high toxicity, and that the toxicity decreases as the substitution moves from ethyl to propyl, etc., it would be reasonable to increase the alkyl chain length to design a safer chemical. Even when the reason for the influence of alkyl chain length on toxicity is unknown, an empirical structure–activity relationship of this kind offers a powerful design tool.

#### *Elimination of toxic functional group*

A class of chemicals is often defined by certain structural features, such as functional groups like aldehydes, ketones, nitriles, or isocyanates. If one doesn't have any information about the specific

variations in a chemical's toxicity with structural modification or in the mechanism by which it produces that toxicity, the assumption that certain reactive functional groups will react similarly within the body or in the environment is often a good one. The assumption is especially good if there are data on other compounds in the chemical class that demonstrate a common toxic effect.

In such cases, the design of a safer chemical could possibly proceed by removing the toxic functionality which defines the class. In some cases, this is not possible because the functionality is what gives the molecule the properties that are required for the chemical to perform in the desired way. In these cases, there are still options, such as masking the functional group as a nontoxic derivative form and only releasing the parent functionality when necessary.

#### *Reduce bioavailability*

If, through the above methods, one cannot identify the structural feature of the molecule that needs to be modified in order to make it less hazardous, then there is still the option of making the substance less bioavailable. If the substance is unable, due to structural design, to reach the target of toxicity, then it is in effect innocuous. This can be done through a manipulation of the water-solubility/lipophilicity relationships that often control the ability of a substance to pass through biological membranes such as skin, lungs, or the gastrointestinal tract. The same principle applies to designing safer chemicals for the environment, such as replacement for ozone-depleting substances. In order for a substance to have a significant ozone-depleting potential, it must be able to both reach the altitudes and have a sufficient lifetime in those altitudes in order to cause damage. Many substances are now being designed, which have the same properties as those of known ozone depleters, but without the ability to be available to the target of the hazard, in this case the stratospheric ozone layer.

#### *Design for innocuous fate*

It was often the goal of the chemist to design substances which were robust and could last as long as possible. This philosophy has resulted in a legacy of wastes, persistent toxic and bioaccumulative substances, and lingering toxic waste sites. It is now known that it is more desirable to avoid substances that persist indefinitely in the environment or a landfill, and to replace them with those that are designed to degrade after their useful life is over. Therefore, the design of safer chemicals cannot be limited to only hazards associated with the manufacture and use of the chemical but also that of its disposal and ultimate end of life cycle.

Polymeric materials, for instance, should not have any negative effect on the environment during their production or service and at the end of their life. Polyolefin technology is presented by Romano (this issue, pp. 1383–1388) as a safe alternative to the use of potentially dangerous monomers and chemicals and to polymer processing and manufacturing with high environmental impact. The recent developments in the field of polyolefins (polyethylene, polypropylene and ethylene-propylene copolymers and terpolymers) is reviewed in the light of the positive impact that they will have on several aspects of the environmental issue.

### **Minimization of energy consumption**

The design of chemical transformations can reduce the required energy input in terms of mechanical, thermal, and other energy inputs, and the associated environmental impacts of excessive energy usage. Design for energy minimization is inherently coupled to the design for material efficiency in many aspects and is therefore addressed in numerous examples in the Symposium-in-Print. For instance, when utilizing new solvents such as supercritical carbon dioxide, one is often also greatly affecting the ease of separation, which requires significant energy inputs. Further, if a synthetic transformation is developed using a catalytic system rather than a stoichiometric process, we know that catalysis is useful in lowering activation energy required for the conversion. Therefore, rather than identify specific chapters and research that exclusively address energy concerns, the reader is instead encouraged to appreciate the intrinsic design changes which are providing extensive benefit for energy minimization through the use of green chemistry methodologies.

## FUTURE PERSPECTIVES

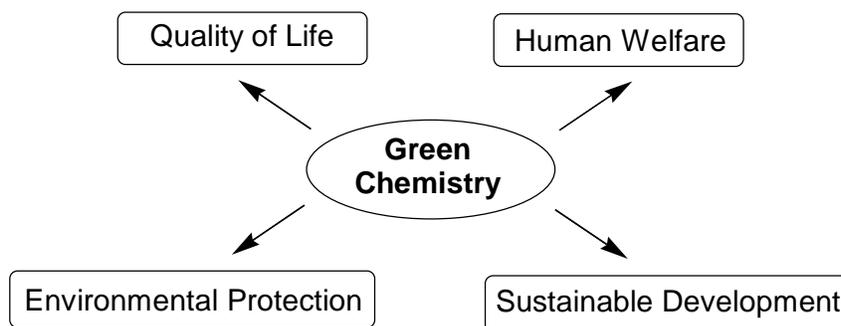
### Future challenges and opportunities for the chemical profession and the science of chemistry

The principles of green chemistry are also a substantial beginning for the chemical profession in trying to deal with the novel ethical context in which humanity has been placed by the unprecedented power afforded to it in the 20<sup>th</sup> century by science and technology [12]. Thus, green chemistry is unusual in that it is here that what has hitherto been called “pure chemistry” must be integrated into the much broader questions associated with sustainability and vice versa.

Although green chemistry will underpin many activities in environmental protection, Scheme 2 shows that its overall impact is potentially much wider.

Green chemistry has major contributions to make to the quality of life, human welfare, and sustainable development. However, before green chemistry can contribute fully to these areas, it must be integrated into the discipline of chemistry itself. This requirement presents a number of major challenges to the chemical profession:

- Chemists will need to integrate into pure chemistry the questions of why or why not, on environmental protection grounds, a particular technology should be abandoned, improved, or adopted. These questions must become as important in research and education and made as concrete as the ubiquitous questions associated with what comprises chemical technology and how it actually works.
- It is vital that green chemistry not become a fad, in which chemistry that is not really “green” gets paraded as such before the scientific community and the world. Such fraud will inevitably bring the type of disenchantment and confusion that might simply discredit the field and would deny future generations the great good of experiencing the chemical dimension essential to a sustainable technologically advanced civilization.
- Certain of the largest sustainability issues, where chemists have so much to offer, will require new approaches that can only be built with long-term commitment. For example, finding efficient methods for converting solar to chemical energy is a large sustainability issue. The culture of present-day chemistry places too many short-term obstacles in the path of strategic research problems of this type. But chemists must solve such problems to achieve sustainability. Thus, the culture must adapt to recognize that certain sustainability problems will require novel approaches with inherently longer incubation times. Chemists must learn how better to evaluate and sustain



**Scheme 2** Green chemistry in the context of the major drivers for new developments in modern chemistry.

- research programs that, while they may not rapidly produce large numbers of publications, do offer reasonable promise of bringing within the fullness of time those critical advances that will genuinely promote the cause of sustainability.
- There is the very difficult issue of achieving a wholeness of scientific intelligence where more than the current specialized and professionalized expertise is paid due homage. The science of chemistry cannot escape this growth and remain meaningful and important to humanity. Chemistry exerts an enormous influence on human action and is thus inextricably intertwined with the forces that guide human action, especially ethics and certain forms of passion. As such a wholeness is achieved, the power of scientific objectivity will be more openly directed by the action-orienting insights and passions that make us all human, such as our love of life and our desire to protect it. Such passions are neither vacuous nor disorienting. Rather, they are forces for great good that are fully capable of directing chemists toward research that really matters to each and every human being living and to come. Chemistry will have much more to offer, become more meaningful to humanity, increase in attractiveness as a career choice, grow to be more worthy of support, spawn large new economic developments, and progress to be more interesting and compelling if chemists work to define and follow their natural and unique role in achieving a virtuous civilization that sees broad validity within the community of living things for the claim to continuity of existence in an environment of natural genesis.

### **An environmentally friendly economy from green chemistry**

Chemistry is the central and essential science necessary to deal with the very large questions of global sustainability. Chemists have proven over time that they possess the imagination, the technical ability, and the opportunities to produce the brilliant science that will be needed to decisively solve the technical problems of sustainability. Chemistry needs to begin work on sustainability problems with a force that befits their importance. The most obviously important research fields center on finding alternatives to nonrenewable (depleting) resources and pollution prevention through hazard reduction.

#### *Renewable energy sources*

In an energy-hungry world that has demonstrated an inability to engage in effective conservation measures on the scale necessary, the question of energy becomes paramount. The vast majority of energy production in the world is being generated through the use of finite depleting resources. These same finite resources (petroleum) are the basic feedstock for over 95% of all high value organic chemicals. It is clear that burning of fossil fuels is not sustainable, and the research of alternative sources is not proceeding at a rate necessary to address the problem in the necessary timeframe.

#### *Renewable feedstocks*

It is undeniable that the fossilized carbon reserves of the planet, built up over millions of years, are being consumed at a rapid and ever increasing pace. These reserves are consumed not only as energy sources, but also to produce feedstocks for the chemical industry. How are we going to achieve renewable feedstock alternatives? It is the role of creative chemists who will learn how to process renewable biomass into the chemical building blocks of future economies. In this area, chemists could have a great deal to offer also. Again, chemists need to develop a strategic plan and ensure that it is adequately backed.

#### *Pollution reduction*

While progress is clearly being made in many arenas, it is still clear that much needs to be done to reduce the pollution pressure on the environment. Pollution largely results from imperfect applied chemistry. So who will reduce and eliminate this pressure, if not chemists? There are different kinds of pollutants. Persistent pollutants are more troubling than others because the environment does not have sufficiently rapid ways of dealing with them. By designing products and processes throughout the life

cycle such that hazards are reduced, it will be to the benefit of sustainability, both environmentally and economically.

### **Interdisciplinary approach**

Authentic green chemistry is designed to eliminate pollution at its source with the intention that the new chemistry cannot imperil beneficial life forms. However, the earth's environment is perhaps the most complex chemical system we know about. The realization that a multitude of conundrums lie in the path of green chemistry does not constitute a reason not to proceed. Rather, it provides us with a clear warning to temper our natural enthusiasm for the good we might do with a healthy scepticism of our ability to foresee the future. We must be careful and aim this scepticism at avoiding environmental harm. Designers of the best green chemistry technologies will design for flexibility and deal with unknown perils in a prudent and correctable manner. Because of the complexity of the environment, green chemistry projects will require a certain level of multidisciplinary expertise reaching beyond the actual chemistry. This will be best achieved by collaborations among appropriate specialists.

Green chemistry is a new and innovative approach to furthering the interests of the chemical enterprise within the context of sustainability. However, it has the potential to strengthen, enrich, and promote chemistry. In particular, it promises to excite talented young scientists and to attract them to the chemical profession.

Green chemistry interacts with the activities of all seven IUPAC Divisions as well as with the Committee on Chemistry and Industry. This expertise places IUPAC in an extremely strong position to provide leadership in green chemistry, to promote this new approach, and to ensure that green chemists follow and uphold the highest scientific standards.

### **Green chemistry education**

In order to allow for the full potential of green chemistry to explore the scientific, economic, and humanitarian advances that its promise holds, the scientific community needs to provide educational opportunities to train chemists of the future to the scientific principles and technical methodologies that comprise green chemistry. Since green chemistry requires the same skills and abilities of traditional chemistry, students of all ages can learn fundamental concepts in ways that are more environmentally benign. The same rigor and intellectual thoroughness that is an intrinsic part of all chemistry is essential in the successful and scientifically uncompromising practice of green chemistry.

This educational endeavor can take several forms, including traditional courses in chemistry for students at primary, secondary, and university levels, as well as professional training for practicing chemistry in industry. Both of these target audiences need curriculum materials to be developed and a suitable educational infrastructure in green chemistry to be made available to teachers, instructors, and professors. Textbooks, laboratory training, student/instructor exchange, and internship programs are all necessary components of adequate training in green chemistry.

In addition to classical educational mechanisms, there needs to be outreach to science students in developing nations in many of the same areas as mentioned above. In addition, nonscience students and professionals (especially those involved in the business/finance communities) need to be aware of the recent developments and advances green chemistry has brought to the chemical enterprise. Only through a far-reaching educational initiative will the development, implementation, and achievements of green chemistry be realized to the benefit of society and the enrichment of the science of chemistry.

### **CONCLUSIONS**

To combine the technological progress with the safeguard of the environment is one of the challenges of the new millennium. Chemists will play a key role in the realization of the conditions for a sustainable development, and green chemistry may be their winning strategy.

The following Symposium-in-Print will give some examples of the potentialities of such a new and rapidly emerging field, but does not intend to cover it entirely. The projects and programs mentioned in this report, as well, are only the most visible part of all the initiatives that scientists all over the world are undertaking in the field of green chemistry. Other projects are coming from many organizations, and IUPAC is on the way of launching an official green/sustainable program aimed at attracting and stimulating the active participation of more and more chemists.

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