Concept of Green Chemistry

Redesigning Organic Synthesis

Bharati V Badami

Green chemistry is the utilization of a set of principles that will help reduce the use and generation of hazardous substances during the manufacture and application of chemical products. Green chemistry aims to protect the environment not by cleaning up, but by inventing new chemical processes that do not pollute. It is a rapidly developing and an important area in the chemical sciences. Principles of green chemistry, developments in this field and some industrial applications are discussed.

Bharati V Badami was a Professor of Organic Chemistry Karnatak University, Dharwad. Her research interests are synthesis, reactions and synthetic utility of sydnones. She is currently working on electrochemical and insecticidal/antifungal activities for some of these compounds.

Chemistry has provided valuable materials in the form of medicines, food products, cosmetics, dyes, paints, agrochemicals, biomolecules, high-tech substances like polymers, liquid crystals and nanoparticles. Chemists have used their knowledge and skill to prepare a large number of new materials which are far better and more useful than the natural products, such as high-tech polymers, liquid crystals, tough ceramics, nonlinear optical substances, novel electronics, designer drugs, genetic materials and new energy sources.

The processes on industrial scale involve many chemical reactions using huge quantities and wider varieties of smaller molecules, reagents, solvents, acids, alkali, etc. These chemical processes not only produce the required products but also large quantities of undesired and harmful substances in the form of solids, liquids and gases and have become the biggest challenge that chemistry has to face. So, the pressing need for the synthetic chemists is to minimize chemical pollution. During the last two decades much work has been going on in this direction. The term *Green Chemistry* was coined in 1991 by Anastas. The purpose is to design chemicals and chemical processes that will be less harmful to human health and environment. Green chemistry

Key words
Green chemistry, green syntheses, green solvents, benign processes.

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The terms 'Environmental Chemistry' and 'Green Chemistry' are two different aspects of environmental pollution studies. The former is the study of chemical pollutants in natural environment while the latter is an attempt to design chemical products and processes to reduce the harm they cause to the environment. Green chemistry seeks to reduce pollution at source, whereas environmental chemistry focuses on the study of pollutant chemicals and their effect on nature.

Commercial applications of green chemistry have led to novel academic research to examine alternatives to the existing synthetic methods. The fundamental idea of green chemistry is that, the designer of a chemical is responsible for considering what will happen to the world after the chemical agent is put in place.

The principles of green chemistry and some examples of their applications to basic and applied research are illustrated below:

***Prevention of Waste*:** It is better to prevent waste than to treat or clean up waste after it is formed. The ability of chemists to redesign chemical transformations to minimize the generation of hazardous waste is an important first step in pollution prevention.

***Maximize Atom Economy*:** Atom Economy is a concept that evaluates the efficiency of a chemical transformation, and is calculated as a ratio of the total mass of atoms in the desired product to the total mass of atoms in the reactants.

$$\%\ \text{Atom Economy} = \frac{\text{No. of atoms incorporated}}{\text{No. of atoms in the reactants}} \times 100.$$

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Choosing transformations that incorporate most of the starting materials into the product are more efficient and minimize waste, e.g., Diels–Alder reaction is 100% Atom Economy reaction as all the atoms of the reactants are incorporated in the cycloadduct.

***Less Hazardous Chemical Syntheses*:** Synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and environment. Some toxic chemicals are replaced by safer ones for a green technology, when reagent choices exist for a particular transformation. This principle focuses on choosing reagents that pose the least risk and generate only benign by-products. For example, in the manufacture of polystyrene foam sheet packing material, chlorofluorocarbons which contribute to O_3 depletion, global warming and ground level smog, have now been replaced by CO_2 as the blooming agent.

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***Metathesis*:** Developed by Grubbs, Schrock and Chauvin, metathesis is a major advance for green chemistry. It is a reaction in which double bonds are broken and made between carbon atoms in ways that cause atom groups to change places, with the help of special catalyst molecules. It is used in the development of pharmaceuticals and advanced plastic materials, and is a great step forward for green chemistry, reducing hazardous waste through smarter production.

***Designing Safer Chemicals*:** New products can be designed that are inherently safer for the target application. Pharmaceutical products often consist of chiral molecules, and the difference between the two forms can be a matter of life and death – for example, racemic thalidomide when administered during pregnancy, leads to horrible birth defects in many new borns. Evidence indicates that only one of the enantiomers has the curing effect while the other isomer is the cause of severe defects. That is why it is vital to be able to produce the two chiral forms separately. Catalysts that can catalyse important reactions that produce only one of the two mirror image forms are developed.

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***Safer Solvents and Auxilliaries*:** Solvents are extensively used in most of the syntheses. Widely used solvents in syntheses are toxic and volatile – alcohol, benzene (known carcinogenic), CCl_4, $CHCl_3$, perchloroethylene, CH_2Cl_2. Purification steps also utilize and generate large amounts of solvent and other wastes (e.g., chromatography supports). These have now been replaced by safer *green solvents* like ionic liquids, supercritical CO_2 fluid, water or supercritical water and also solvent-free systems that utilize the surfaces or interiors of clays, zeolites, silica, and alumina. These are the basis of many of the cleaner chemical technologies that have reached commercial development.

a) Ionic liquids are liquids at RT and below. They are nonvolatile and have no vapour pressure. They can serve as optimal replacements for volatile organic traditionally used industrial solvents. The reactions in ionic liquids need no special apparatus and methodologies, and they can be recycled. However, large-scale applications are still not known.The first ionic liquid **I** was discovered in 1914 and many binary ionic liquids of type **II** are also used as green solvents.

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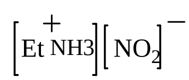

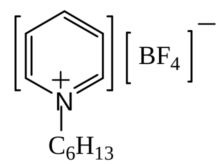

I **II**

b) Supercritical CO_2 fluid is another versatile green solvent which has low viscocity and no surface tension. It has the unique ability to diffuse like gas through solids, and to dissolve a wide range of organic substances, catalysts, etc. Supercritical CO_2 fluid is now becoming an important commercial and industrial solvent for chemical separation because of its low toxicity and non-inflammability. Its stability and the relatively low temperature of the process allows most compounds to be extracted with little damage and denaturation (e.g., fragrance compounds used in perfumery). Because CO_2 is obtained as a byproduct of other industrial processes it is inexpensive and being a gas it is easily evaporated leaving no residue.

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c) Supercritical water*:* Organic substances are insoluble in water. Many compounds are soluble in water when it becomes supercritical at 374 °C and 218 Atm. Hence, this clean and cheap solvent is used as a green solvent for many synthetic reactions.

d) Reactions in aqueous phase*:* The use of ordinary water for organic reactions was unknown till the middle of the 20th century. However, replacement of organic solvents with eco-friendly water has found success with many reactions, some of which may occur at higher rates because of its high polarity. Reactions carried out in aqueous medium include oxidations, reductions, epoxidations, polymerizations (with or without catalysts) and many named reactions.

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e) Reactions in solid phase: Large number of reactions occur in solid state without the solvent, These reactions are simple to operate, economical and solvent-related pollution is avoided.

***Use of Renewable Feedstocks*:** Chemical transformations should be designed to utilize raw materials and feedstocks that are renewable, but technically and economically practicable. Examples of renewable feedstocks include agricultural products, and those of depleting feedstocks include raw materials that are mined or generated from fossil fuels (petroleum, natural gas or coal). For green synthesis, the feedstock should replace the traditional petroleum sources, e.g., benzene used in the commercial sythesis of adipic acid which is required in the manufacture of nylon, placticizers and lubricants, has been replaced to some extent by the renewable and nontoxic glucose and the reaction is carried out in water.

Use of Catalysts: Catalysts are used in small amounts and can carry out a single reaction many times and so are preferable to stoichiometric reagents, which are used in excess and work only once. They can enhance the selectivity of a reaction, reduce the temperature of a transformation, reduce reagent-based waste and potentially avoid unwanted side reactions leading to a clean technology**.** Catalysis is crucial to the chemical and related industries. Apart from heavy metal catalysts softer catalysts like zeolites, phase transfer catalysts, e.g., crown ethers, are finding increasing industrial applications.

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Biocatalysts – Microorganisms and Enzymes: One ploy of green chemistry is to work more like Mother Nature. Plants, for example, have access only to air, a few trace minerals in the soil and energy from the sun, yet they carry out hugely complex chemical transformations. Nature has provided hints for ways to carry out environmentally sound reactions by using microorganisms and/or enzymes. Enzymes are the most efficient and commonest of the catalysts found in nature. The earliest biocatalysed conversion known to mankind is the manufacture of ethyl alcohol from molasses by the enzyme invertase. Enzymes have been used as important tools in organic syntheses and are widely recognised as practical alternatives to traditional (non-bio) syntheses. In pharmaceutical industry, the largest scale biocatalytic process is the conversion of the fermentation product of Penicillin G into 6-amino penicillanic acid by enzyme penicillin acylase. Many chemically modified penicillins, amino acids, vitamins, fructose syrup and many biopharmaceuticals are obtained by this method. A milestone in this area was the commercial use of enzyme nitrile hydratase to convert acrylonitrile to acrylamid, which eliminated the formation of acrylic acid as a byproduct in the chemical process. Biocatalysed reactions are advantageous as they are performed in aqueous medium, all conversions are single step, protection and deprotection of functional groups are not neceessary, reactions are fast, stereo-specific. Such transformations are either impossible or extremely difficult to achieve by conventional chemical methods.

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Avoid Chemical Derivatives: Unnecessary derivatization (use of blocking groups, protection/deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate more waste. Instead, more selective and better alternative synthetic sequences that eliminate the need for functional group protection should be adopted.

Design Synthesis for Energy Efficiency: Energy requirements of the chemical processes should be recognized for their environmental and economic impacts and should be kept to a minimum.

a) *Microwave irradiation*: Reactions with microwave sources have been carried out in a solid support like clay, silica gel, etc., eliminating the use of solvents or with minimum amount of solvents. The reactions take place at a faster rate than thermal heating. For example, Beckmann rearrangement of oximes in the solid state with microwave irradiation gave quantitative yields of the products without the use of acid catalysts.

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b) *Sonochemistry (Ultrasound energy)*: Reactions using ultrasound energy are carried out at RT with excellent yields. For example, Ullmann's coupling which takes place at higher temperature giving low yields by conventional method, gives increased yields at low temperature and in short duration with ultrasound energy.

***Design for Degradation*:** Chemical products should be designed so that at the end of their function, they do not accumulate and persist in the environment but break down into innocuous hazardless substances.

Inherently Safer Chemistry for Accident Prevention: Design chemicals and their forms (solid, liquid, or gas) to minimize the chemical accidents including explosions, fires and releases to the environment, e.g., manufacture of gold atom nanoparticles used diborane (highly toxic and bursts into flame near room temperature) and cancer-causing benzene. Now, diborane has been replaced by environmentally benign $NaBH_4$ which also eliminates the use of benzene.

Nanoscience and nanotechnology is another important contribution to green chemistry. Nanotechnology provides huge savings in materials by development of microscopic and submicroscopic electronic and mechanical devices.

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Some examples of green chemistry in the use of industrial synthesis:

Now, many industrial applications are found that fulfill several of the 12 principles of green chemistry at the same time.

a) The most polluting reaction in industry is oxidation. Implementation of green chemistry has led to the use of alternative less polluting reagents viz., metal ion contamination is minimized by using molecular O_2 as the primary oxidant and use of extremely high oxidation state transition metal complexes.

b) Conventional methylation reactions employing toxic alkyl halides or methylsulfate leading to environmental hazard are replaced by dimethylcarbonate with no deposit of inorganic salts e.g., methylaton of arylacetonitriles in presence of K_2CO_3 to 2-arylpropionitriles (> 99%).

c) The use of phosgene and methylene chloride in the synthesis of polycarbonates has been replaced by diphenylcarbonate.

d) Use of CO_2 as a reaction medium for asymmetric catalytic reductions particularly hydrogenation and H_2 transfer reactions.

e) A convenient green synthesis of acetaldehyde is by Wacker-chemie's oxidation of ethylene with O_2 in presence of a catalyst, in place of its synthesis by oxidation of ethanol or hydration of acelylene with H_2SO_4.

It is important to teach the values of green chemistry to tomorrow's chemists. They should learn to assess hazard with this knowledge and to adopt more sustainable chemical practices throughout their academic and industrial career. The practice of green chemistry means doing clean chemistry, and it cannot be less chemistry.

Suggested Reading

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Address for Correspondence
Bharati V Badami
H.No. 80 (Upstairs)
1st Main, 3rd Cross
Narayanpur
Dharwad 580 008, India.