Green Chemistry

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Green Chemistry is essentially chemistry for the environment. It can be defined as the design of chemical products and processes that reduce or eliminate the use of generation of hazardous substances. The hazards in this definition include but are not limited to toxicity, physical hazards, global climate change and resource depletion. Chemical industries contribute more than 40% of the total environmental pollution (Fig.1)[1]. Heterogeneous catalysis, solventless synthesis, use of microwaves, ultrasound, etc. are a few attempts made by many researchers all over the world in this green chemistry direction, the emphasis also is to suggest how atom economical processes are also the most cost effective.
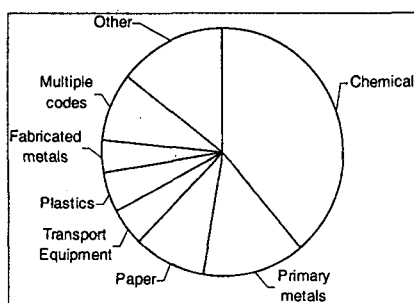

Fig.1 Proportion of hazardous waste released to the environment by the major industrial sectors

Green chemistry differs from historical approaches to environmental protection in several ways. The term GREEN CHEMISTRY, first defined by the US 'Environmental Protection Agency' (EPA) as 'the utilisation of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products', is now widely accepted.

The EPA has issued 12 principles of green chemistry, which elaborate the definition of green chemistry (EPA website, www. epa.gov/dfe/greenchem). The principles of green chemistry focus on reducing, recycling, or eliminating the use of toxic chemicals in chemistry by finding creative ways to minimise the human and environmental impact without stifling scientific progress.

Principles of Green Chemistry:

1. **Prevention** - It is better to prevent waste formation than to treat or clean up waste after it has been created.
2. **Atom economy** - Synthetic methods should be designed to maximise the incorporation of all the materials used in the process into the final product.
3. **Less hazardous chemical synthesis** - Wherever practicable, synthetic methods should be designed use and generate substances that possess little or no toxicity to people or the environment.
4. **Designing safer chemicals** - Chemical products should be designed to effect their desired function while minimising their toxicity.
5. **Safer solvents and auxiliaries** - The use of auxiliary (e.g. solvents or separation agents) should be made unnecessary wherever possible and innocuous when used.
6. **Design for energy efficiency** - Energy ts of chemical processes should be recognized for their environmental and
7. **Use of renewable feedstocks** - A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.
8. **Reduce derivatives** - Unnecessary derivatisation (useof blocking groups, protection/deprotection, and temporary modification of physical/chemical processes) should be minimised or avoided if possiblebecause such steps require additional reagents and can generate waste.
9. **Catalysis** - Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. **Design for degradation** - Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.
11. **Real-time analysis for pollution** - Analytical

methodologies need to be further developed to time, in process monitoring a control prior to the formation of hazardou substances.

12. **Inherently safer chemistry for accident Prevention:-** Substances and the form of a substance used in a chemical process should be chosen to minimise chemical accidents, including releases, explosions, and fires.

Although much of this may appear to be a common sense, it is surprising how many chemists in research and process development do not think in these terms. In chemical synthesis, the ideal will be a combination of a number of environmental, health, safety, and economic aspects (Fig.2)[2].
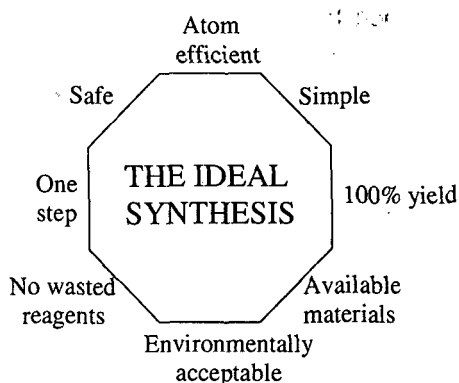

Fig. 2 The ideal synthesis

The stage in the product life cycle most usually associated with green chemistry is manufacture. Even if the product being made is innocuous, the manufacturing process itself can have significant environmental impacts. It is not uncommon, e.g. to have pharmaceutical manufacturing processes that create 100-1000 units of waste for each unit of product. We will therefore review all associated manufacturing processes to see the green chemistry opportunities to reduce environmental impacts.

1. Atom economy

The efficiency of a process can be described using Sheldon's relatively simple "atom utilization" quantification approach [3,4]. How much of the reactant end up in the product compared with the amount in waste-the atom economy of the process- is often ignored. Consider e.g., acylation of toluene by acetyl chloride with $AlCl_3$. A Friedel-Crafts acylation reaction ends up producing a complex

between product and the Lewis acid activating agent. The products are liberated by the addition of water, which also reacts with the activating agent to generate a large volume of a non-recoverable effluent stream
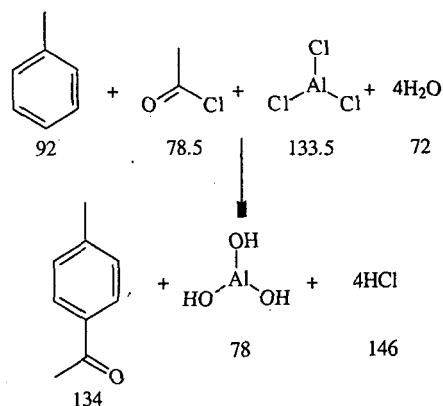
The proportion of atoms in the end product is a poor 37.4% (134/(134+78+146)), even ignoring the sodium carbonate or whatever base is used to wash the product and converting the hydrogen chloride by-product to salts. A hypothetical route from acetic acid, toluene and a catalyst would generate only water as the by-product and have an 88% atom utilisation.

The process efficiency can also be calculated from the E-factor, the ratio (by weight) of the by-products to the desired product(s). The table below illustrates that the 'dirty' end of the chemical industry, oil refining, and bulk chemicals, is remarkably waste conscious; it is the fine chemicals and pharmaceutical companies who are using inefficient, dirty processes, albeit on a much smaller scale.

Industry	Production / tons pa	E-factor
Oil refining	10^6-10^8	0.1
Bulk chemicals	10^4-10^6	1-5
Fine chemicals	10^2-10^4	5-50
Pharmaceuticals	10^1-10^3	25-100

BHC Company (a joint venture of BASF and Hoechst Celanese) has developed an improved process for the manufacture of ibuprofen that increases atom economy. The new technology has three catalytic steps with about 80% atom economy

and this increases to about 99% atom economy with the recovery of the by-product acetic acid. Anhydrous hydrogen fluoride is both a catalyst and a solvent in this synthesis; hydrogen fluoride improves the reaction selectivity and reduces waste.

Over 99% of hydrogen fluoride is recovered and recycled. This process replaces the previous technology that has six stoichiometric steps and less than 40% atom economy (Scheme 1)[5].
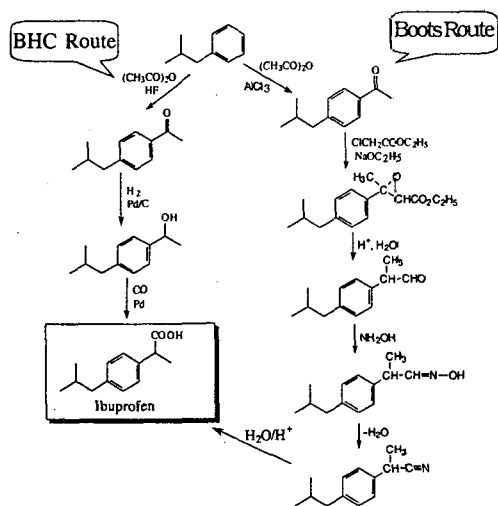
Scheme 1: Two routes to Ibuprofen.
**Only BHC route involves catalytic steps.**

2. Catalysis

Catalysis played a major role in establishing the economic strength of the chemical and related industries in the first of the 20th century and an estimated 90% of all the chemical processes since 1930 depend on catalysis. This has resulted in the build up of an enormous world-wide market for catalysts, which is valued today at some $5000 million per annum with the product value dependent upon them being a staggering $250000 million.

Heterogeneous catalysis is especially important in industry and playing an increasingly important role in small-scale chemical manufacturing; often with the result of a major reduction in waste. Some of the major industrial processes that use solid catalysts include the synthesis of inorganic chemicals such as NH_3, SO_3, and NO, the various reactions used in the refining of crude petroleum such as cracking, isomerisation, and reforming and many of the major reactions of the petrochemical industry, such as the synthesis of

methanol, the hydrogenation of aromatics and various controlled oxidations.

A good example of this is the new heterogeneous route to hydroquinone based on the titanium silicate catalyst TS-1. The traditional homogeneous route involved the oxidation of aniline with manganese dioxide and sulphuric acid followed by reduction with Fe/HCl. This route led to very large volumes of hazardous waste (e.g. 4 mole equivalents of manganese sulphate are produced).
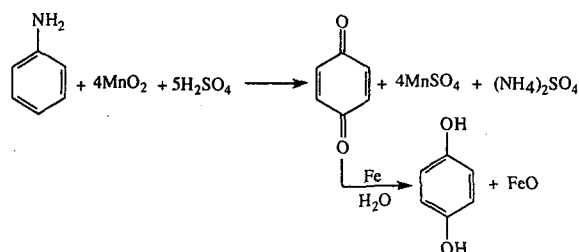
The new route is an excellent example of clean synthesis. The catalyst is reusable, the oxidation is relatively safe to handle and the by-products are either innocuous (water) or marketable (catechol).
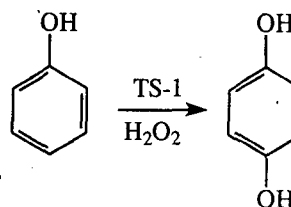
Catalysis using solid catalysts is rapidly emerging as a new enviro-technology designed to enhance process efficiency and reduce process waste through more efficient use of plant, lower energy costs and reduced side products. In the last decade clay and zeolite catalysed reactions are rapidly substituting most of the acid catalysed reactions. There are several significant examples of new industrial processes based on this concept[6]. In fact we can say that hidden among the tiny galleries, pores and cavities of solid acid catalysts is the basis for much of the manufacturing industry!

Clays are layered aluminosilicates, whereas zeolites have a rigid three-dimensional aluminosilicate structure containing channels. Both of them possess high surface area, ion exchange property and high acidity and their properties can be

manipulated as per the requirement. Clays have proven themselves as popular solid catalysts for many years. They form the basis of new commercial supported reagent catalysts developed for the liquid phase synthesis of fine chemicals. Particularly significant is their use in Friedel-Crafts reactions, which represent a remarkably diverse and frequently employed class of organic reactions used in the manufacture of countless intermediates and products. The essential logic behind the use of catalysts and supports such as acid-treated clays in these reactions is that their mesoporous nature makes them more likely candidates for many liquid phase reactions. The microporous zeolitic materials are often more suitable for vapour phase reactions. Zeolites are also shape selective catalysts

The new solid catalysts are meant to replace existing reagents and catalysts, which are environmentally unacceptable. Most notoriously, aluminium chloride, perhaps the most widely used Friedel-Crafts catalyst is the source of enormous quantities of toxic waste. This is a good example of the type of chemical process that is unlikely to be environmentally unacceptable in the future, and where the costs of clean-up and waste disposal will make it difficult to maintain economically.

Another example of the problems associated with liquid acid/base catalysts is the production of gasoline alkylates from isobutane and butenes. A typical alkylation plant of 10000barrels/day capacity requires 4,00,000 lbs. of anhydrous HF[7]. Although the HF can be recycled, it is highly toxic and extremely corrosive. Alternatively, H_2SO_4 can be used to produce gasoline alkylate. However, large amounts of spent acid must be continuously removed. It is speculated that if a safe catalyst, e.g., a solid acid, could be used to perform the alkylation, then the current world-wide capacity of approximately 1.5 million barrels/day could be significantly increased.

The nitration of aromatics is a common reaction in the fine chemicals industry, producing intermediates for dyes, plastics and pharmaceuticals. A typical industrial process involves using a large excess of fuming nitric acid with sulphuric acid, leading to large amounts of acidic waste. Recent research, however, using lanthanide triflate catalyst, e.g., $Yb(CF_3SO_3)_3$, has opened up the possibility for industry to use molar equivalents of nitric acid, thus avoiding the use of sulphuric acid [8]. These so-called rare earth elements are not that rare or expensive and offer real commercial possibilities; their value lies

in the fact that they behave as Lewis acids, but are water tolerant and can be readily recovered and recycled.

Enzyme catalysts are also widely used for chemoselective synthesis. Frost has demonstrated a variety of syntheses using glucose as a starting material. Using biotechnological techniques to manipulate the shikimic acid pathway compounds such as hydroquinone, catechol all of which are important large volume chemicals can be synthesised [9]. Recently researchers at Michigan University have found that adipic acid can be prepared by a green process where microbes are used for environmentally benevolent process from glucose[10]. Glucose is first converted to cis,cis-muconic acid using a genetically-engineered microbe, and this acid is then hydrogenated to give adipic acid.
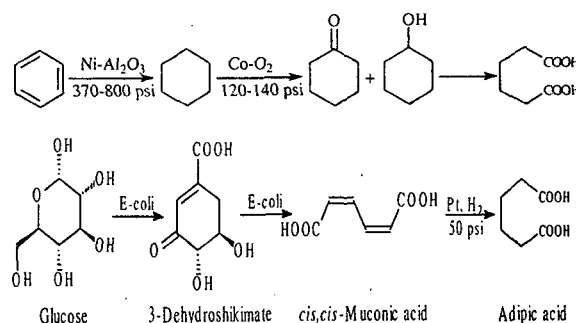
Scheme 2: Conventional and new route for the synthesis of adipic acid

This process eliminates both the use of benzene (carcinogenic agent) as a starting material and formation of nitrous oxide as a by-product. The process uses a renewable feedstock and the process material are of little or no toxicity.

2.1 Asymmetric Synthesis

Asymmetric synthesis deals with the production of excess of one of the enantiomers/ diastereomers. Why is this so important? Let us go back to nature to find the answer. One may well think that both forms of chiral molecules ought to be equally common in nature, the reactions should be symmetrical. But when we study the molecules of the cells in close-up, it is evident that nature mainly uses one of the two enantiomers and this applies to all living material. A table below shows the relationship between absolute configuration and biological effect of chiral compounds (Table 1).

Table 1 Relationship between absolute configuration and biological effect of chiral compounds

Compound	Configuration	Biological effect
Limonene	R	Orange smell
	S	Lemon smell
Asparagine	R	Sweet taste
	S	Bitter taste
Propanolol	R	Contraceptive
	S	antihypertensive, antiarrhythmic
Chloramphenicol	R,R	antibacterial
	S.S	inactive
Ethambutol	R,R	Causes blindness
	S,S	Causes blindnesstuberculosis

Thus the enzymes in our cells are chiral, as are other receptors that play an important part in cell machinery. This means that they prefer to bind to one of the enantiomers. In other words, the receptors are extremely selective; only one of the enantiomers fits the receptor's site like a key that fits a lock

Since the two enantiomers of a chiral molecule often have totally different effects on cells, it is importantto be able to produce each of the two forms pure. One can realise the importance of asymmetric synthesis from the fact that this year's Nobel Prize for chemistry is conferred on three researchers- Sharpless, Knowles and Noyori for their contribution to asymmetric synthesis.

Most drugs consist of chiral molecules. And since a drug must match the molecules it should bind to itself in the cells, it is often only one of the enantiomers that is of interest. In certain cases the other form may even be harmful. This was the case, for example, with the drug thalidomide, which was sold in the 1960s to pregnant women. One of the enantiomers of thalidomide helped against nausea, while the other one caused foetal damage.
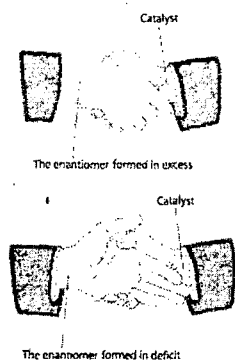

Fig. 3 The hands in a handshake between two right hands match better than a handshake between a right and a left hand.

Two strategies are available for the production of a single enantiomer. The first, and more elegant strategy, involves the direct manufacture of the pure enantiomer through asymmetric catalysis. The second is

to produce a racemic mixture through traditional routes. The desired product is then separated from the racemic mixture using techniques that include crystallization, chromatography, and kinetic resolution. These methods are often laborious and expensive. Despite this, these procedures are used regularly because the desired enantiomer is so valuable. The undesired enantiomer must be recycled, discarded, or destroyed. The large amounts of by-products and the high volumes of solvents used in the purification make these systems targets for environmentally benign replacements.

Noyori, together with Takaya, discovered an atropisomeric chiral diphosphine, BINAP. Rh(I) complexes of the enantiomers of BINAP are remarkably effective in various kinds of asymmetric catalysis.

(S)-BINAP   mirror plane   (R)-BINAP
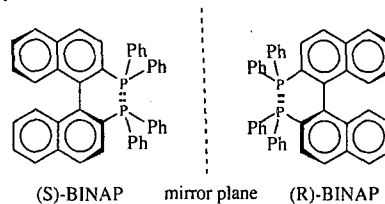
Noyori's discovery of the BINAP-Ru(II) complex catalyst was a major advance in steroselective organic synthesis. These chiral Ru(II) complexes serve as catalyst precursors for the highly enantioselective hydrogenation of a range of α,β- and β,γ-unsaturated carboxylic acids. An example is shown below.

(S)-naproxen
an anti-inflammatory agent
92% yield, 97%ee
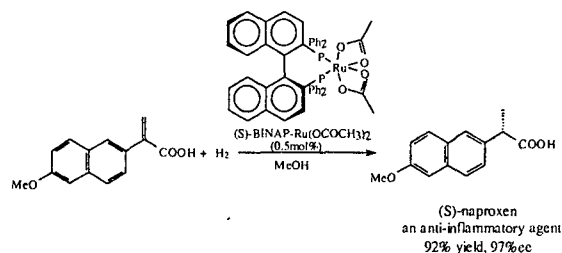
3. Green Solvents

The replacement of toxic and noxious solvents by more environmentally benign ones is an area of prime interest for the 'green' chemists. Many solvents, which can be harmful, if handled without proper safety; and to the environment, if released directly as an effluent, are still in use. Volatile organic solvents are the normal media for the industrial synthesis of organics mainly petrochemicals and pharmaceuticals, with a current

world-wide usage of ca. £4,000,000,000 p.a. Because of increasingly strict legislation on the release of volatile organic compounds and on trace solvents in water, industry is focusing on the use of water as a solvent.

There are four main alternate strategies: (a) solvent free synthesis, (b) the use of water as a solvent, (c) the use of supercritical fluids as solvent, and (d) the use of ionic liquids as solvent.

3a. Solvent free synthesis: Tanaka and Toda have reviewed cycloaddition, polymerisation, photocatalytic, rearrangement, coupling reactions in dry state11. Contrary to common belief, molecules can move quite freely in the solid state and organic reaction can occur by mixing powdered reactant and reagents in the absence of solvent and the reaction product can be obtained efficiently.

3b. The use of water as a solvent: Water is not normally a good solvent for organic molecules. At high temperatures, however, the ionic product of water increases dramatically, being 1000 times higher at 240°C than at room temperature, making it a stronger acid and base. At the same time, the polarity is significantly reduced as the temperature increases. These properties suggest that water may be a useful solvent for some high temperature organic reactions, including condensation, isomerisation, decarboxylation, and hydration of alkenes.

Thus, the replacement of organic-based solvents will require a significant amount of effort. A commercial process that has successfully made the transition from organic to aqueous solvent is described below:

Hydroformylation is the addition of CO and H_2 to an olefin to yield an aldehyde. A typical propene hydroformylation process involves the use of $[HRh(CO)(P(C_6H_5)_3)_3]$ (1a) in organic solvent. Propene, CO and H_2 enter the reactor and n - and i -butyraldehyde are the products formed. The desired isomer is the linear aldehyde. This is an example of homogeneous catalysis, and the products are distilled off of the reaction solution. However, this process is not able to accommodate heavier olefins due to the low volatility of the product aldehyde.

Rührchemie/Rhöne-Poulenc have developed propene hydroformylation process that uses water as the solvent[12]. Two plants now produce 3,00,000 tons of butyraldehyde/year[13]. The key to the success of this process is the ligand triphenylphosphone trisulfonate, TPPTS. This ligand has a solubility of 1100 g/L in water. Thus, $[HRh(CO)(TPPTS)_3]$ (1b) is extremely water soluble, and is not soluble in most organics. Propene is slightly soluble in water. Therefore, the hydroformylation can take place homogeneously in water and as the reaction proceeds a second, water immiscible butyraldehyde phase forms. The product phase is easily separated from the aqueous phase without significant catalyst loss.
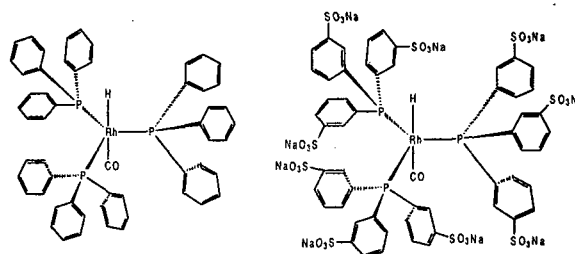
Li has reviewed carbon-carbon bond formation reactions successfully carried out in aqueous media such as Diels-Alder reaction, carbonylation, alkylation, and polymerisation reactions[14].
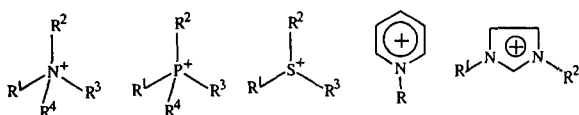
3c. The use of supercritical fluids (SCFs) as solvents: Every stable compound has a triple point and a critical point. Any gaseous compound becomes supercritical when compressed to a pressure higher than the critical pressure (Pc) above the critical temp (Tc). Properties of SCFs are different from those of ordinary liquids and gases and are tunable simply by changing the pressure and temperature. In particular, density and viscosity change drastically at conditions close to the critical point. The solvating power is much smaller than that of conventional fluid solvents, but this can be utilised to generate unique molecular clusters or assemblies in homogenous phase.

$scCO_2$, readily accessible with Tc of 31°C and a Pc of 73 atm, has excellent potential for achieving this goal. It is abundant, inexpensive, non-flammable, non-toxic and environmentally benign. It has high solubility for non-polar organic compounds and even a small amount of polar entrainer and appropriate surfactant change the microenvironment to greatly increase the solubility of such substances. Thus, it allows the facile separation of reactants, catalysts and products.

Surprisingly, unlike ambient liquid water, scH_2O is relatively non-polar but highly acidic, although under harsh conditions (Tc=374°C, Pc=218 atm). A recent review covers various reactions with supercritical fluids[15].

3d. The use of ionic liquids as solvents: The term ionic liquid implies a material that is fluid at ambient temperature, is colourless, has a low viscosity and is easily handeled, i.e. a material with attractive properties for a solvent. Room temperature ionic liquids are generally salts of organic cations, e.g., tetraalkylammonium, tetraalkylphosphonium, N-alkylpyridinium, 1,3-dialkylimidazolium and trialkylsulfonium cations.

Cations:

Anions:

BF_4^-, PF_6^-, SbF_6^-, NO_3^-, $CF_3SO_3^-$, $(CF_3SO_3)_2N^-$, $ArSO_3^-$, $CF_3CO_2^-$, $CH_3CO_2^-$, $Al_2Cl_7^-$
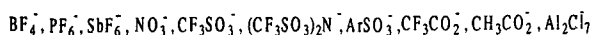
Ionic liquids are currently under investigation and development in a variety of laboratories, around the world. Many of these processes utilise the ability of many ionic liquids e.g. N-butylpyridinium chloride-aluminium(III) chloride, to selectively immobilise transition metal catalysts for liquid-liquid two-phase catalysis while permitting easy, often trivial, extraction of products. Ionic liquids exhibit many properties which make them potentially attractive media for homogeneous catalysis: (a) They have essentially no vapour pressure, (b) They generally have reasonable thermal stability, (c) They are able to dissolve a wide range of organic, inorganic and organometallic compounds, (d) The solubility of gases, e.g. H_2, CO and O_2 is generally good, which makes them attractive solvents for catalytic hydrogenations, carbonylations, hydroformylations and aerobic oxidations. The areas under study include alkylation reactions, Diels-Alder cyclisations, Heck coupling reactions, hydrogenation, hydroformylation, oligomerisation, dimerisation and polymerisation of olefins[16].

Conclusion

The success or failure of the green chemistry movement will be ultimately decided by industry. However, in order to move industry forward much can be done in teaching the chemistry to ensure that future generations of research and process development chemists are more aware of the possibilities for developing environment-friendly products and processes. What is clear is that environmental issues are here to stay, and chemical industries will not be allowed to cause as much pollution in the 21st century as they have done in 20th. The most successful chemical companies of the future will be those which will exploit its opportunities to their competitive advantage, and the most successful chemists of the future will be those who use Green Chemistry concepts in R & D, innovation and education. Chemists now have the tools required to become protectors of the environment.

Green Chemistry Awareness

EPA Green Chemistry Programme: EPA introduced green chemistry as a formal focus area in 1991. Under the EPA office of Pollution Prevention and Toxics, the Green Chemistry Programme fosters research, development, and implementation of innovative chemical technologies that prevent pollution in a scientifically sound and cost-effective manner. (www.epa.gov/greenchemistry)

The Green Chemistry Institute (GCI): GCI, a not for profit organization in Rockville, Md., promotes and fosters green chemistry through information dissemination, chemical research, conferences and symposia, and chemical education (www.lanl.gov/internal/projects/green/index/html).

The 'Green Chemistry' Journal published by the Royal Society of Chemistry contains current research, reviews and information covering all chemical aspects of clean technology (www.rsc.org/greenchem).

The Royal Society of Chemistry Green Chemistry Network offers three annual awards (UK Green Chemistry Awards) for Green technology that offers significant improvements in chemical processes, products and services through research and commercial exploitation of novel chemistry, so to achieve a more sustainable, cleaner and healthier environment as well as creating competitive advantage (www.chemsoc.org/gcn).

Green Chemistry Websites:

www.acs.org/education/greenchem/

www.bama.ua.edu/~cgm
www.chemsoc.org/gcn
www.epa.gov/opptintr/greenchemistry/
www.grc.uri.edu/programs/2002/green.htm
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www.web.chem.monash.edu.au/GreenChem

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