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# RELEVANCE OF GREEN CHEMISTRY 12 PRINCIPLES IN ORGANIC SYNTHESIS

A. Kulshrestha and J. Pandey *

Department of Chemistry, Amity University Uttar Pradesh, Lucknow Campus, Lucknow - 226010, Uttar Pradesh, India.

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**Correspondence to Author:**
**Dr. Jaya Pandey**

Department of Chemistry,
Amity School of Applied Sciences,
Amity University Uttar Pradesh
Lucknow Campus, Gomti Nagar
Extension, Lucknow - 226028,
Uttar Pradesh, India.

**E-mail:** jpandey@lko.amity.edu

**ABSTRACT:** Green chemistry or sustainable chemistry focuses on designing products and processes that minimize the generation or use of hazardous substances. Green chemistry, though not a new area, has recently gained much importance because of increasing environmental concerns. Industries now focus on adopting processes which are mainly non- hazardous, easier to undertake, lesser energy and time consuming, using re-usable reagents, degeneration of drastic materials, and more economical. These concepts have identified and developed various technologies such as microwave, ultrasonic, UV radiation, electrochemistry, *etc*., as green technologies. Solvents such as water, has significant importance, being non-hazardous, easily recoverable, and lowering unnecessary wastage of energy. Other recoverable solvents such as acetone, alcohol, methanol, etc., come under green chemicals. Catalysts that promote chemical reactions, without causing hazardous effect and are recoverable are also a part of green chemistry. All the aspects of green chemistry, improving the level of research in chemistry and advance techniques make the experimental work easier to new researchers. This is a positive and harmless growth in the field of chemistry.

**INTRODUCTION:** A green signal permits to proceed. That is how 'green chemistry' suggests a branch of chemistry that is acceptable and most valuable. Green chemistry is a synthetic process that avoids many technical, environmental problems, hazardous atmosphere, and formation of specific products in high yields, avoids the use of hazardous chemicals, attains more economical status, reduces by-products and creates an environmentally friendly atmosphere.

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Green chemistry addresses our future challenges in working with chemical processes and products by inventing novel reactions that can maximize the desired products and minimize by-products, designing new synthetic schemes that can simplify operations in chemical productions, and seeking greener solvents that are inherently environmentally and ecologically benign.

Green chemistry searches for an alternative, environmentally friendly reaction media and at the same time strives to increase reaction rates and lower reaction temperatures [1-5]. Green chemistry takes into account the environmental impact and seeks to prevent or lessen that impact through several key principles outlined below. These principles can be grouped into "Reducing Risk" and "Minimizing the Environmental Footprint [6-10]."

- Prevention of waste - better to minimize the formation of waste than to remove it or reduce its toxicity when formed.
- Atom economy - atom wise maximize the incorporation of all reactants used in the process into the final products.
- Less hazardous chemical synthesis - use of chemical reactants and formation of final products with minimized or no toxicity.
- Designing safer chemicals and products - preparation of effective chemicals with reduced toxicity.
- Safer Solvents and Auxiliaries - avoid auxiliary substances such as solvents, separating agents, etc., wherever applicable.
- Design for Energy Efficiency - energy requirements should be recognized for environmental and economic impacts and to be minimized to conduct the synthetic procedure at ambient temperature and pressure.
- Renewable feedstock - a raw material or feedstock should be renewable rather than depleting whenever possible.
- Reduce derivatives- use of derivatives as reactants with protecting groups and temporary modified structures should be avoided wherever possible.
- Catalysis- catalytic reagents are superior to stoichiometric reagents. It can enhance the extent of product formation under reduced temperature and pressure and reduce the waste formation
- Design for degradation- 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 and do not persist in the environment.
- Real-time analysis for pollution prevention- analytical methodology be developed to allow real-time in-process monitoring and control before the formation of hazardous substances.
- Safety- substances should be chosen to minimize the potential for chemical accidents, explosion, fire, *etc.*

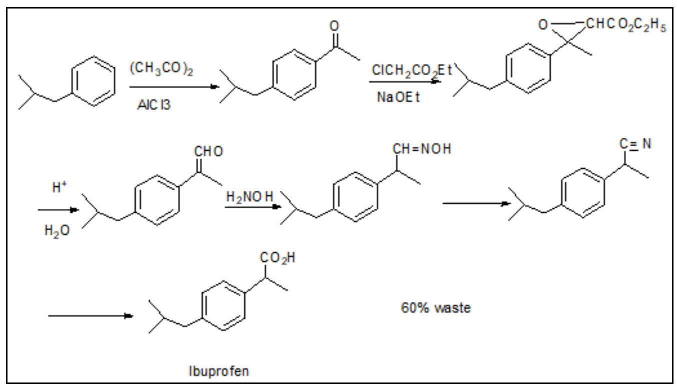
These principles, along with suitable examples of reactions carried out under these mentioned 12 principles, are covered in this article [11].

**I) Prevention of Waste:** It is better to prevent waste formation that to treat it after it is formed. An example is the manufacture of phenol. It used to be made from benzene using sulfuric acid and sodium hydroxide in a multi-stage process with 78% yield; the reaction can be expressed as:

$$C_6H_6 + H_2SO_4 + 2NaOH \longrightarrow C_6H_5OH + Na_2SO_3 + 2H_2O$$

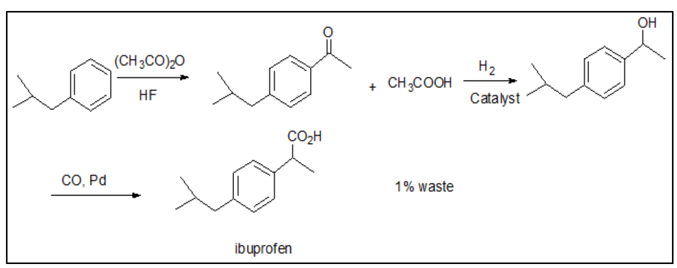
Sodium sulfite is the by-product, can be used in other processes. However, if it is not in demand, that would mean this may not be the most suitable reaction for manufacturing phenol [12, 13].

Another example of green synthesis is the synthesis of ibuprofen. Traditional synthesis of ibuprofen produces 60% waste, as shown below.




**SCHEME 1: CONVENTIONAL METHOD OF SYNTHESIZING IBUPROFEN**

Alternate green chemistry of ibuprofen produces just 1% waste.

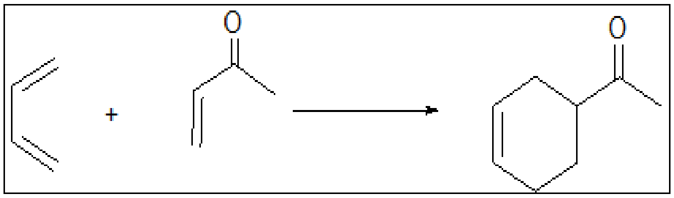



**SCHEME 2: GREEN CHEMISTRY METHOD OF SYNTHESIZING IBUPROFEN**

**II) Atom Economy:** Atom economy is a measure of the amount of atoms from the starting material that is present in the useful products at the end of a chemical process. Side products from reactions that aren't useful can lead to a lower atom economy and more waste. Therefore, processes that maximize the atom economy are preferred.

Atom economy % = Relative molecular mass of desired products / Relative molecular mass of all reactants × 100

An example of Diel's Alder Reaction with 100% atom economy is as follows: [14-18]



**SCHEME 3: DIEL'S ALDER REACTION**

Another example is the manufacture of phenol from benzene and propene,

$C_6H_6 + CH_3CH{=}CH_2 + O_2 \longrightarrow C_6H_5OH + CH_3CO$

The byproduct propanone, which is a valuable chemical and so the atom economy for this process can be regarded as 100%.

The addition, condensation and rearrangement reactions will generally have higher atom economies than either elimination or substitution.

For example, the addition of chlorine to ethene, to form 1,2-dichloroethane (an important reaction in the manufacture of poly (chloroethene) (PVC)) has an atom economy of 100%:

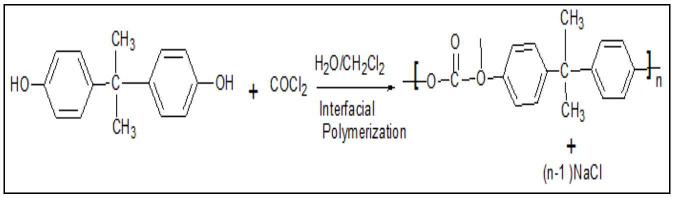
$H_2C{=}CH_2 + Cl_2 \longrightarrow ClCH_2CH_2Cl$

However, if the product is hydrolyzed, the atom economy falls:

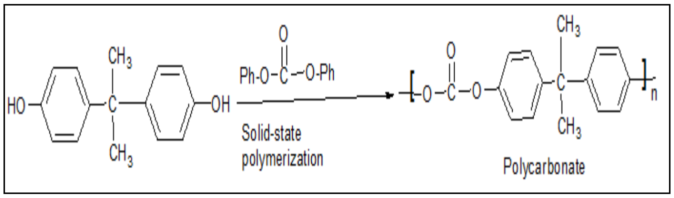
$ClCH_2CH_2Cl + 2H_2O \longrightarrow HOCH_2CH_2OH + 2HCl$

The first is an addition reaction; the latter is a substitution reaction.

**III) Less Hazardous Chemical Synthesis:** It is also important that chemicals that are produced are safe for the environment. In all cases, the material should degrade to harmless products. Synthetic methods should where practicable, use or generate materials of low human toxicity and environmental impact. For example, polycarbonate synthesis is carried out using phosgene ($COCl_2$). To avoid phosgene, the hazardous chemical, solid-state polymerization is undertaken, which also leads to polycarbonate formation under green chemistry [19, 20].



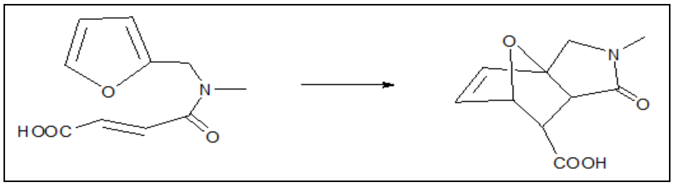

**SCHEME 4A: GREEN CHEMISTRY METHOD OF SYNTHESIZING POLYCARBONATE**




**SCHEME 4B: GREEN CHEMISTRY METHOD OF SYNTHESIZING POLYCARBONATE**

**IV) Designing Safer Chemicals:** The design of safer chemical targets requires a knowledge of how chemicals act in our bodies and the environment. In some cases, a degree of toxicity to animals or humans may be unavoidable, but alternatives should be sought. Toxic chemicals used, such as repellent DEET as an insecticide, bisphenol- A, as a plasticizer, *etc.*, and some acidic catalysts, need their replacement to achieve a safer side. Designing such requirements, safer chemicals is an important part of green chemistry, *e.g.* solid acid catalysts Zeolite H-FER, as a safer catalyst [21].

**V) Safer Solvents and Auxiliaries:** Many chemical reactions require the use of solvents or other agents to facilitate the reaction. They can also have a number of hazards associated with them, such as flammability and volatility. Solvents might be unavoidable in most processes, but they should be chosen to reduce the energy needed for the reaction, should have minimal toxicity, and should be recycled if possible. Solvents are also the major contributors to the overall toxicity profile and because of that, compose the majority of the materials of concern associated with a process. Water is also capable of accelerating the process even when the diene and the dienophile are associated [22].

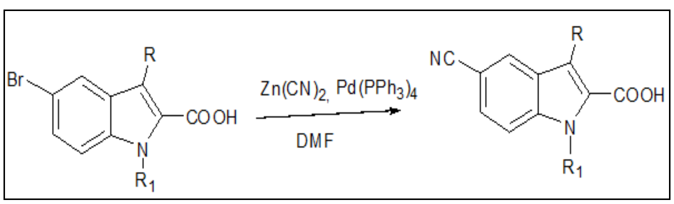


**SCHEME 5: CONVERSION OF DIENE INTO DIENOPHILES BY WATER**

On average, they contribute the greatest concern for process safety issues because they are flammable and volatile, or under the right conditions, explosive. They also generally drive workers to don personal protective equipment of one kind or another. The use of auxiliary substances (*e.g.*, solvents or separation agents) should be made unnecessary whenever possible and innocuous when used. Some of the safer auxiliaries (*e.g.*, solvents, separating agents, etc.) are water and carbon dioxide. Water is used as a solvent in catalytic reactions [1, 2,] and $CO_2$ is also used as a solvent for chemical reaction and extraction [23].

Some reactions use water as a solvent, for example, in the manufacture of inorganic compounds such as hydrogen peroxide, phosphoric acid, sodium carbonate, and organic compounds such as ethane-1,2-diol and ethanol. Water is not a harmful solvent, but it is a precious resource, and it is important to ensure that it is not wasted. Supercritical (liquid) carbon dioxide is widely used as a solvent in the extraction of caffeine from coffee beans and in the latest dry cleaning equipment it replaces chlorinated solvents such as perchloroethylene, $C_2Cl_4$.

**VI) Design for Energy Efficiency:** Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.




**SCHEME 6: GREEN CHEMISTRY METHOD OF SYNTHESIS LESS TIME CONSUMING**

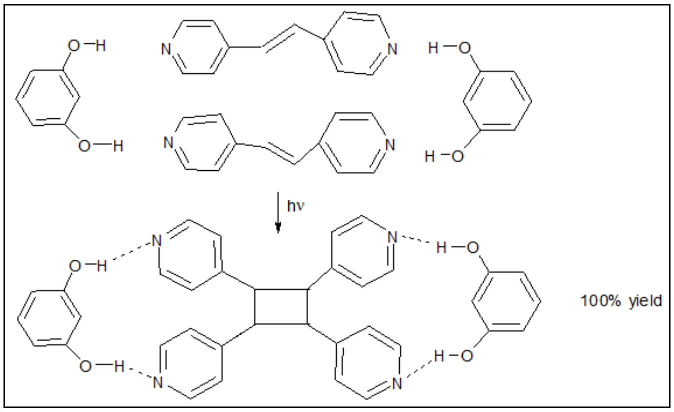
Various Microwave-Assisted Diels-Alder reactions have been carried out for energy effective reaction, as a part of green chemistry. One such example is shown below. Replacement of Br with CN under conventional condition takes place at 100 °C with around 75% conversion in 72 h. Under Micro Wave, 100% conversion in only 10 min is produced at 200 °C. Traditional processes are being overhauled, and more energy efficient ones substituted. Catalysts are being developed so that a process can be run at lower temperatures and pressures (high temperatures and pressures are very energy consuming. Similarly, the development of molecular sieves means that processes such as the purification of ethanol can be carried out at ambient temperatures instead of by distillation [24].

**VII) Renewable Feedstock:** Renewable biomass feedstock forms the basis of many successful industries such as pulp & paper, and wood product industries. Crops grown for fiber, oils or other materials, provide necessary feedstock to such industries. One renewable resource hydrogen is obtained from biomass such as water, natural gas, crude oils, hydrocarbon, and organic fossil materials. Recently glycerin has become increasingly available as a by-product of the manufacture of bio-diesel, and this renewable feedstock has improved the production of epichlorohydrin, a largely used chemical for the manufacture of epoxy resins [25]. Some other solvents which can be distilled, purified, and reused such as acetone, methanol, ethanol, acetonitrile, *etc*. are considered as green solvents.

**VIII) Reduce Derivatives:** Unnecessary derivatization (use of blocking groups, protection/ de-protection, and temporary modification of physical/chemical processes) should be minimized or avoided if possible because such steps require additional reagents and can generate waste. An alternative that has been explored in some processes is the use of enzymes. As enzymes are highly specific, they can be used to target particular parts of a molecule's structure without the need for the use of protecting groups or other derivatives. Enzymes are so specific that they can often react with one site of the molecule and leave the rest of the molecule alone and hence protecting groups are often not required.

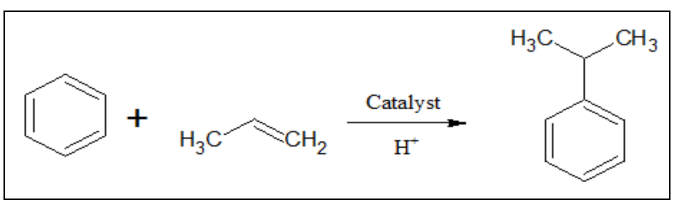
A great example of the use of enzymes to avoid protecting groups and clean up processes is the industrial synthesis of semi-synthetic antibiotics such as ampicillin and amoxicillin. In the first industrial synthesis Penicillin G (R=H) is first protected as its silyl ester [R = $Si(Me)_3$] then reacted with phosphorus pentachloride at -40 °C to form the chlorimidate 1 subsequent hydrolysis gives the desired 6-APA from which semi-synthetic penicillins are manufactured [27].

Covalent bond formation in solid state condition under hv, in high yields, with limited by-products, and with minimal waste has been reported [28].



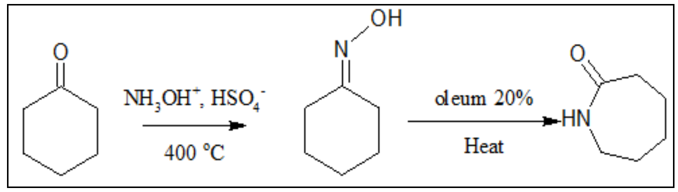

**SCHEME 7: GREEN CHEMISTRY METHOD OF SYNTHESIS MINIMIZING WASTE**

**IX) Catalysis:** A primary goal of green chemistry is the minimization or preferably the elimination of waste in the manufacture of chemicals and allied products. The use of catalysts can enable reactions with higher atom economies. Catalysts themselves aren't used up by chemical processes, and as such can be recycled many times over, and don't contribute to waste. They can allow for the utilization of reactions which would not proceed under normal conditions, but which also produce less waste. For example, benzene and propane are converted into cumene in the manufacture of phenol. This reaction needs an acid catalyst, such as aluminum chloride. A solid zeolite with acid groups, such as ZSM-5 is now the favored catalyst:



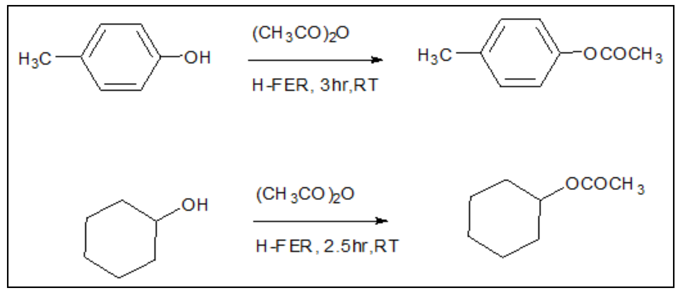

**SCHEME 8: SYNTHESIS OF CUMENE**

The zeolite is more environmentally friendly as the effluent is much cleaner and lower temperatures and pressures can be used [29]. Another similar example is in the manufacture of one of the most important polymers used to make fabrics, nylon 6,6. In this process, cyclohexanone is converted into caprolactam via the oxime (produced by the reaction of the ketone with hydroxylamine hydrogensulfate). The oxime is isomerized by sulfuric acid to caprolactam; the released sulfuric acid is converted to ammonium sulfate.



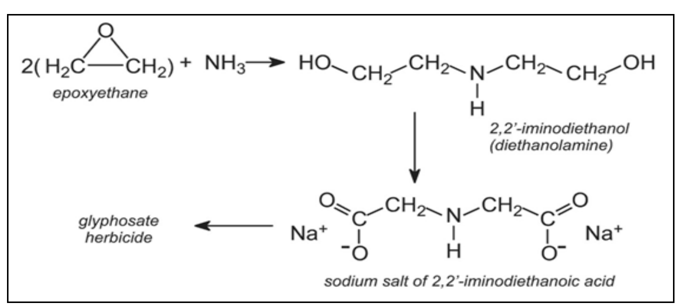

**SCHEME 9: SYNTHESIS OF CAPROLACTAM**

However, again, a zeolite catalyst, with acidic sites, is now being used to effect the rearrangement. The zeolite is regenerated and saves the use and subsequent waste of sulfuric acid. Catalytic reagents are better than stoichiometric reagents. It has higher activation energy enhancing the selectivity of a reaction, reduce transformation temperature, enhance the yield of the conversion product, and reduce reagent- based waste [30].




**SCHEME 10: GREEN CHEMISTRY METHOD OF SYNTHESIS REDUCING WASTE AND INCREASING YIELD OF PRODUCT**

**X) Degradation Design:** 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. Exposure to persistent chemicals can be significant as a result of global dispersion enabled by properties such as volatility or sorption to particles and partitioning into organisms based on properties such as fat solubility. In green chemistry, chemical products should be designed in a way that at the end of their function, it degrades into hazard less substance without persisting environmentally [31].




**SCHEME 11: GREEN CHEMISTRY METHOD OF SYNTHESIS DEGRADING LESS HAZARDS SUBSTANCE**

**XI) Pollution Preservation Analysis:** Analytical methodologies need to be further developed to allow for real-time, in-process monitoring, and control before the formation of hazardous substances. Monitoring a chemical reaction as it is occurring can help prevent the release of hazardous and polluting substances due to accidents or unexpected reactions. With real-time monitoring, warning signs can be spotted, and the reaction can be stopped or managed before such an event occurs. There should be a provision to analyze and estimate the progress of product formation and detect the production of any unwanted by-product creating hazardous environment [32].

**XII) Safety:** Safety can be defined as the control of recognized hazards to achieve an acceptable level of risk. Substances and the form of the substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires. Safer solvents such as water, liquid $CO_2$, or avoiding the use of solvents is a part of green chemistry. Diels-Alder reactions of neat reactive dienes and dienophiles are sometimes very vigorous and are, therefore, limited preparative value. Addition of a limited amount of water in such reaction makes it valuable by lowering its temperature, increasing its rate of formation and creating higher purity product [33].

**CONCLUSION:** Though the tenets of green chemistry might seem simple to implement, improvements can still be made in a large number of chemical processes. A lot of the chemical products we all utilize come from processes that still fail to meet a number of these principles; plenty of these products are still derived from chemicals from crude oil, and many still produce large amounts of waste.

There are, of course, challenges involved in meeting some of the principles in a large number of processes, but it can also drive new research and the discovery of new chemistry. It is to be hoped that, in the coming years, many more processes will be adapted with these principles in mind.

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**CONFLICT OF INTEREST:** Nil

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