

# Green Chemistry

There is absolutely no doubt that green chemistry has brought about medical revolution (e.g., synthesis of drugs etc.). The world's food supply has increased many folds due to the discovery of hybrid varieties, improved methods of farming, better seeds and use of agro chemicals like fertilizers, insecticides and herbicides etc. Also the quality of life has improved due to the discovery of dyes, plastics, cosmetics and other materials. All these developments increased the average life expectancy from 47 years in 1900 to about 80 years in 2010. However, the ill-effects of all the development became pronounced. The most important effect is the release of hazardous byproducts of chemical industries and the release of agro chemicals in the atmosphere, land and water bodies; all these are responsible for polluting the environment including atmosphere, land and water bodies. Due to all these, green chemistry assumed special importance.

## 1.1 THE NEED OF GREEN CHEMISTRY

It has already been stated that various scientific developments in the 20th century brought about various benefits to the mankind, but all this was responsible for a number of environmental problems at the local and global levels. It is, of course, important to formulate guidelines and pass strict rules for the practising chemists. But the most important is to bring about changes at the grass root level. Which can be achieved by bringing about necessary changes in the chemistry curriculum in the colleges and the universities as well as also in the secondary schools. A concerted and pervasive effort is needed to reach the widest audience. Bringing green chemistry to the classroom and the laboratory will have the desired effect in educating the students at various levels about green chemistry.

## 1.2 PRINCIPLES OF GREEN CHEMISTRY

Green chemistry deals with environmentally benign chemical synthesis with a view to devise pathways for the prevention of pollution. According to Paul T.

## 2 Green Chemistry - Environmentally Benign Reactions

Anastas,<sup>1</sup> the following twelve basic principles of green chemistry have been formulated:

- 1. It is better to prevent waste than to treat or clean up waste after it is formed.**

It is best to carry out a synthesis by following a pathway so that formation of waste (byproducts) is minimum or absent. It must be kept in mind that in most of the cases, the cost involved in the treatment and disposal of waste adds to the overall cost of production. The unreacted starting materials (which may or may not be hazardous) form part of the waste. The basic principle 'prevention is better than cure' should be followed. If the waste is discharged in the atmosphere, sea or land, not only causes pollution, but also requires expenditure for cleaning up.

- 2. Synthetic materials should be designed to maximize the incorporation of all materials used in the process into the final product.**

It has so far been believed that if the yield in a particular reaction is about 90 per cent, it is considered to be good. The percentage yield is calculated by

$$\% \text{ yield} = \frac{\text{Actual yield of the product}}{\text{Theoretical yield of the product}} \times 100$$

The above calculation implies that if one mole of a starting material produces one mole of the product, the yield is 100%. However, such a synthesis may generate significant amount of waste or byproducts which is not visible in the above calculation. Such a synthesis, even though is 100 per cent (by above calculation) is not considered to be a green synthesis. For example, reactions like Grignard reactions and Wittig reaction may proceed with 100 per cent yield, but they do not take into account for the large amount of byproducts obtained.

A reaction or a synthesis is considered to be green if there is maximum incorporation of the starting materials or reagents in the final product. One should take into account the percentage atom utilization, which is determined by the following equation

$$\% \text{ atom utilization} = \frac{\text{MW of desired product}}{\text{MW of desired product} + \text{MW of waste products}} \times 100$$

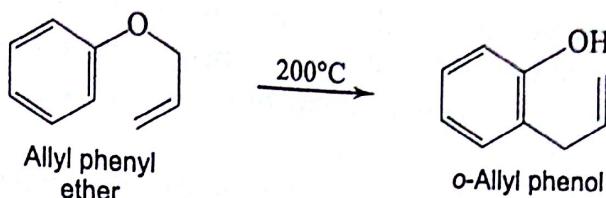
This concept of atom economy was developed by B.M. Trost<sup>2</sup> in a consideration of total amount of the reactants end up in the final product. The same concept was also determined by R.A. Sheldon<sup>3</sup> as given below.

$$\% \text{ atom economy} = \frac{\text{FW of atoms utilized}}{\text{FW of the reactants used in the reaction}} \times 100$$

The most common reactions we generally come across in organic synthesis are rearrangement, addition, substitution and elimination reactions. Let us find out which of the above reactions are more atom economical.

### (a) Rearrangement Reactions

These reactions involve rearrangement of atoms that make up a molecule. For example, allyl phenyl ether on heating at 200°C gives *o*-allyl phenol (Scheme-1).

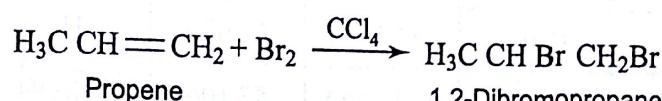


**(Scheme-1)**

The rearrangement reaction (in fact all rearrangement reactions) is 100 per cent atom economical reaction, since all the reactants are incorporated into the product.

### (b) Addition Reactions

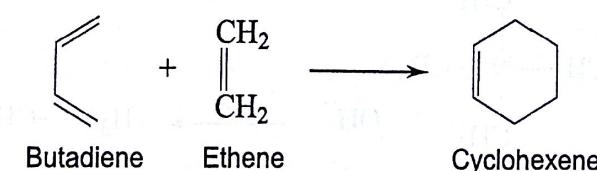
Consider the bromination of propene (Scheme-2)



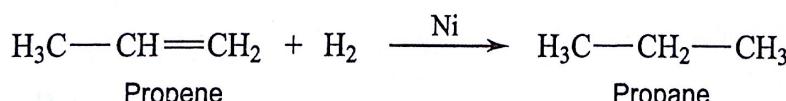
(Scheme-2)

Here also all elements of the reactants (propene and bromine) are incorporated into the final product (1,2-dibromopropane). So this reaction is also 100 per cent atom economical reaction.

In a similar way, cycloaddition reaction of butadiene and ethene (Scheme-3) and addition of hydrogen to an olefin (Scheme-4) is 100 per cent atom economical reaction.



**(Scheme-3)**



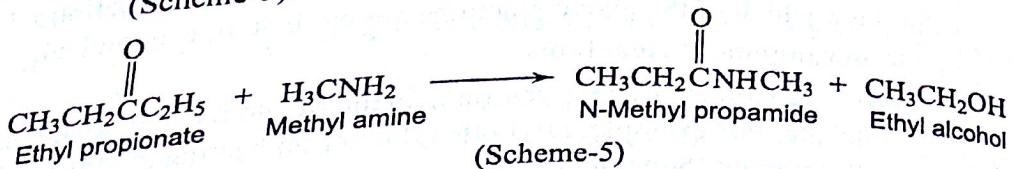
(Scheme-4)

### (c) Substitution Reactions

In substitution reactions, one atom (or group of atoms) is replaced by another atom (or group of atoms). The atom or group that is replaced is not utilized in the final product. So the substitution reactions are less atom economical than rearrangement or addition reactions.

#### 4 Green Chemistry - Environmentally Benign Reactions

Let us consider the reaction of ethyl propionate with methyl amine (Scheme-5).



In the above reaction, the leaving group ( $\text{OC}_2\text{H}_5$ ) is not incorporated in the formed amide and also, one hydrogen atom of the amine is not utilized. The remaining atoms of the reactants are incorporated into the final product.

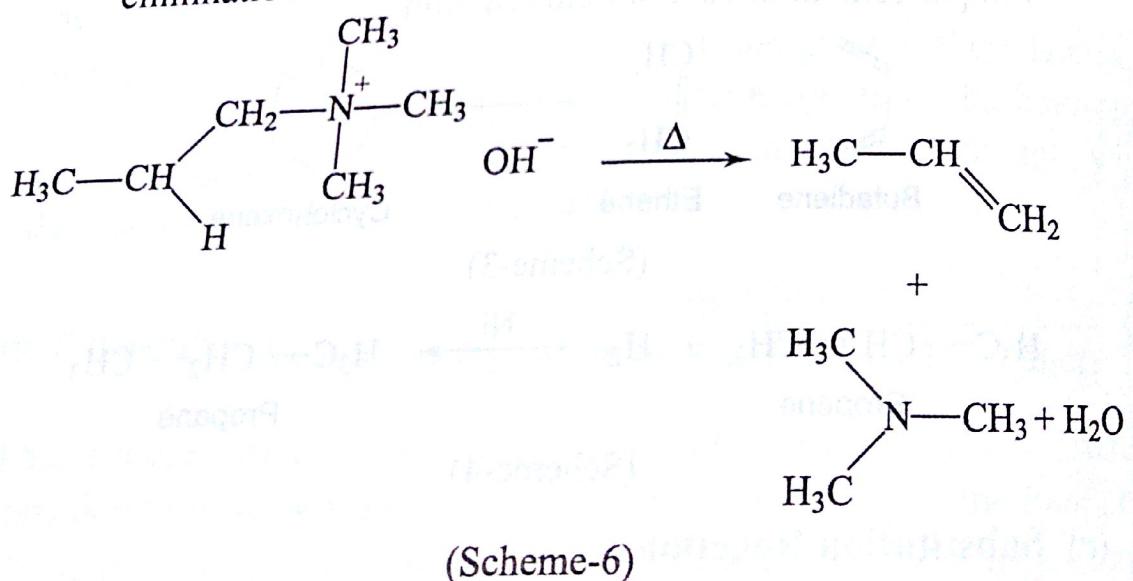
The total of atomic weights of the atoms in reactants that are utilized is 87.106 g/mole, while the total molecular weight including the reagent used is 133.189 g/mole. Thus, a molecular weight of 46.069 g/mole remains unutilized in the reaction.

Reactants		Utilized		Unutilized	
Formula	FW	Formula	FW	Formula	FW
$\text{C}_5\text{H}_{10}\text{O}_2$	102.132	$\text{C}_3\text{H}_5\text{O}$	57.057	$\text{C}_2\text{H}_5\text{O}$	45.061
$\text{CH}_5\text{N}$	31.057	$\text{CH}_4\text{N}$	30.049	H	1.008
Total $\text{C}_6\text{H}_{15}\text{NO}_2$	133.189	$\text{C}_4\text{H}_9\text{NO}$	87.106	$\text{C}_2\text{H}_5\text{OH}$	46.069

$$\text{Therefore, the atom economy (\%)} = \frac{87.106}{133.189} \times 100 = 65.40\%$$

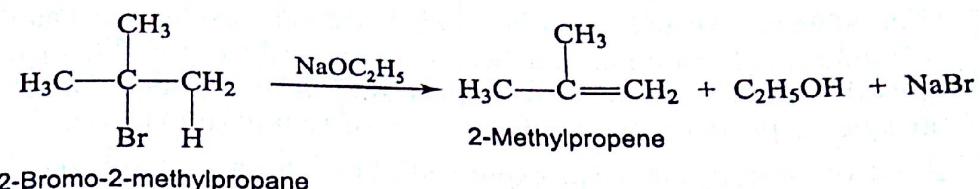
#### (d) Elimination Reactions

In an elimination reaction, two atoms or groups of atoms are lost from the reactant to form a  $\pi$  bond. Consider the following Hofmann elimination reaction (Scheme-6).



The above elimination reaction is not very atom economical. The percentage atom economy is 35.30% and is the least atom economical of all the above reactions.

Consider another elimination reaction involving dehydrohalogenation of 2-bromo-2-methylpropane with base to give 2-methylpropene (Scheme-7).



(Scheme-7)

The above dehydrohalogenation reaction (an elimination reaction) is also not very atom economical. The percentage atom economy is 27 per cent which is even less than the Hofmann elimination reaction.

**3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.**

One of the most important principle of green chemistry is to prevent or at least minimize the formation of hazardous products which may be toxic and or environmentally harmful. In case hazardous products are formed, their effects on the workers must be minimized by the use of protective clothing, respirator etc. This, of course, will add to the cost of production. At times, it is found that the controls may fail and there may be more risk involved. Green chemistry, in fact, offers a scientific option to deal with such situations.

**4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.**

It is extremely important that the chemicals synthesised or developed (e.g., dyes, paints, cosmetics, pharmaceuticals etc.) should be safe to use. A typical example of an unsafe drug is thalidomide (introduced in 1961) for reducing the effects of nausea and vomiting during pregnancy (morning sickness). The children born to women taking thalidomide suffered birth defects. Subsequently, the use of thalidomide was banned, the drug withdrawn and strict regulations passed for testing all new drugs.

With the advancement of technology, the designing and production of safer chemicals has become possible. In fact, it is possible to manipulate the molecular structure to achieve this goal.

**5. The use of auxiliary substances (solvents, separation agents, etc.) should be made unnecessary whenever possible and, when used, innocuous.**

A number of solvents like methylene chloride, chloroform, perchloroethylene, carbon tetrachloride, benzene and other aromatic hydrocarbons have been used (in a large number of reactions) due to their excellent solvent properties. However, the halogenated solvents (mentioned above) have

In the above procedure, the protecting group is not incorporated into the final product, their use makes a reaction less atom economical. Thus, as far as possible, the use of protecting groups be avoided. Though atom economy is a valuable criterion in evaluating a particular synthesis as 'green', other aspects of efficiency must also be considered.

9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

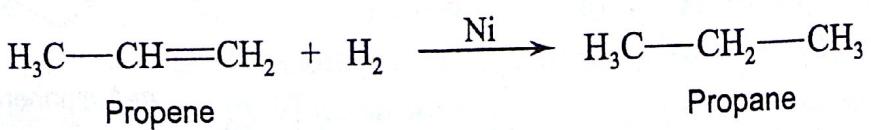
In some reactions, the reactants (A and B) react to form a product (C), in which all the atoms contained within A and B are incorporated in the product (C). In such cases, stoichiometric reactions are equally environmentally benign from the point of material usage as any other type of reactions. However, if one of the starting material (A or B) is a limiting reagent; in such cases, even if the yield is 100 per cent, some unreacted starting material will be left over as waste. In other cases, if the reagents A and B do not give 100 per cent yield of the product (C), both the excess of unreacted reagents will form part of waste. It is found that due to the reason mentioned above, catalysts, wherever available offer distinct advantages over typical stoichiometric reagents. The catalyst facilitates the transformations without being consumed or without being incorporated into the final product.

Catalysts are selective in their action, in that the degree of reaction that takes place is controlled, e.g., mono addition vs multiple addition; also the stereochemistry is controlled (e.g., R vs S enantiomer). By using catalysts, both starting-material utilization is enhanced and formation of waste reduced. An additional advantage of the use of catalyst is that the activation energy of a reaction is reduced and so the temperature necessary for the reaction is also lowered. This results in saving the energy.

It should be understood that in stoichiometric processes, the product obtained is one mole for every mole of the reagent used. However, a catalyst will carry out thousands of transformations before being exhausted.

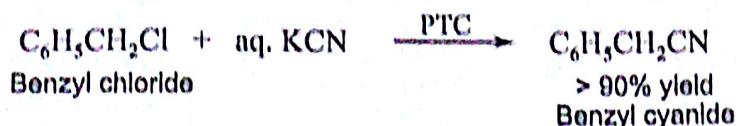
Following are given some of the applications of the use of catalysts:

- (i) Hydrogenation of olefins in presence of nickel catalyst gives much better yields (Scheme-9).



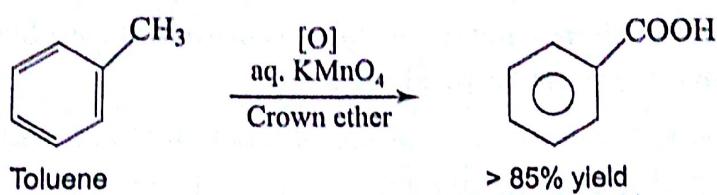
**(Scheme-9)**

(ii) Conversion of benzyl chloride into benzyl cyanide in much better yields using phase transfer catalysts (Scheme-10).



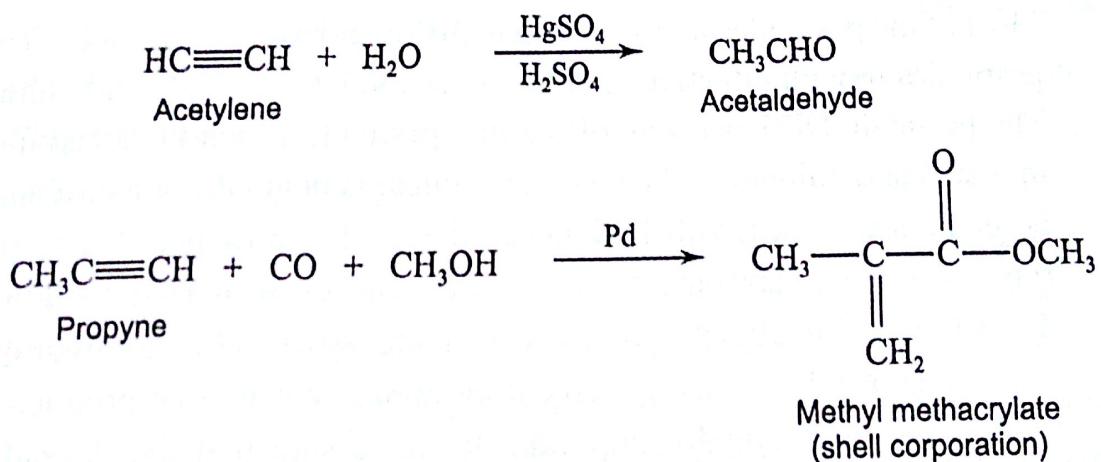
(Scheme-10)

(iii) Oxidation of toluene with  $\text{KMnO}_4$  in presence of crown ether gives much better yield (Scheme-11).



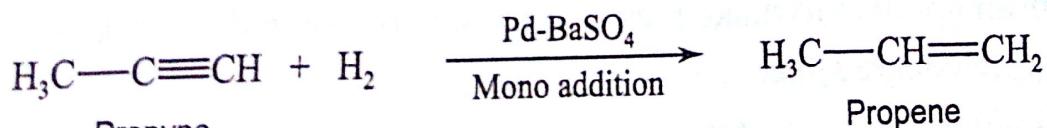
(Scheme-11)

(iv) Even in those cases where no reaction occurs usually, the reaction becomes feasible. An example is the hydration of alkynes to give aldehydes or ketones (Scheme-12).



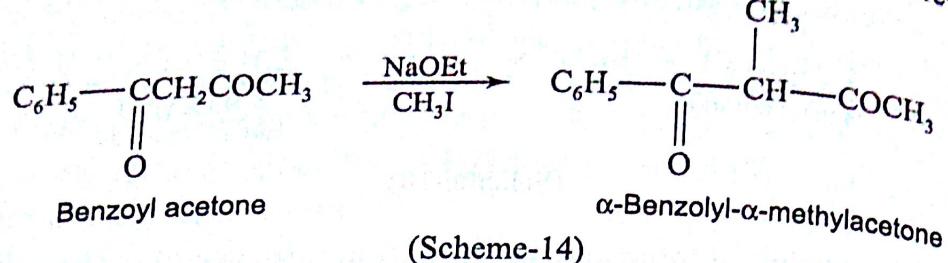
(Scheme-12)

(v) The selectivity enhancement takes place as shown by reduction of a triple bond to double bond (Scheme-13).



(Scheme-13)

(vi) Selectivity in C-methylation versus O-methylation (Scheme-14).



- 10. Chemical products should be so designed that at the end of their function they do not persist in the environment and break down into innocuous degradation products.**

It is of utmost importance that the products that are synthesised should be biodegradable; they should not be 'persistent chemicals' or 'persistent bioaccumulators'. Such chemicals (which are non-biodegradable) remain in the same form in the environment or are taken up by various plants and animal species, and accumulate in their systems; this is detrimental to the concerned species. The problem of non-biodegradability is generally associated with pesticides, plastics and a host of other organic molecules.

Most of the pesticides in use are organohalogen-based compounds. These pesticides though effective tend to bioaccumulate in plants and animals. The pesticide DDT was one of the first pesticide which bioaccumulated in plants and animals. Whenever a chemical is being designed, it should be made sure that it will be biodegradable. It is now possible to place functional groups and other features in the molecule which will facilitate its degradation. Functional groups which are susceptible to hydrolysis, photolysis or other cleavage have been used to ensure that products will biodegrade. It is equally important to make sure that the degradation products should not possess any toxicity and be detrimental to the environment.

Plastics are known to remain persistent and are not biodegradable. The waste plastics were mostly used for landfills etc. However, it has now been possible to make plastics (particularly for garbage bags etc.) which are biodegradable.

- 11. Analytical methodologies need to be further developed to allow for real-time, in-process monitoring, and control prior to the formation of hazardous substances.**

Analytical methodologies and technology have been developed which allow the prevention and minimization of the generation of hazardous substances in chemical processes. One needs to have accurate and reliable sensors, monitors, and analytical techniques to assess the hazards that

are present in the process stream. Using various techniques, a chemical process can be monitored for generation of hazardous byproducts and side reactions. These procedures can prevent any accident which may occur in chemical plants.

**12. Substances and the forms 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 occurrence of accidents in chemical industry must be avoided. The accidents in Bhopal (India) and Seveso (Italy) and many others have resulted in the loss of thousands of life.

At times, it is possible to increase accident potential inadvertently in an attempt to minimize the generation of waste in order to prevent pollution. It has been noticed that in an attempt to recycle solvents from a process (in order to be economical and also prevent escape of solvent to the atmosphere) increases the potential for a chemical accident or fire. In fact, a process must balance the accident prevention with a desire for preventing pollution. A possible course is not to use volatile solvents, instead solids or low vapour pressure substance can be used.

### **1.3 PLANNING A GREEN SYNTHESIS IN A CHEMICAL LABORATORY**

Following are given some of the points, which should be kept in mind for carrying out a synthesis in a chemical laboratory:

**1. Percentage atom utilization**

There should be maximum incorporation of the starting materials and reagents into the final product (also see Section 1.2).

**2. Evaluating the type of the reaction involved**

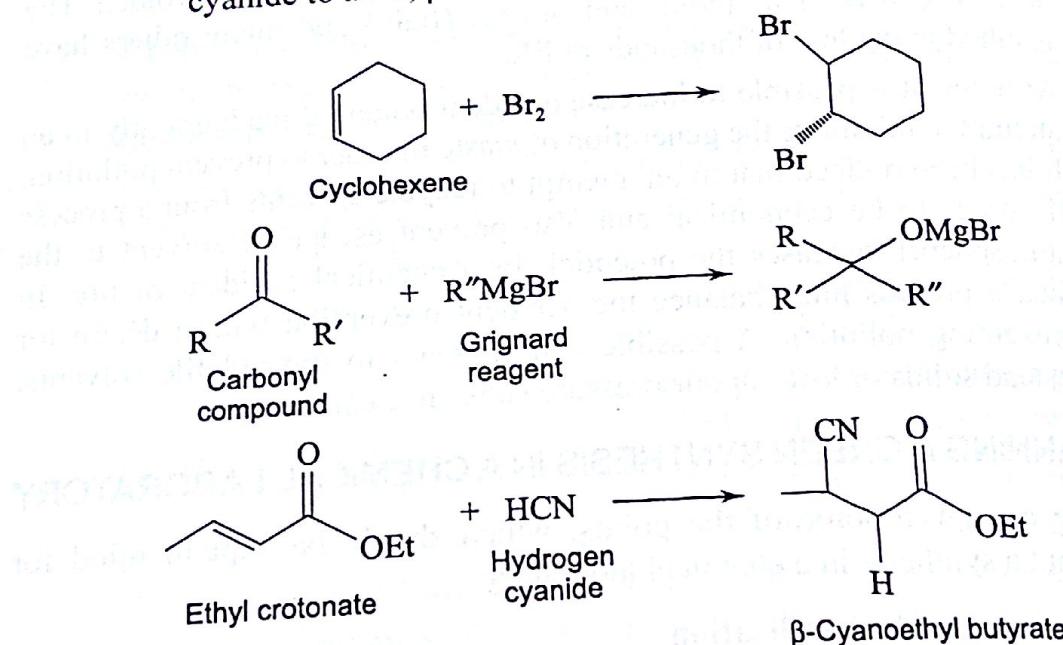
The reaction involved must be evaluated with regard to its environmental impact or consequences. For this purpose, the nature of the starting material and the byproducts (if formed) must be examined. Following are given the different types of reactions which may be involved in a particular synthesis:

**(a) Rearrangement Reactions**

These reactions, as the name indicates in which the atoms that comprise a starting molecule change its orientation relative to one another including their connectivity and bonding pattern. Such reactions can be performed using a variety of procedures including thermal, photo and chemical means. From the point of green chemistry, in such reactions, both the starting materials and the end products contain the same atoms and so there is no waste generated. In fact, a rearrangement reaction is 100 per cent atom economical and fully efficient.

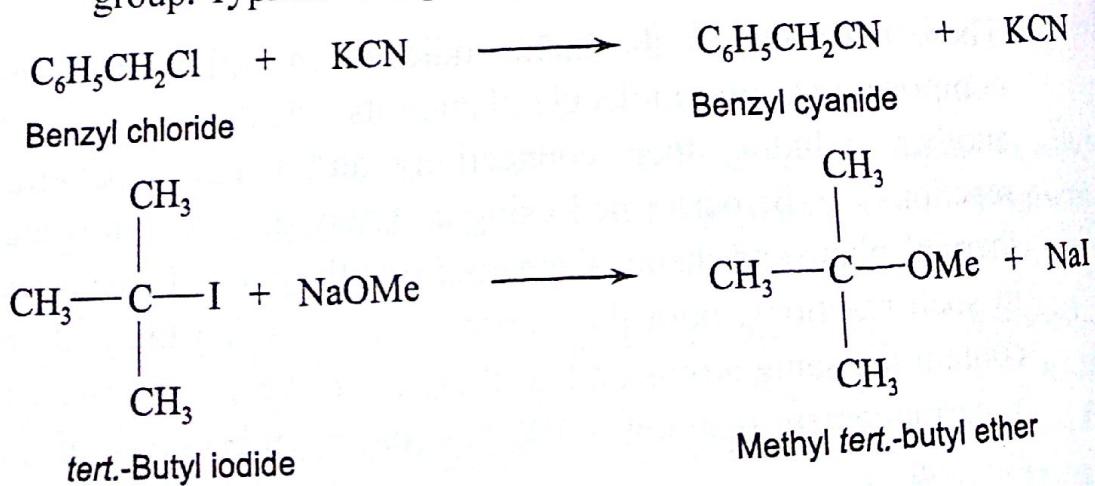
(b) Addition Reactions

In these reactions, a reagent adds to a substrate, all reagents and the substrates are consumed during the reaction. No additional byproducts are generated and such reactions are very efficient, and like rearrangement reaction are also 100 per cent atom economical. Some typical addition reactions include the addition of bromine to an olefin, Grignard reagent to a carbonyl compound and hydrogen cyanide to an  $\alpha, \beta$ -unsaturated carbonyl compounds (Scheme-15).

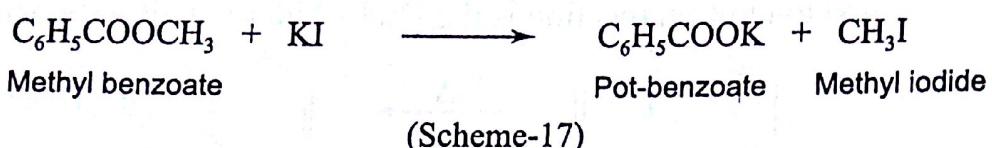


(c) Substitution Reactions

In these reactions, the functional group of a substrate is replaced with another functional group. Typical examples include the well-known  $S_N1$  and  $S_N2$  reactions. In these reactions, nucleophilic reagents displace a leaving group in an aliphatic carbon atom; the product formed incorporates the nucleophile with removal of the leaving group. Typical examples are given below (Scheme-16).



In some cases, the leaving group is the desired product. For example, potassium iodide demethylation of a carboxylic acid methyl ester to give free carboxylate salt and methyl iodide (Scheme-17).

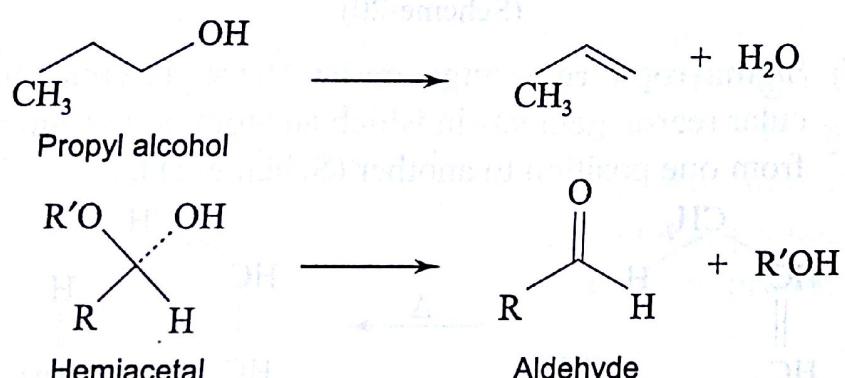


(Scheme-17)

The usefulness of the methods depends on the nature of the leaving group generated. This pathway can be convenient and efficient if a substitution reaction sequence can be designed where the leaving group has been carefully selected.

#### (d) Elimination Reactions

These are reverse of addition reactions and are procedures to generate unsaturation in the molecule. Examples of this type include dehydration of an alcohol to generate an olefin and loss of an alcohol from a hemiacetal to give an aldehyde (Scheme-18).



(Scheme-18)

As in the case of substitution reactions, the environmental implications of the leaving group should be examined, evaluated and controlled.

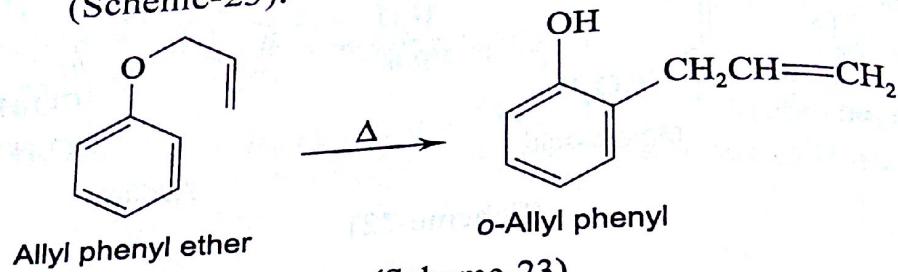
### (e) Pericyclic Reactions

These are concerted reactions and are characterised by the making or breaking of bonds in a single concerted step through a cyclic transition state involving  $\pi$  or  $\sigma$  electrons. Energy of activation for pericyclic reaction is supplied by heat in a thermally induced reaction and by ultraviolet light in a photo-induced reaction. Pericyclic reactions are highly stereospecific, often the thermal and photochemical processes yield products with different but specific stereochemistry. Since pericyclic reactions do not involve ionic or free radical intermediates; solvents, and nucleophiles or electrophilic reagents have no effect on the course of the reaction. We normally come across three types of pericyclic reactions.

(iii) **Organic synthesis in solid state:** The organic synthesis in solid state (viz., solvent-free organic synthesis and transformations) are mostly green reactions. These are of two types:

**(a) Solid phase organic synthesis without any solvent**

The earliest record of an organic reaction in dry state is the Claisen rearrangement of allyl phenyl ether to *o*-allyl phenol (Scheme-23).



(Scheme-23)

A large number of reactions have now been performed without any solvent. These will be discussed subsequently.

**(b) Solid supported organic synthesis**

In these reactions, the reactants are stirred in a suitable solvent (for example, water, alcohol, methylene chloride etc.) with a suitable adsorbent or solid support like silica gel, alumina, phyllosilicate ( $m^{n+}$ -montmorillonite etc.). After stirring, the solvent is removed *in vacuo* and the dried solid support on which the reactants have been adsorbed are used for carrying out the reaction under microwave irradiation.

#### 4. Selection of starting materials.

As far as possible, the starting materials selected should be obtainable from renewable sources. The starting materials should not cause any harm (e.g., allergy etc.) to the person handling these.

#### 5. Use of protecting group

should be avoided as far as possible, since these generate wastes.

#### 6. Use of catalyst

We know that catalysts facilitate transformation and the conversions can be affected in short duration of time and consume less energy. Such reactions should be preferred. Use of phase transfer catalysts and crown ethers is very well known.

#### 7. Use of microwaves, sonication

saves lot of energy and time, and gives much better yields.