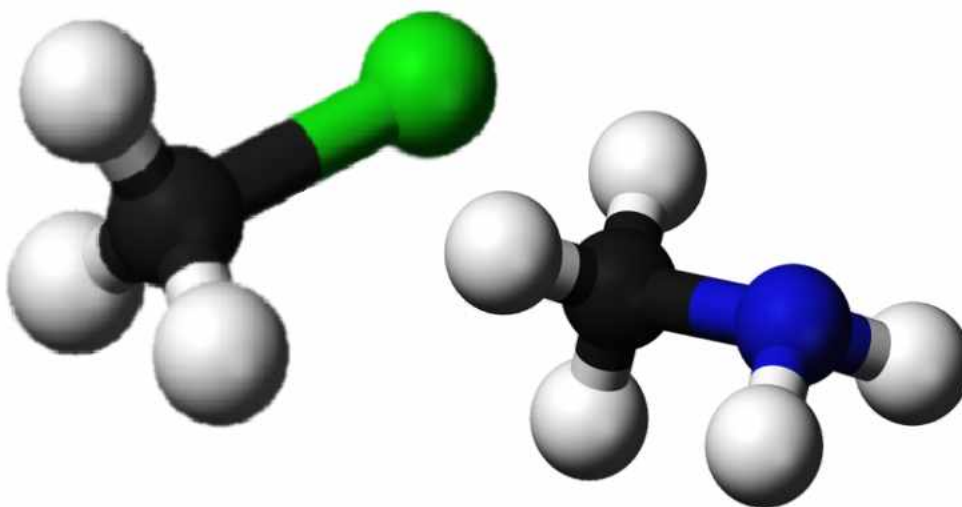


CHAPTER 6

ALKYL HALIDES & AMINES



Teaching Periods	10	Assessment	01	Weightage %	08
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Students will be able to:

- ✓ Discuss the physical properties, structure and reactivity of RX. (Understanding)
- ✓ Describe the preparation of RX by the reaction of alcohols with HX, SOCl₂ and PX₃ and by halogenation of alkanes. (Understanding)
- ✓ Explain the mechanism and types of nucleophilic substitution reactions. (Applying)
- ✓ Explain the mechanism and types of elimination reactions. (Applying)
- ✓ Compare the nucleophilic substitution versus elimination reaction. (Analyzing)
- ✓ Explain the preparation and reactivity of Grignard's Reagents. (Applying)
- ✓ Applications of Grignard's reagent (Water, esters and carbon dioxide and amines). (Applying)
- ✓ Explain the structure and basicity of amines. (Applying)
- ✓ Describe the preparation of amines by alkylation of ammonia to RX and reduction of nitriles, nitro and amide functional groups. (Understanding)
- ✓ Explain the reactions of amines (RX, aldehydes, and ketones) and preparation of amides and diazonium salts. (Understanding)
- ✓ Enlist the important compounds of Alkyl Halides and Amines with their applications. (Applying)
- ✓ Explain the reactivity of alkyl halide with respect to polarity of C- X bond. (Understanding)
- ✓ Explain why primary alkyl halide favors S_N² reactions and tertiary alkyl halide S_N¹. (Understanding)



INTRODUCTION

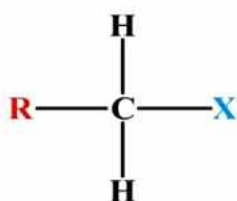
“Organic compounds that contain at least one halogen atom (fluorine, chlorine, bromine, or iodine) bonded to an alkyl group are called haloalkanes”. These compounds are classified on the basis of number of halogen atoms attached to alkyl group. Monohaloalkanes have only one halogen atom, dihaloalkanes have two halogen atoms and trihaloalkanes have three halogen atoms.

Monohaloalkanes are usually called alkylhalides and represented by a formula $R-X$, where R is an alkyl group and X is halogen atom (functional group). The general formula of monohaloalkanes is $C_nH_{2n+1}X$ where n , represents the number of carbon atoms.

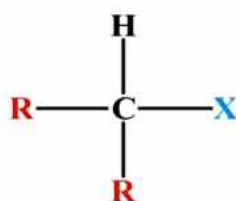
Alkyl halides are widely used in the synthesis of organic compounds as they are versatile compounds that can undergo a wide variety of reactions. They are also used as solvents and in the production of plastics, pharmaceuticals and agrochemicals.

6.1 ALKYL HALIDES

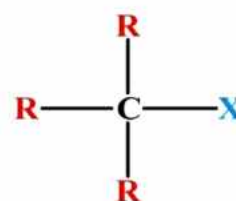
Alkyl halides can be classified according to the carbon atom to which the halogen atom is attached. A primary (1°) alkyl halide refers to an alkyl halide where the halogen-bearing carbon is bonded to only one other carbon atom. When two carbon atoms are attached to the halogen-bearing carbon, it is known as a secondary (2°) alkyl halide. Finally, a tertiary (3°) alkyl halide is characterized by the halogen-bearing carbon being bonded to three carbon atoms.



(1° - Alkyl halide)



(2° - Alkyl halide)



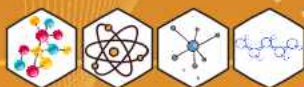
(3° - Alkyl halide)

Examples of alkyl halides are given below

Primary alkyl halide: 1-Bromopropane ($\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}$)

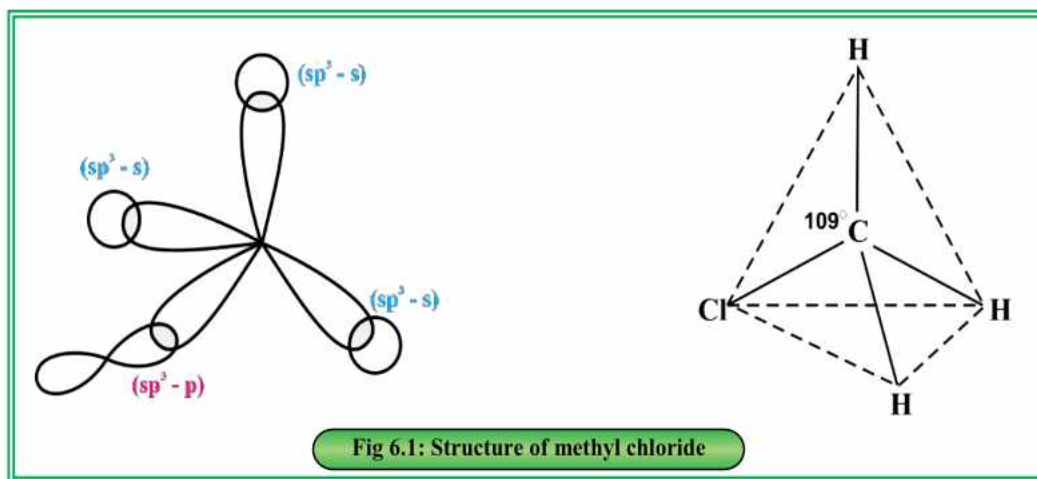
Secondary alkyl halide: 2-Bromopropane ($\text{CH}_3\text{CHBrCH}_3$)

Tertiary alkyl halide: 2-Bromo-2-methylpropane ($\text{CH}_3\text{C}(\text{CH}_3)_2\text{Br}$)



6.1.1 Structure of Alkyl Halide

Let us consider methyl chloride ($\text{CH}_3\text{-Cl}$) as an alkyl halide. The geometry of molecule is explained by hybrid orbital theory. Carbon of methyl halide is bonded with four atoms which means carbon is utilizing its all four valence electrons to produce four sp^3 hybrid orbitals, which are oriented at an angle of 109° to give a tetrahedral geometry. These four sp^3 hybrid orbitals are shared with three s-orbitals of hydrogen atoms and one p-orbital of chlorine by head on overlapping to make four sigma bonds (Fig.6.1).



6.1.2 Physical Properties of Alkyl Halides

(i) Physical state

Alkyl halides with lower number of carbon atoms and different halogen atoms exist as gas or liquid at room temperature, whereas alkyl halides with higher carbon atoms i.e. beyond 18-carbon atoms are colourless solids.

(ii) Solubility

Alkyl halides are soluble in organic solvents but are slightly soluble in water, this is due to the inability of alkyl halides to form hydrogen bonds with water.

(iii) Melting and boiling points

Alkyl halides possess higher melting and boiling points than alkanes of comparable molecular weight, this is due to increasing strength of intermolecular forces.

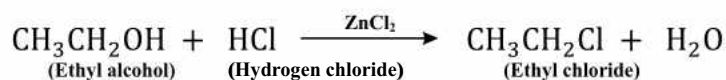


6.1.3 Preparation of Alkyl Halides

Alkyl halides can be prepared by various methods. Some of which are given below:

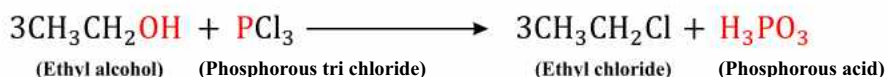
6.1.3.1. Reaction of Alcohol with Hydrogen Halides:

Alcohols can be converted to alkyl halides by the reaction with hydrogen halides. The reactivity of an alcohol with halogen acid follows the trend $\text{HI} > \text{HBr} > \text{HCl}$. When producing an alkyl halide from hydrogen chloride, anhydrous zinc chloride (ZnCl_2) is used as a catalyst.

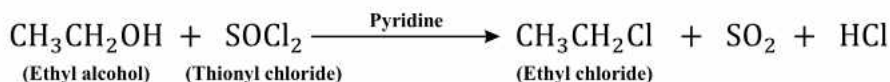


6.1.3.2. Reaction of Alcohols with other halogenated agents

Alcohols react with phosphorous trihalide (PCl_3 , PBr_3 , PI_3) to form alkylhalides. Since phosphorus trichloride is more easily available, the reaction is generally carried out by using this reagent.



Alcohols reacts with thionyl halide (SOX_2) in the presence of pyridine as catalyst to produce an alkyl halides. This is preferred method for the preparation of alkyl halide because both the by products are in gaseous state.



6.1.3.3 By the halogenation of alkane

The reaction between alkanes and halogens in the presence of sun light or high temperature produces alkyl halides. This reaction involves the substitution of one or more hydrogen atoms in alkanes by halogen atoms,



potassium hydroxide (KOH), the hydroxide ion (OH^-) acts as strong nucleophile which attacks the partially electropositive carbon atom of alkyl halide, as a result, new bond is formed between carbon and attacking nucleophile.

Different strong nucleophilic can produce a variety of organic compounds when treated with an alkyl halide.

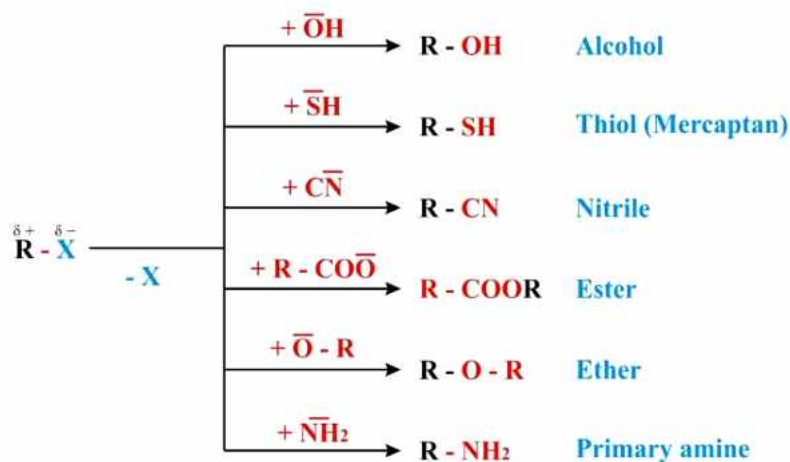


Table 6.1 Some common strong Nucleophiles along with their typical reagents.

Nucleophiles	Typical Reagent
OH^-	NaOH, KOH
SH^-	KSH
CN^-	NaCN
$\text{CH}_3\text{-COO}^-$	$\text{CH}_3\text{-COONa}$
$\text{CH}_3\text{-CH}_2\text{-O}^-$	$\text{CH}_3\text{-CH}_2\text{-ONa}$
NH_2^-	NaNH_2



Self-Assessment

Why alkyl halide undergoes nucleophilic substitution reaction? Which reagent is required to convert a methyl iodide into:

(i) Methanol (ii) Methyl cyanide (iii) Dimethyl ether (iv) Thiol



Mechanism of nucleophilic substitution reactions

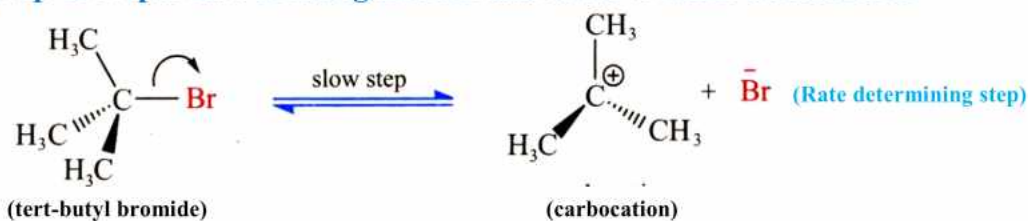
The mechanism of nucleophilic substitution reaction is divided into:

- (i) S_N^1 Reactions
- (ii) S_N^2 Reactions

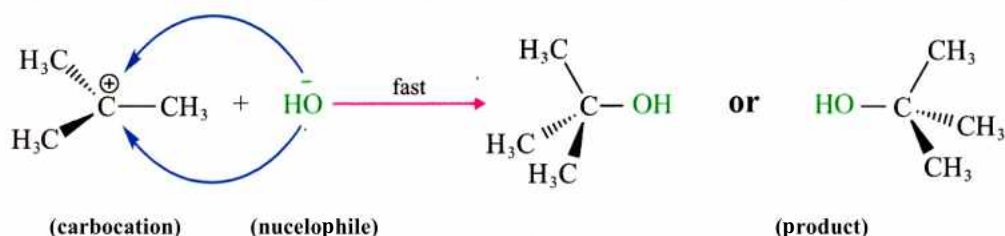
S_N^1 mechanism

It is unimolecular bi-step S_N reaction. “The S_N1 reaction mechanism proceeds in two distinct steps, with the first step involving the departure of the leaving group (the halogen atom) from the substrate molecule, leading to the formation of a carbocation intermediate, followed by nucleophilic attack in the second step”.

Step-1: Departure of halogen from substrate to form carbocation



Step-2: Attack of strong nucleophile on carbocation to form product



Tertiary alkyl halides undergo S_N1 reactions more readily than primary or secondary alkyl halides due to the stabilizing effect of electron-donating alkyl groups, and favoring the formation of the carbocation intermediate, thus facilitating the S_N1 reaction.

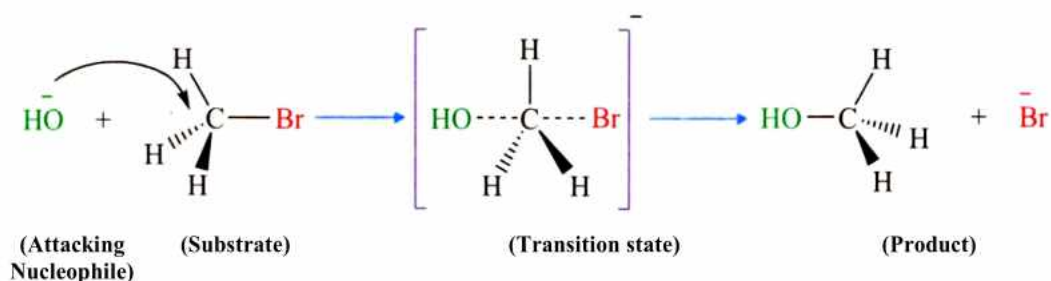
Chemical reactions that processed via the S_N1 mechanism exhibit first-order Kinetics, and the rate of the reaction is dependent on the concentration of the substrate, not on the nucleophile involved in the reaction.

$$R = K [\text{Substrate}]$$



SN² mechanism

It is bimolecular single step SN reaction **“In the SN² mechanism, bond formation and bond breaking occur simultaneously in a single step process”**. The nucleophile directly attacks the electrophilic carbon atom of the substrate, leading to the departure of the halogen atom attached to the electrophilic carbon. The nucleophile attacks from the back side because the front side is sterically hindered by the nucleophile of the substrate.



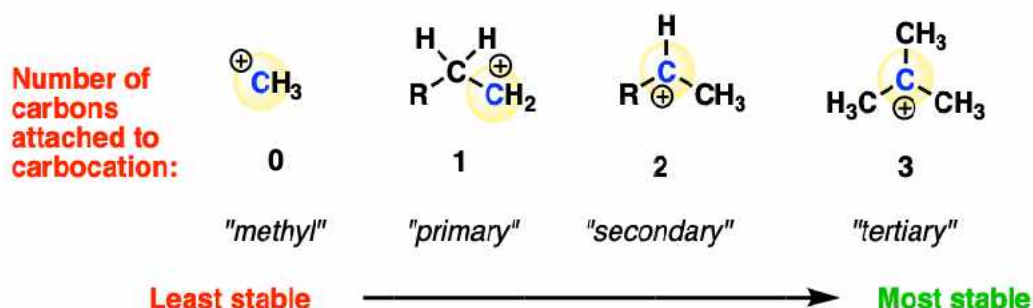
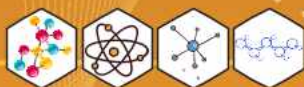
The SN² mechanism is typically observed in primary alkyl halides and methyl halides because primary carbocation and methyl carbocation are highly unstable due to the lack of electron donating alkyl groups.

The SN² mechanism is followed by second order kinetics which means that the reaction rate is dependent upon the concentration of both substrate and attacking nucleophile.

$$R = K [\text{Substrate}] [\text{Nu}^-]$$

Carbocations and their stability

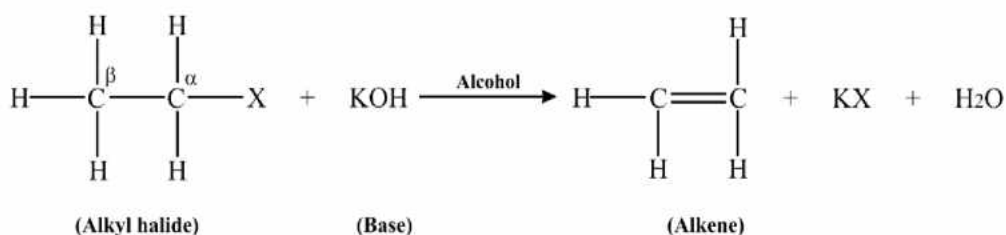
“Carbocations are organic ions that have a positively charged carbon atom. They are formed when a carbon atom loses a pair of electrons”. Carbocations are classified into primary, secondary and tertiary depending upon the number of carbon atoms bonded to positively charged carbon atom. Carbocations are highly reactive species, they can be formed as intermediates during a chemical reaction. Tertiary carbocations are more stable than secondary and primary carbocation because of electron donating tendency of alkyl group.



6.1.5. Elimination Reactions

An elimination reaction refers to a type of organic reaction where the substituents are removed from the adjacent carbon atoms of substrate molecule. **"When an alkyl halide reacts with alcoholic potassium hydroxide, the removal of hydrogen and halogen atoms from two adjacent carbon atoms of substrate takes place, giving a multiple bond product".** It is referred as 1, 2-elimination or β -elimination reaction.

In β -elimination reaction, base initiates the reaction by abstracting a proton from substrate. It leads to the formation of carbocation intermediate, which then eliminated a halogen atom from the adjacent carbon to form a new π bond.



There are two common types of β -elimination reactions named as E_1 and E_2 .



Self-Assessment

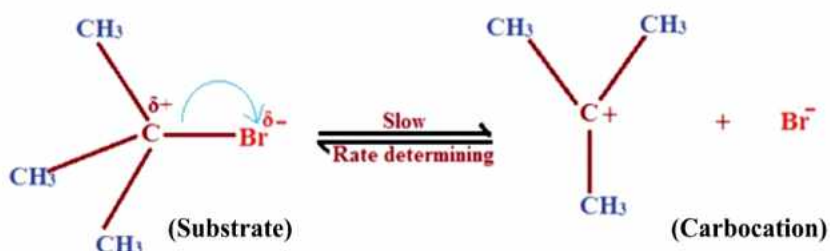
Explain the following:

- Why β -elimination reactions are not possible in methyl halides?
- Why S_N2 reaction is not favourable in tertiary alkyl halides?
- Why tertiary carbocation is more stable than secondary and primary carbocations?

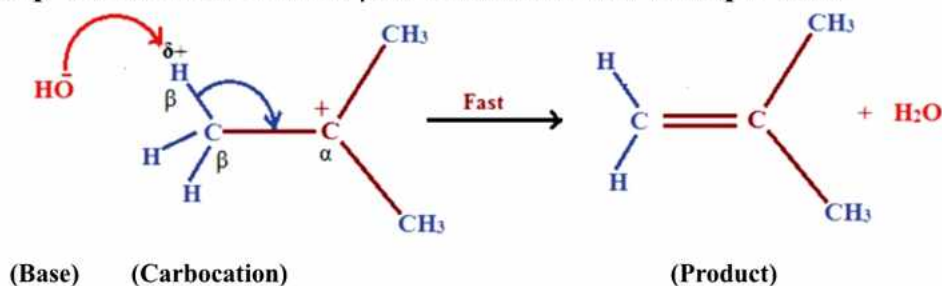
6.1.5.1 Mechanism of E_1 Reaction

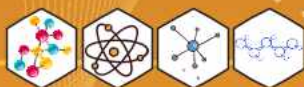
E_1 reactions, known as unimolecular elimination reactions, occur in two steps. In the first step, the halogen atom departs from the substrate, forming a carbocation intermediate, which is the slow and rate-determining step. In the second step, a base abstracts a proton from the carbon next to the halogenated carbon, leading to the formation of a double bond between the two adjacent carbon atoms.

Step-1: Formation of carbocation



Step-2: Attack of Base on β -H & formation of multiple bond



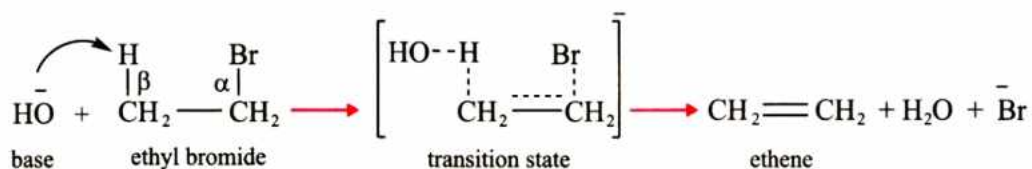


The rate determining step in E^1 mechanism involves the unimolecular ionization of the substrate molecule. Therefore, the rate of the reaction depends only on the concentration of reactant, and not on the concentration of base.

$$R = K [\text{Substrate}]$$

Mechanism of E_2 – reaction

E_2 -reaction is referred as bimolecular elimination reaction. The mechanism completes in single step in which both substrate and attacking base are involved.



Mechanism of E_2 reaction is feasible in primary alkyl halides for example when ethyl bromide is allowed to react with hot alcoholic potassium hydroxide, it gives ethene followed by E_2 -mechanism. Base first attacks on ethyl bromide and abstracts a proton from β -carbon. Simultaneous halide ion eliminates from α -carbon and the lone pair of electrons is shifted between α and β carbon to give an ethene.

Therefore, as far as kinetics of E_2 reaction is concerned, the rate of this reaction depends upon the concentration of both substrate and attacking base, the rate law may be written as

$$R = K [\text{Sub}] [\text{base}]$$

6.1.6. Substitution Versus Elimination Reactions

Nucleophile substitution reactions can occur alongside the elimination reactions because nucleophile can also act as a base. However, nucleophilic substitution reactions occur when the nucleophile attacks on the α -carbon atom where as elimination reaction occurs when the nucleophile attacks on the β -hydrogen. Several factors can influence the formation of products via either substitution or elimination mechanisms.

- **Solvent effect:** Substitution reactions are favoured in polar solvents while elimination reaction are favoured in non polar solvents.



- **Base effect:** A strong base promotes elimination reaction and hinders substitution reaction.
- **Temperature effect:** The rise in temperature encourages elimination reaction over substitution reaction.
- **Substrate effect:** If the substrate molecule is a tertiary alkyl halide, it favours elimination reaction while if it is primary alkyl halide, it favours substitution reaction. Secondary alkyl halide is consented to both substitution and elimination.

6.2 GRIGNARD'S REAGENTS (ORGANOMETALLIC COMPOUNDS)

Organometallic compounds are defined as **“organic compound that possess at least one bond between a carbon atom and a metal atom”**.

Some common examples of organometallic compounds are given as:

- Grignard reagent: It is a highly reactive organic compound and used in organic synthesis.
- Methylcobalamine: It is a derivative of vitamin B-12.
- Dimethyl Zinc: It is used as insecticide.
- Tetraethyl lead: It is used as knock inhibitor in petroleum industry.



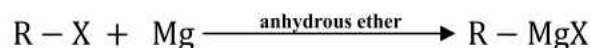
DO YOU KNOW?

Organometallic compounds are being studied as a potential therapeutic agents for a variety of diseases including cancer, HIV and tuberculosis. They are also used as contrasting agents in magnetic resonance imaging (MRI).

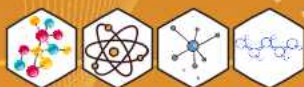
6.2.1 Preparation of Grignard Reagent

“Grignard reagent is an organometallic compound that contains a carbon-magnesium (C-Mg) bond”. Grignard reagents are well-known organometallic compounds. The name Grignard is derived from a French chemist Victor Grignard, who first synthesized this compound and was subsequently awarded the Noble Prize in Chemistry in 1912.

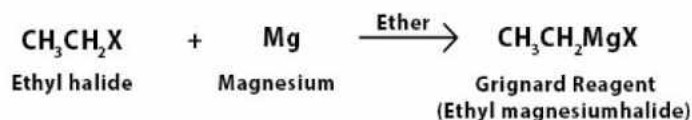
Grignard reagents are prepared in the laboratory by the reaction of an alkyl halide with magnesium metal in the presence of anhydrous ether.



Where R = alkyl group, for example -CH₃, -C₂H₅ etc



X = halogen, for example – Cl, –Br, –I



The formation of Grignard reagent depends on two factors that determine its ease of production.

- (i) **Size of alkyl group:** The larger the size of alkyl group, the more difficult is the formation of Grignard reagent.
- (ii) **Nature of halogen atom:** The ease of formation of Grignard reagent also depends upon nature of halogen atom attached to an alkyl group of alkyl halide. The order is $\text{I} > \text{Br} > \text{Cl}$ because the bond between iodine and carbon is weaker than corresponding bond with other halogens.



Self-Assessment

- How are Grignard reagents prepared?
- What are the key properties of organometallic compounds?

6.2.1 Reactivity

In Grignard reagent the carbon-magnesium bond is covalent and highly polar due to high electronegativity of carbon atom than magnesium metal, which creates more electron density on carbon of alkyl group. As a result the carbon atom bears a partial negative charge and acts as nucleophile. Due to this nucleophilic nature of alkyl parts, Grignard reagent reacts with polarized molecules either by nucleophilic substitution or nucleophilic addition.

6.2.3 Reactions of Grignard Reagent

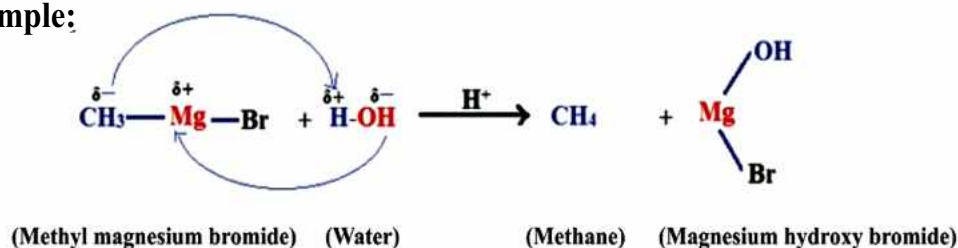
Grignard reagent is a versatile chemical; it is used as starting material for the synthesis of various organic compounds such as alkanes, alcohols, carboxylic acids and ketones.



6.2.1 Reaction with Water

When Grignard reagent reacts with water in an acidic medium, it yields alkanes.

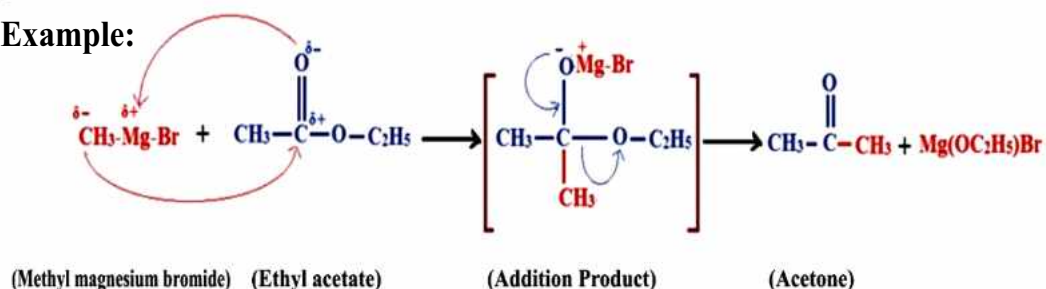
Example:



6.2.3.2. Reaction with ester

Grignard reagent when reacts with ester, it first forms unstable addition product which is later on stabilized with the formation of ketone.

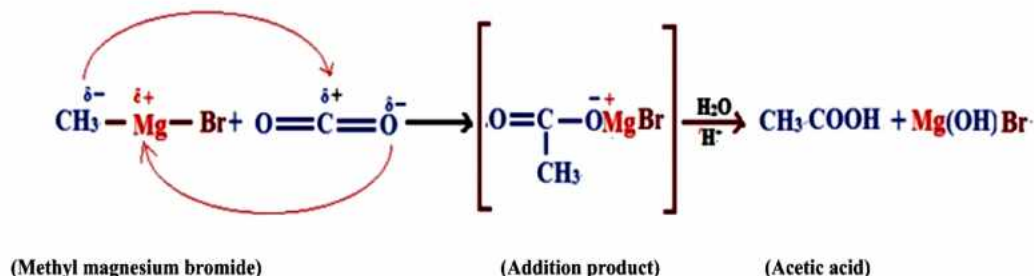
Example:

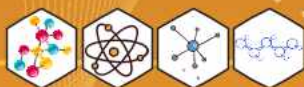


6.2.3.3. Reaction with carbon dioxide

Grignard reagent when reacts with carbon dioxide, it gives unstable addition product, later on hydrolysis in an acidic medium produces carboxylic acid.

Example:

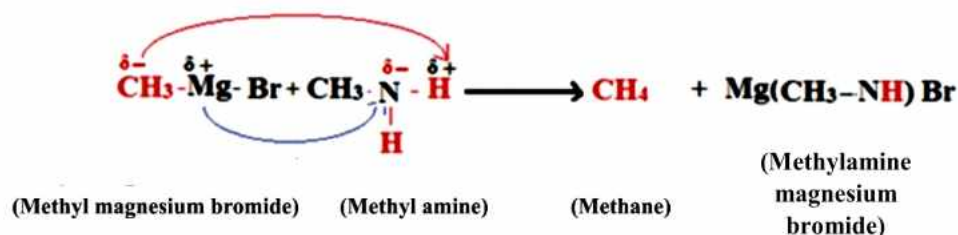




6.2.3.4. Reaction with primary amine

Grignard reagent reacts with primary amine to produce an alkane.

Example:



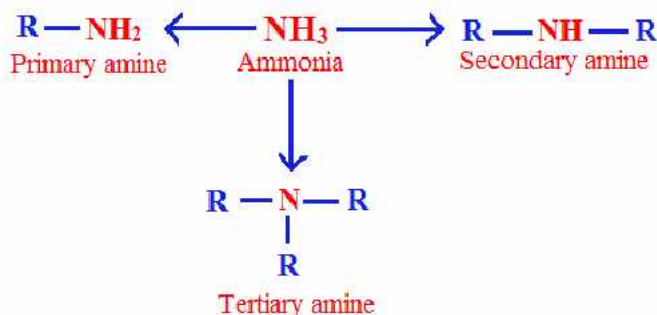
6.3. AMINES

“Organic compounds that contain a nitrogen atom bonded to one or more alkyl or aryl groups are known as amines”. These are derivatives of ammonia where one or more hydrogen atoms of ammonia are replaced by an alkyl or aryl group.



DO YOU KNOW?

Many drugs including antibiotics, anti-depressant and antihistamine contain amine functional groups.



6.3.1. Physical Properties

- **Physical state:** Lower members exist in gaseous states (i.e. Methylamine CH_3NH_2) at room temperature whereas higher members are liquids (i.e. Ethylamine $\text{C}_2\text{H}_5\text{NH}_2$).
- **Odour and Colour:** Mostly they are colourless with an unpleasant smell. For example: Trimethylamine $\text{N}(\text{CH}_3)_3$ has a strong fishy odor and is found in decaying fish and other organic matter.

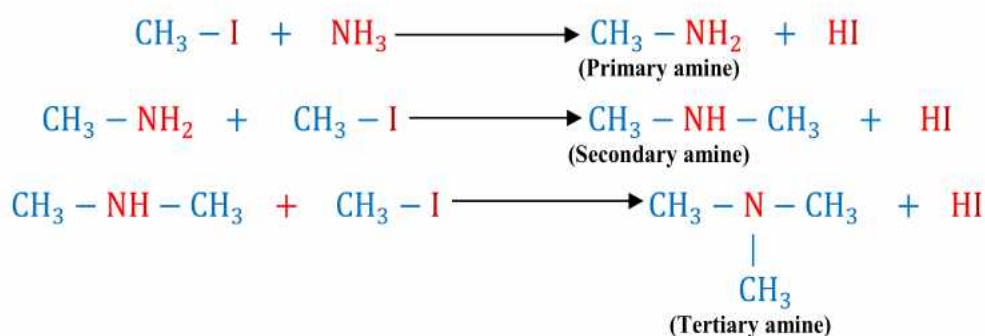


6.3.4. Preparation of Amines

Amines are prepared by different methods:

6.3.4.1. Alkylation of Ammonia by Alkyl Halides

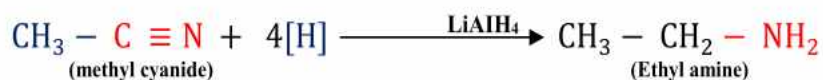
When alkyl halides are heated with alcoholic ammonia in a sealed tube, a mixture of primary, secondary and tertiary amines are obtained.



6.3.4.2. Reduction of Nitrogen Containing Functional Group

6.3.4.2.1. Reduction of Nitriles:

Methyl cyanide (Nitrile) on catalytic hydrogenation can produce ethyl amine.



6.3.4.2.2 Reduction of Amides:

Primary amines can be produced by the reduction of amides with lithium aluminum hydrides.





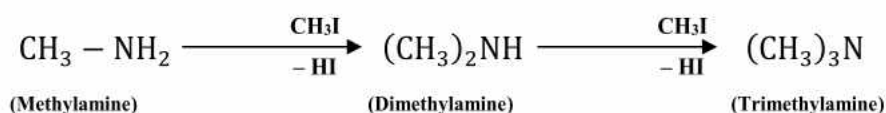
6.3.5. Reactivity

Amines are reactive due to the presence of lone pair of electrons on nitrogen atom and behave as nucleophile or a base. However, the reactivity of amines can be influenced by the nature and number of alkyl groups attached to nitrogen atom.

6.3.6. Reactions of Amines

6.3.6.1 Alkylation of Amines by Alkyl halides

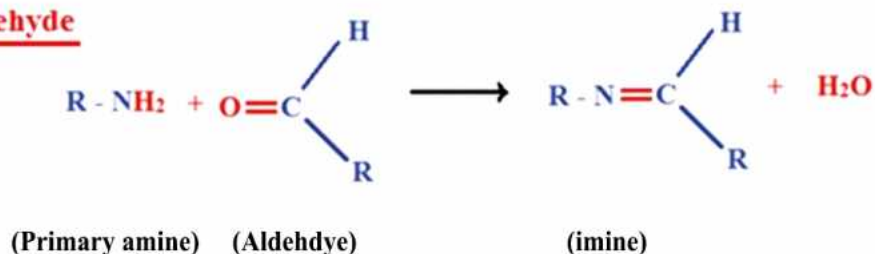
Primary amines react with alkyl halides to form secondary and tertiary amines. In this reaction hydrogen atoms of amines are replaced by alkyl groups.



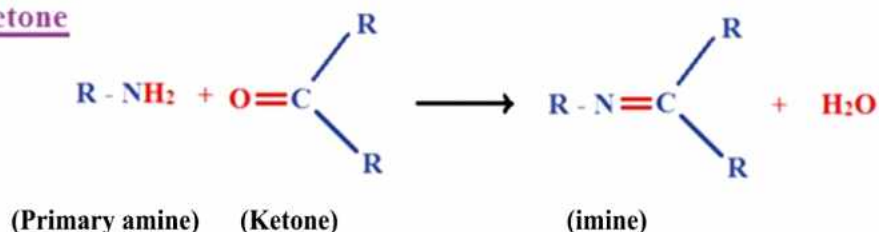
6.3.6.2. Reactions of amine with Aldehydes & Ketones

Primary amines can react with aldehydes and ketones to produce “imines” which also referred as Schiff bases.

with Aldehyde



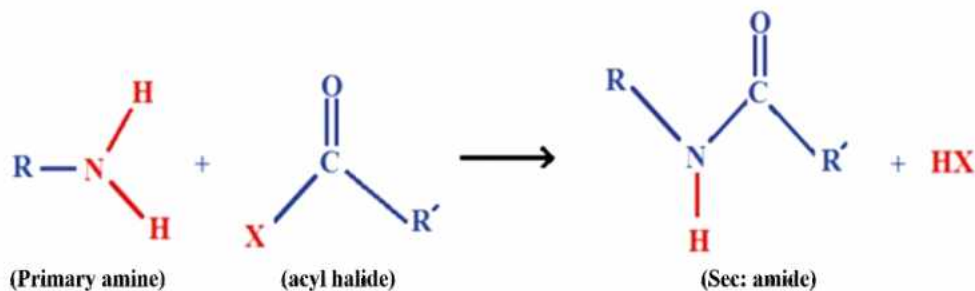
with ketone



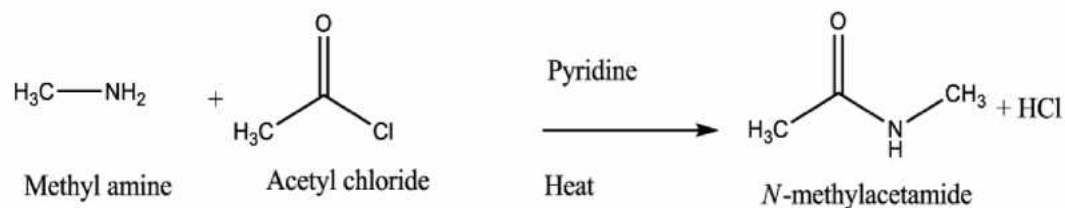


6.3.6.3. Preparation of Amides

When primary amines are reacted with Acyl halide or Acid anhydride, they form amides.

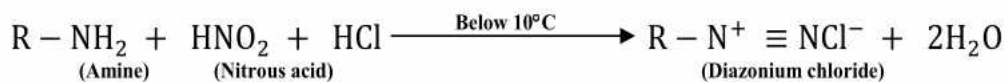


When methyl amine reacts with acetyl chloride to form:

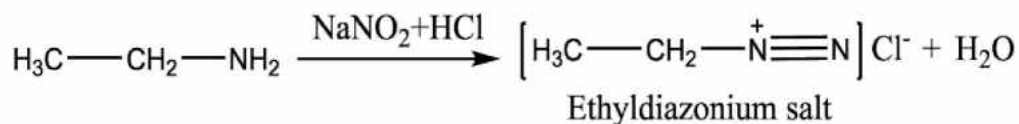


6.3.6.4 Preparation of Diazonium Salt

When amines react with nitrous acid in the presence of hydrochloric acid at below 10°C, a diazonium salt will be obtained.



The reaction of ethylamine with nitrous acid in the presence of hydrochloric acid forms ethyl diazonium, as shown below:





SOCIETY, TECHNOLOGY AND SCIENCE

Haemoglobin and Chlorophyll

Haemoglobin and chlorophyll are coloured organometallic compounds found in animals and plants respectively.

Haemoglobin is a protein, made up of four subunits each containing a heme group with an iron atom that binds to oxygen.

Chlorophyll on the other hand is a large molecule with porphyrin ring structure containing a magnesium atom.

Haemoglobin is involved in the transport of oxygen from lungs to the all body cells, while chlorophyll is responsible for capturing light energy in plants for photosynthesis.



SUMMARY

- Alkyl halides are derivatives of alkanes, they are formed by the replacement of hydrogen of alkanes by halogens.
- Alkyl halides are classified as primary, secondary and tertiary depending upon the nature of carbon to which halogen is bonded.
- Structure of methyl halides is tetrahedral in which carbon atom is bonded to three hydrogen atoms by sp^3 -s sigma bonds and one halogen atom by sp^3 -p sigma bond.
- Alkyl halides are soluble in organic solvents but insoluble in water, this is due to their inability to form hydrogen bonds with water.
- Alkyl halides are reactive due to polar nature of carbon-halogen bond.
- Alkyl halides undergo nucleophilic substitution (S_N) and elimination (E) reactions.
- Grignard reagent is an organometallic compound prepared by the reaction between an alkyl halide and magnesium metal.
- Grignard reagent is very reactive and is used to synthesize many organic compounds like alkanes, carboxylic acids and alcohols etc.



- Amines are derivatives of ammonia, formed by the replacement of one or more hydrogens by alkyl or aryl groups.
- Amines are classified as primary, secondary and tertiary depending upon the number of alkyl groups attached to nitrogen atom.
- Amines serve as bases; due to the presence of lone pair of electrons on nitrogen atom and have ability to accept proton from acids.
- Amines are prepared by alkylation of ammonia, also prepared by reduction of nitriles and amides.

? EXERCISE

Multiple Choice Questions

- (i) Which of the following composition justifies the secondary alkyl halide?

(a) R_3CX	(b) R_2CHX
(c) RCH_2X	(d) CH_3X
- (ii) Which of the following alkyl halide cannot produce an alkene while treated with alcoholic potassium hydroxide:

(a) Methyl bromide	(b) Ethyl bromide
(c) Propyl bromide	(d) Butyl bromide
- (iii) Ethyl magnesium bromide with carbon dioxide yields.

(a) Methanoic acid	(b) Ethanoic acid
(c) Propanoic acid	(d) Butanoic acid
- (iv) Grignard reagent with ester produces:

(a) Aldehyde	(b) Carboxylic acid
(c) Ketone	(d) Ether
- (v) Amines act as bases because:

(a) They accept OH^-	(b) They accept H^+
(c) They donate H^+	(d) They donate the OH^-
- (vi) The structure of Primary amine is:

(a) Planar trigonal	(b) Linear
(c) Tetrahedral pyramidal	(d) Regular tetrahedral



- (vii) Alkyl amine when reacts with nitrous acid in the presence of hydrochloric acid, yields:
- | | |
|--------------------|--------------|
| (a) Diazonium salt | (b) Aldehyde |
| (c) Ketone | (d) Alcohol |
- (viii) SN^2 reaction occurs most easily if the substrate molecule is:
- | | |
|---------------------|---------------------|
| (a) A methyl iodide | (b) An ethyl iodide |
| (c) 2-iodo propane | (d) 2-iodo butane |
- (ix) Suitable reagent required for the synthesis of propane from methyl magnesium iodide is:
- | | |
|----------------------------|------------------------------|
| (a) H_2O | (b) NH_3 |
| (c) CH_3OH | (d) CH_3NH_2 |
- (x) The rate of SN^1 mechanism depends upon:
- Conc. of substrate only
 - Conc. of attacking nucleophile only
 - Conc. of both substrate and attacking nucleophile
 - Polar solvent

Short Questions

- How are alkyl halides prepared by the reaction of alcohol with (i) HX (ii) PX_3 (iii) SOCl_2 . Give the equations.
- How are amines prepared from nitriles, give the equations.
- Why are secondary and tertiary amines more alkaline than primary amines?
- Why the alkyl part of Grignard reagent is nucleophilic in nature?
- Convert the followings:
 - Methyl magnesium bromide into acetone
 - Ethylchloride into ethyl amine
 - Ethyl chloride into ethyl alcohol
 - Ethylamine into imine
- How is primary amine converted into secondary and tertiary amines, give the equations.
- Give an account on the basicity of amines.
- How can you justify the fact that alkyl halides are water insoluble?
- How can you define a nucleophile? Write the names of four nucleophiles along with their typical reagents.
- Why the mechanism of SN^2 reaction completes in one step?



Descriptive Questions

1. How can you define nucleophilic substitution reactions? Describe the mechanisms of SN^1 and SN^2 reactions.
2. What is β -elimination? Discuss the mechanisms of E_1 and E_2 reactions.
3. What are organometallic compounds? How is Grignard reagent prepared? Write down the reactions of Grignard reagent with water, carbon dioxide, ester and amines.
4. What are alkyl halides? Define primary, secondary and tertiary alkyl halides.
5. Draw the orbital structure of methyl iodide and explain the type of hybridization in it.
6. Give a comparative study between nucleophilic substitution reactions and elimination reactions of alkyl halides.