

# Chapter # 6

# ALKYL

# HALIDES AND

# AMINES





## 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.

- Mono haloalkanes have only one halogen atom,
- Dihaloalkanes have two halogen atoms and
- Tri haloalkanes have three halogen atoms.

Mono haloalkanes are usually called alkyl halides and represented by a formula R-X, where R is an alkyl group and X is halogen atom (functional group).

The general formula of mono haloalkanes is  $\text{CH}_{2n+1}\text{X}$  where n, represents the number of carbon atoms.

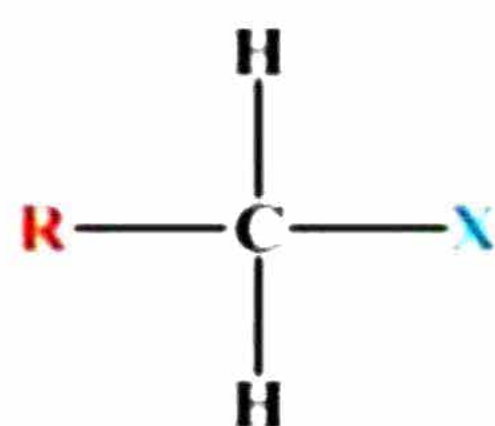
## ALKYL HALIDES

Alkyl halides can be classified according to the carbon atom to which the halogen atom is attached.

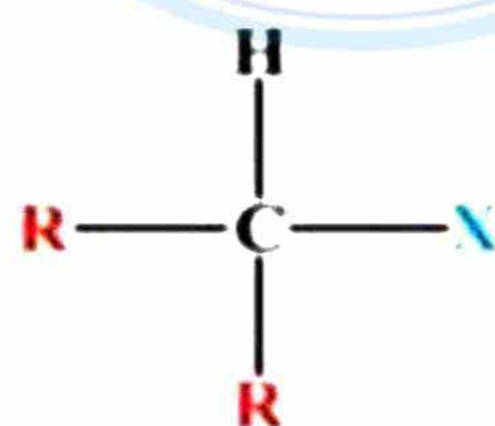
A primary ( $1^\circ$ ) alkyl halide refers to an alkyl halide where the halogen-bearing carbon is bonded to only one other carbon atom.

When two carbon atoms are attached to the halogen-bearing carbon, it is known as a secondary ( $2^\circ$ ) alkyl halide.

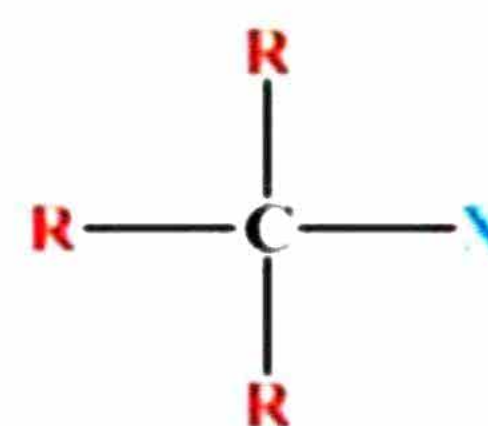
Finally, a tertiary ( $3^\circ$ ) alkyl halide is characterized by the halogen-bearing carbon being bonded to three carbon atoms.



( $1^\circ$ - Alkyl halide)



( $2^\circ$ - Alkyl halide)



( $3^\circ$ - Alkyl halide)

### Examples of alkyl halides are given below

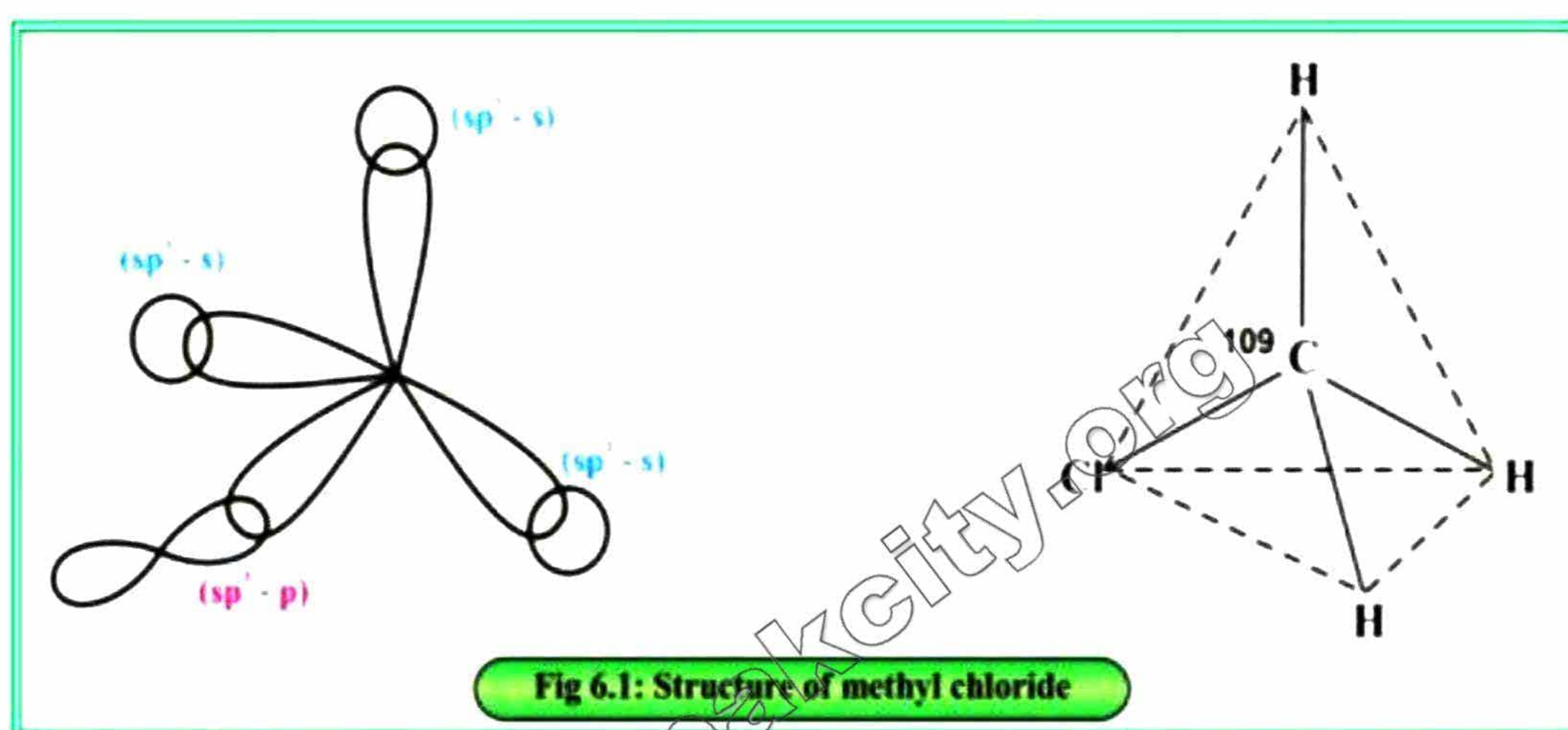
1. Primary alkyl halide: 1-Bromopropane ( $\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}$ )
2. Secondary alkyl halide: 2-Bromopropane ( $\text{CH}_3\text{CHBrCH}_3$ )
3. Tertiary alkyl halide: 2-Bromo-2-methylpropane ( $\text{CH}_3\text{C}(\text{CH}_3)_2\text{Br}$ )



### Structure of Alkyl Halide

Let us consider methyl chloride ( $\text{CH}_3\text{-Cl}$ ) as an alkyl halide.

Carbon of methyl halide is bonded with four atoms which means carbon is utilizing its all four valence electrons to produce four  $\text{sp}^3$  hybrid orbitals, which are oriented at an angle of  $109^\circ$  to give a tetrahedral geometry. These four  $\text{sp}^3$  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.



### 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 colorless 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.

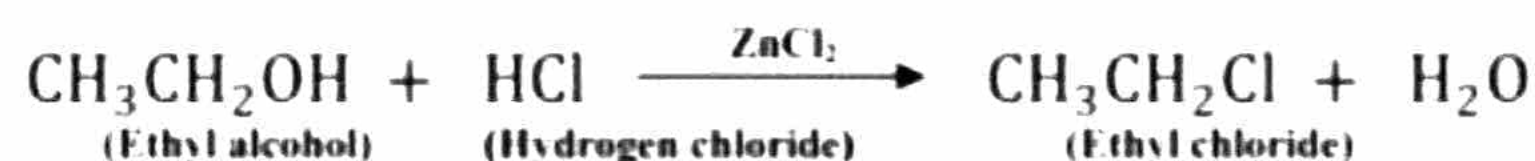
### Preparation of Alkyl Halides

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

#### 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 ( $\text{ZnCl}_2$ ) is used as a catalyst.

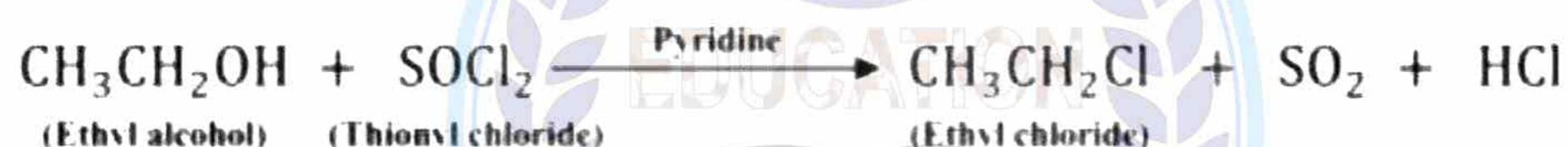


### Reaction of Alcohols with other halogenated agents

Alcohols react with phosphorous trihalide ( $\text{PCl}_3$ ,  $\text{PBr}_3$ ,  $\text{PI}_3$ ) to form alkylhalides. Since phosphorus trichloride is more easily available, the reaction is generally carried out by using this reagent.

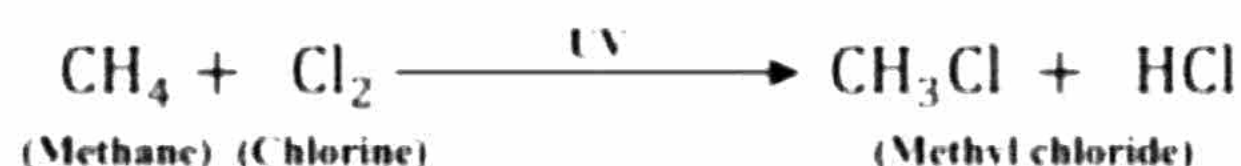


Alcohols reacts with thionyl halide ( $\text{SOX}_2$ ) in the presence of pyridine as catalyst to produce an alkyl halides. This is preferred method for the preparation of alkyl halide because both the by products are in gaseous state.



### 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, resulting in the formation of a mixture of different haloalkanes. However, due to the production of a mixture of different halogenated alkanes, this method is not considered efficient for the preparation of alkyl halides.



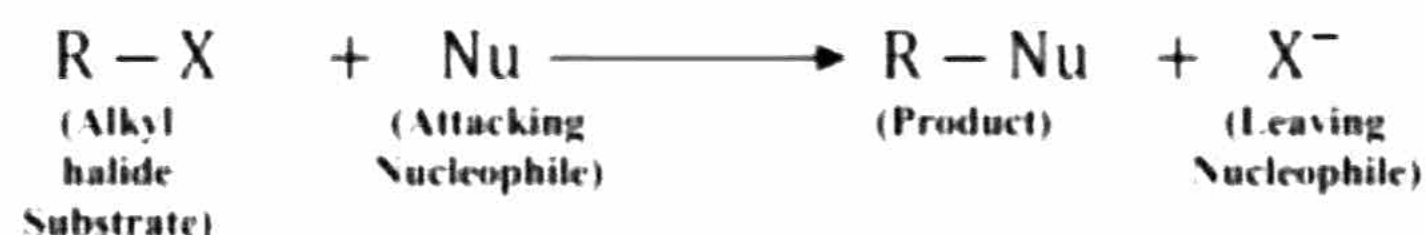
### Nucleophile

Nucleophile is a chemical species within a molecule that can donate a pair of a electrons to forma covalent bond with another atom or molecule.

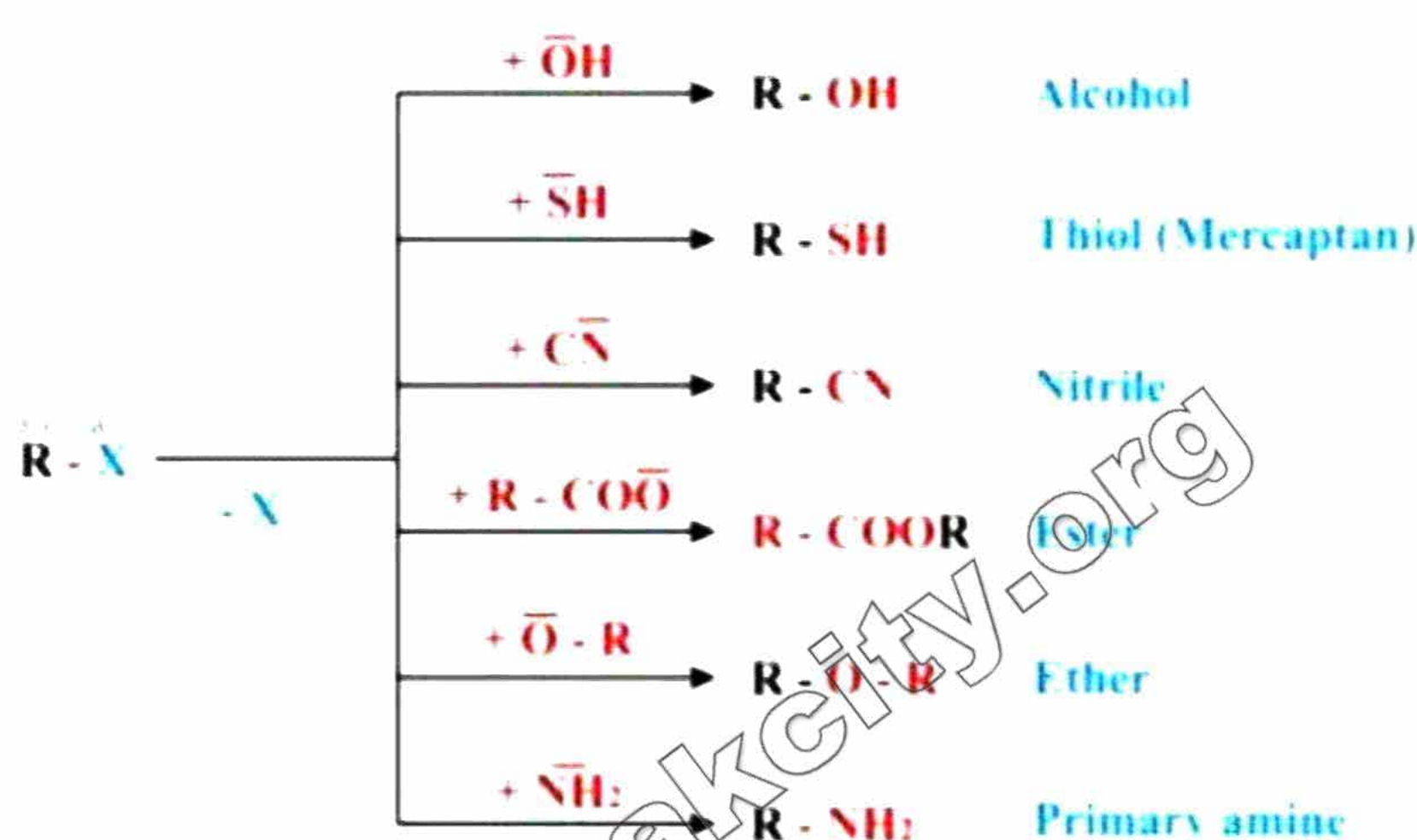


## Nucleophilic Substitution Reactions

“A type of chemical reactions in which strong nucleophile (electron efficient species) replaces the weak nucleophile of the substrate is termed as nucleophilic substitution reactions”.



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



Some common strong Nucleophiles along with their typical reagents.

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

## Mechanism of nucleophilic substitution reactions

The mechanism of nucleophilic substitution reaction is divided into:

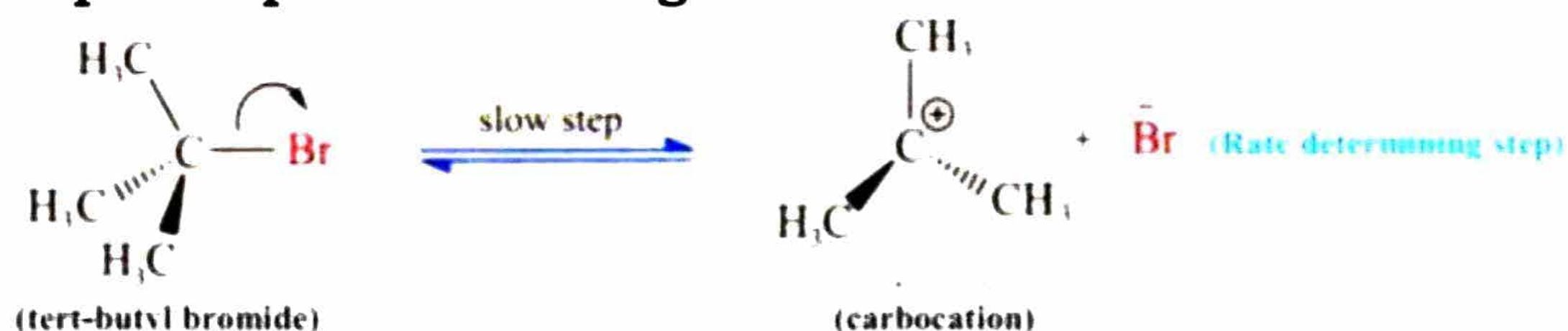
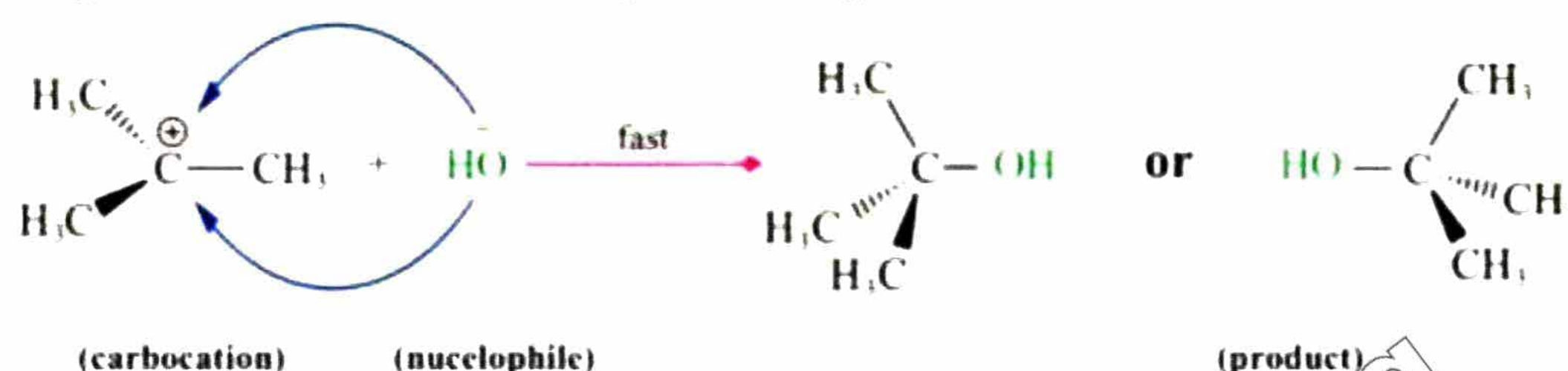
- (i)  $\text{SN}^1$  Reactions
- (ii)  $\text{SN}^2$  Reactions

### $\text{SN}^1$ mechanism

It is unimolecular bi-step  $\text{SN}$  reaction,

“The  $\text{SN}^1$  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  $\text{SN}^1$  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  $\text{SN}^1$  reaction.

Chemical reactions that processed via the  $\text{SN}^1$  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.

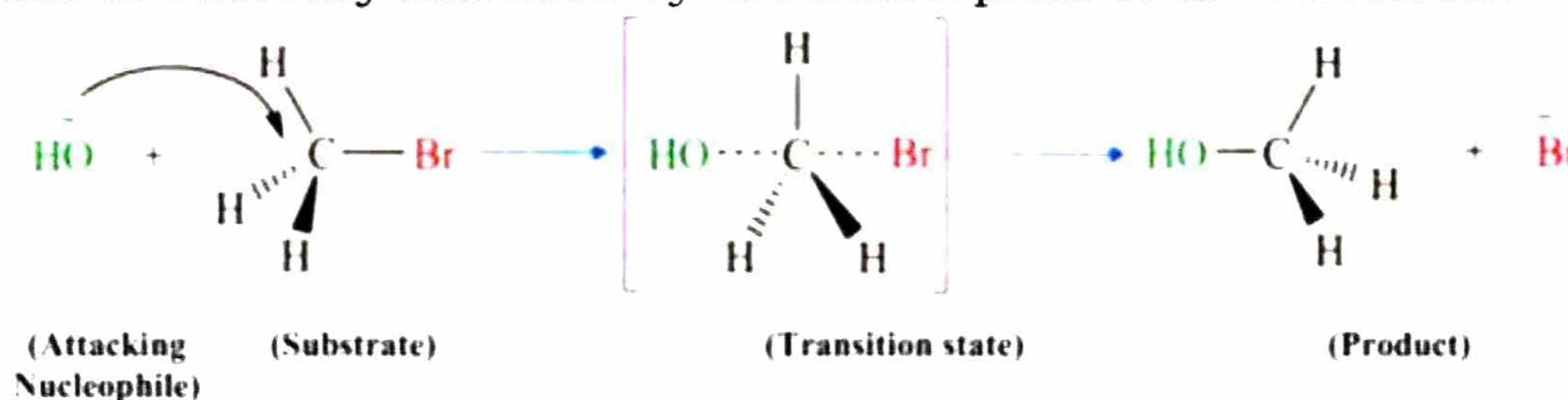
$$R = K [\text{Substrate}]$$

 **$\text{SN}^2$  mechanism**

It is bimolecular single step  $\text{SN}$  reaction

“In the  $\text{SN}^2$  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  $\text{SN}^2$  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.

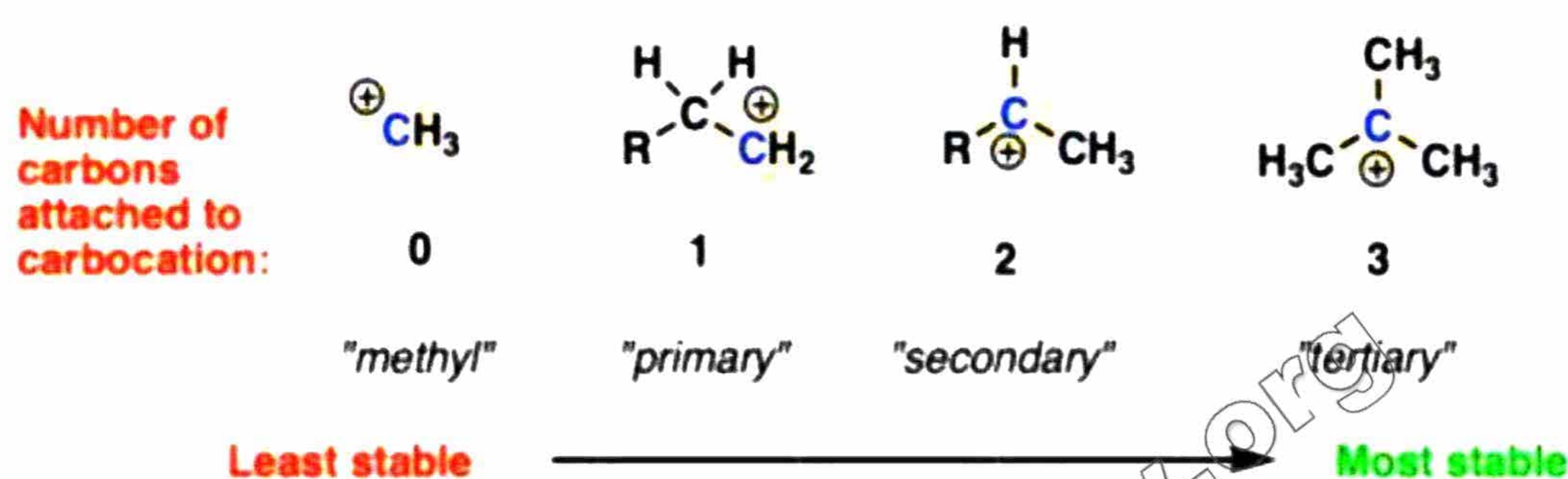


The  $S_N2$  mechanism is followed by second order kinetics which means that the reaction rate is dependent upon the concentration of both substrate and attacking nucleophile.

$$R = k [\text{Substrate}] [\text{Nu}]$$

### 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".

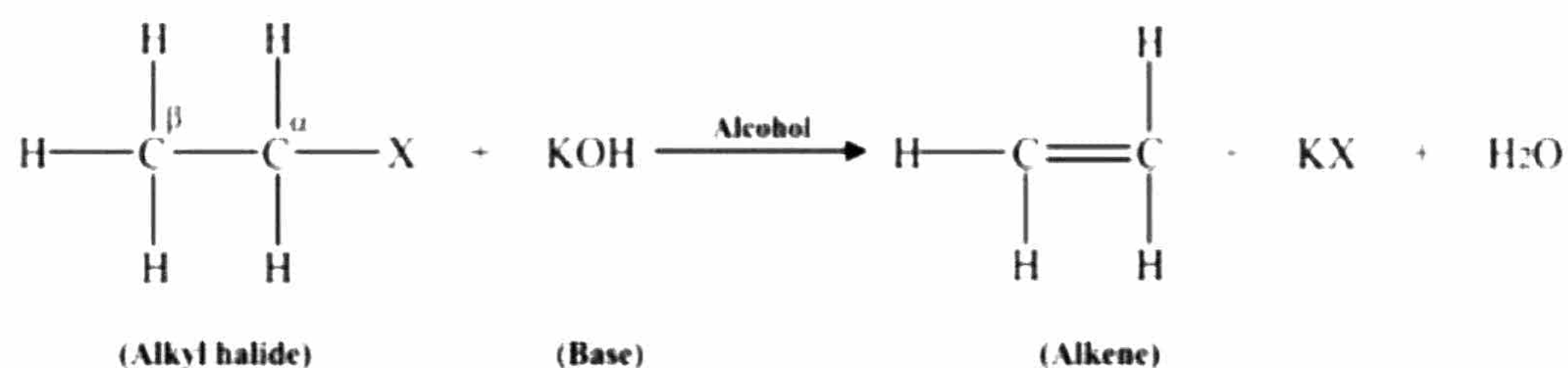


### Elimination Reactions

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  $\beta$ -elimination reaction.

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



There are two common types of  $\beta$ -elimination reactions named as  $E_1$  and  $E_2$ .

### Mechanism of $E_1$ Reaction

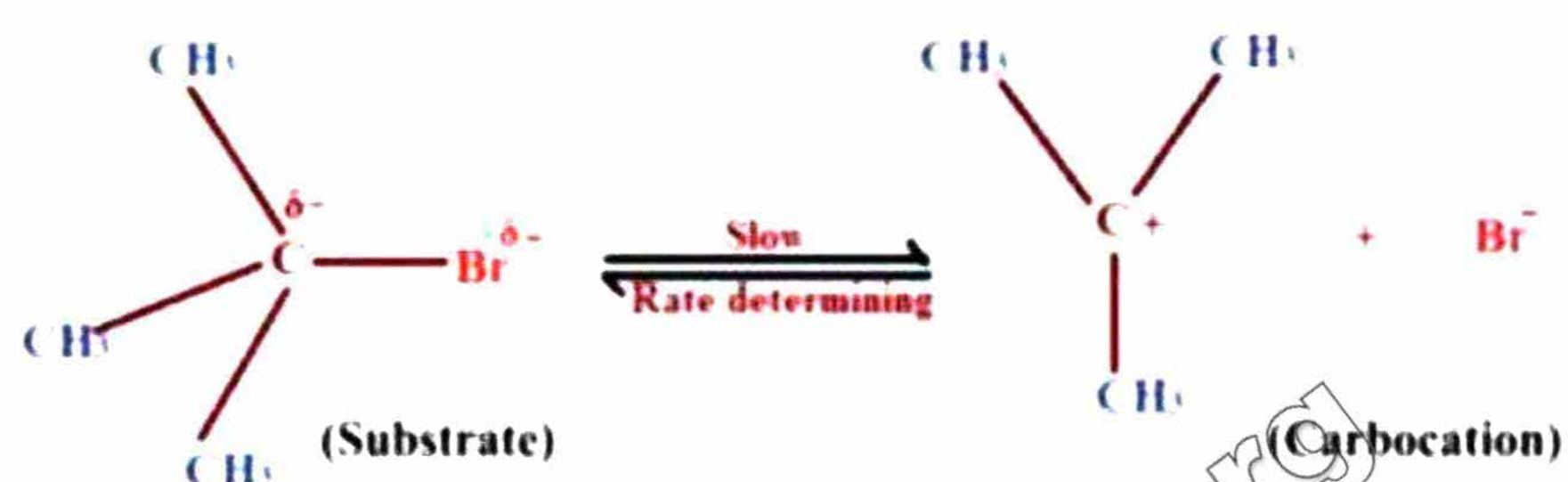


$E_1$  reactions, known as unimolecular elimination reactions, occur in two steps.

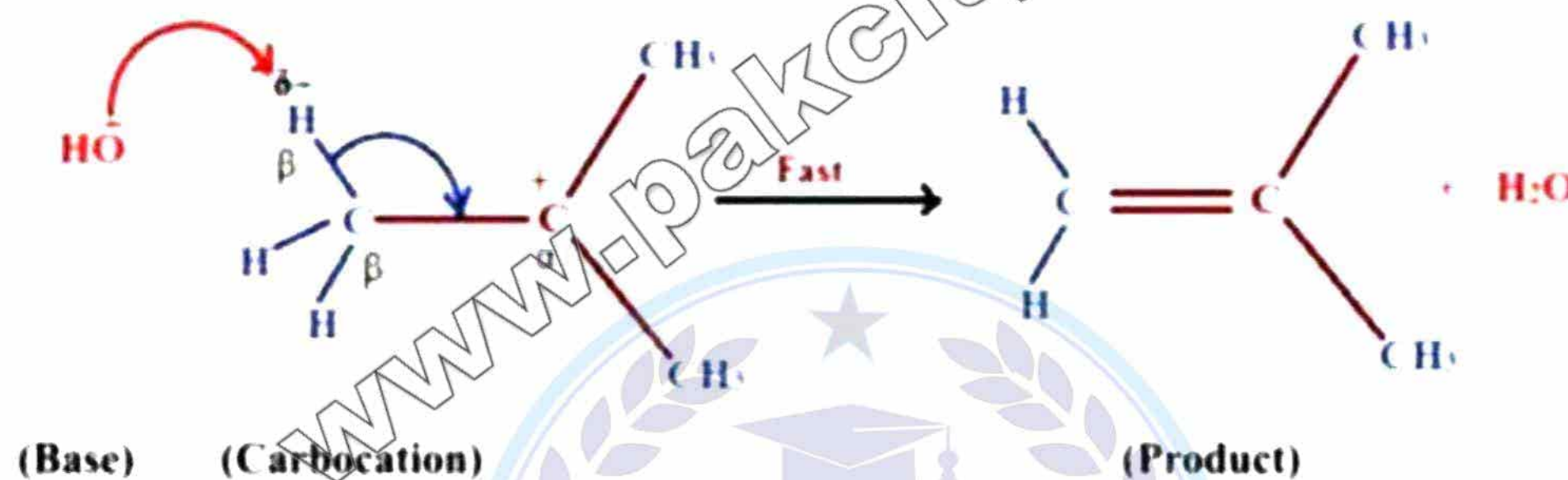
In the first step, the halogen atom departs from the substrate, forming a carbocation intermediate, which is the slow and rate-determining step.

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 B-H & formation of multiple bond

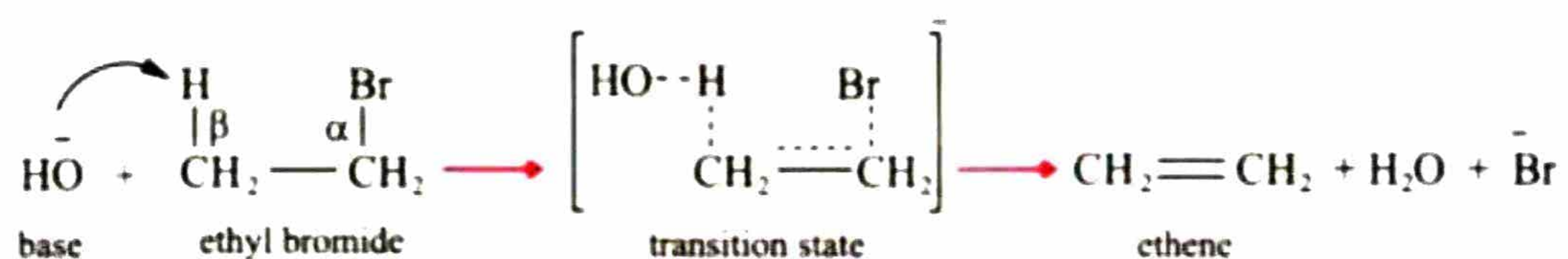


The rate determining step in  $E_1$  mechanism involves the unimolecular ionization of the substrate molecule. Therefore, the rate of the reaction depends only on the concentration of reactant, and not on the concentration of base.

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

### 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  $\beta$ -carbon. Simultaneous halide ion eliminates from  $\alpha$ -carbon and the lone pair of electrons is shifted between  $\alpha$  and  $\beta$  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

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

### **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  $\alpha$ -carbon atom where as elimination reaction occurs when the nucleophile attacks on the  $\beta$ -hydrogen. Several factors can influence the formation of products via either substitution or elimination mechanisms.

#### **Solvent effect:**

Substitution reactions are favored in polar solvents while elimination reaction are favored 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 favors elimination reaction while if it is primary alkyl halide, it favors substitution reaction. Secondary alkyl halide is consented to both substitution and elimination.

### **GRINGARD'S REAGENTS DOYOU (ORGANOMETALLIC COMPOUNDS)**

"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:

- (i) Grignard reagent: It is a highly reactive organic compound and used in organic synthesis.
- (ii) Methyl cobalamine: It is a derivative of vitamin B-12.
- (ii) Dimethyl Zinc: It is used as insecticide.
- (iv) Tetraethyl lead: It is used as knock inhibitor in petroleum industry.

### Preparation of Grignard Reagent

"Grignard reagent is an organometallic compound that contains a carbon-magnesium (C-Mg) bond".

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,

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

The formation of Grignard reagent depends on two factors that determine its case 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 I > Br > Cl because the bond between iodine and carbon is weaker than corresponding bond with other halogens.

### 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.

### Reactions of Grignard Reagent

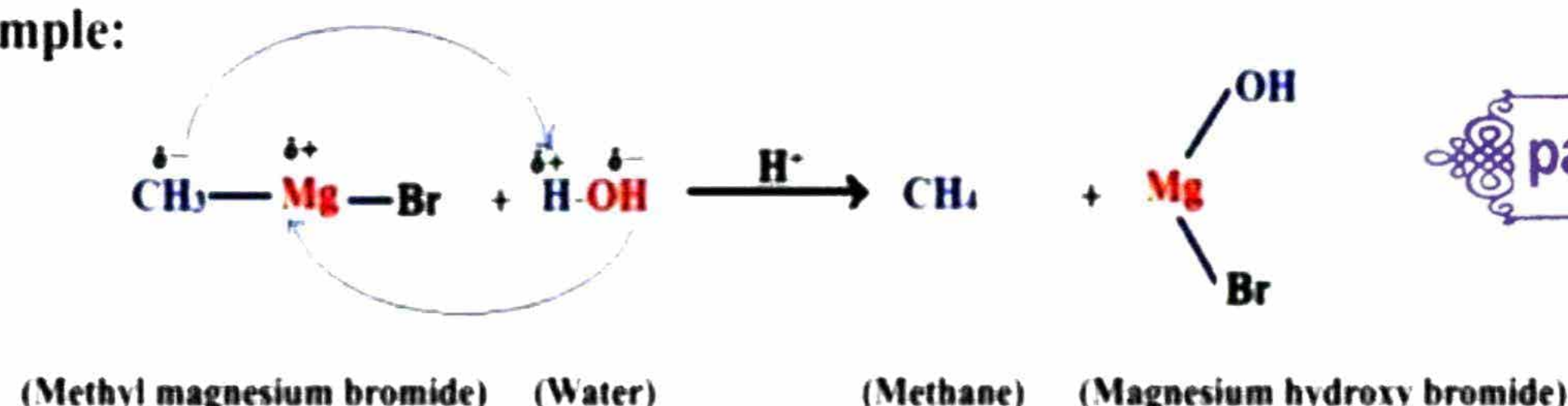


Grignard reagent is a versatile chemical; it is used as starting material for the synthesis of various organic compounds such as alkanes, alcohols, carboxylic acids and ketones.

### Reaction with Water

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

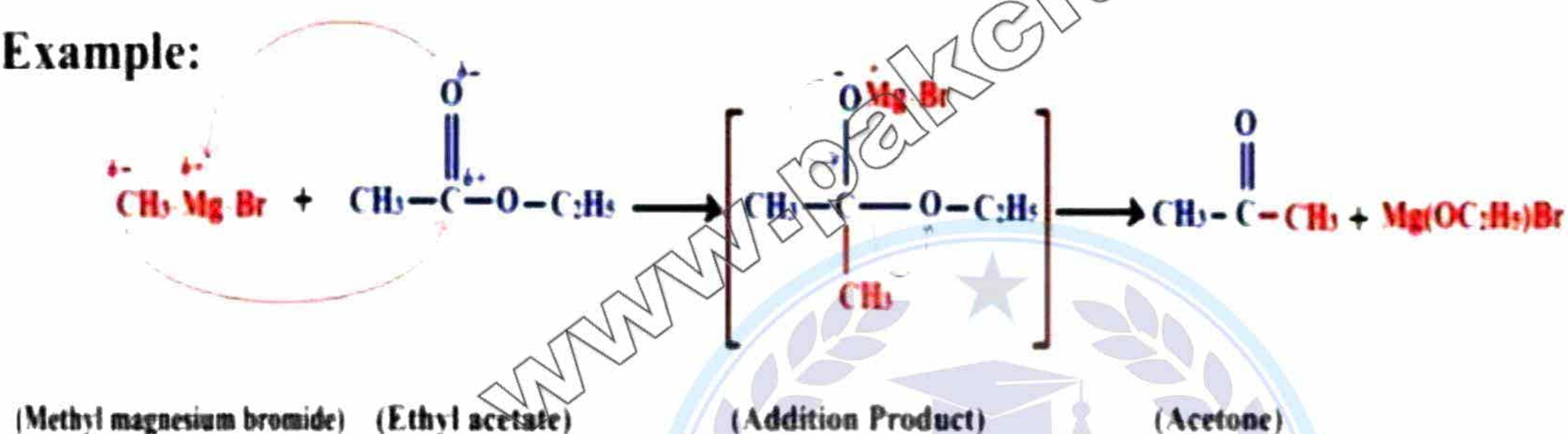
Example:



### 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.

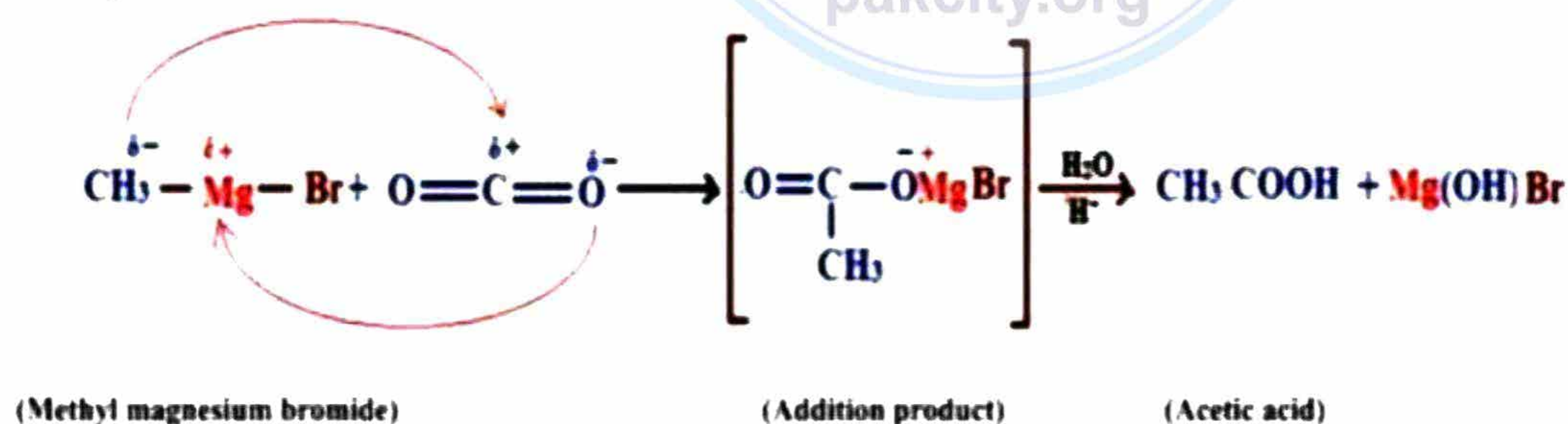
Example:



### 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:

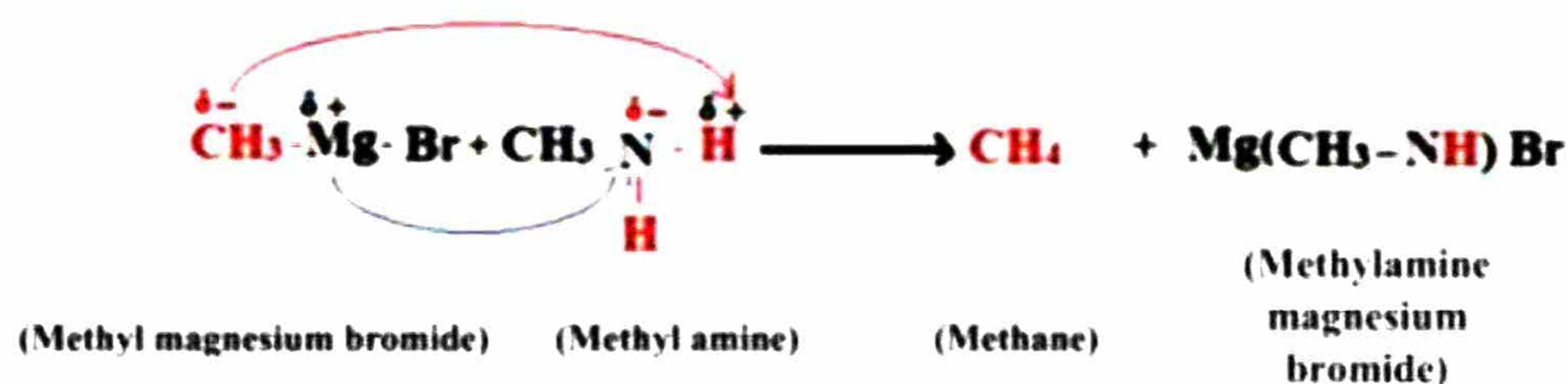


### Reaction with primary amine

Grignard reagent reacts with primary amine to produce an alkane.



**Example:**

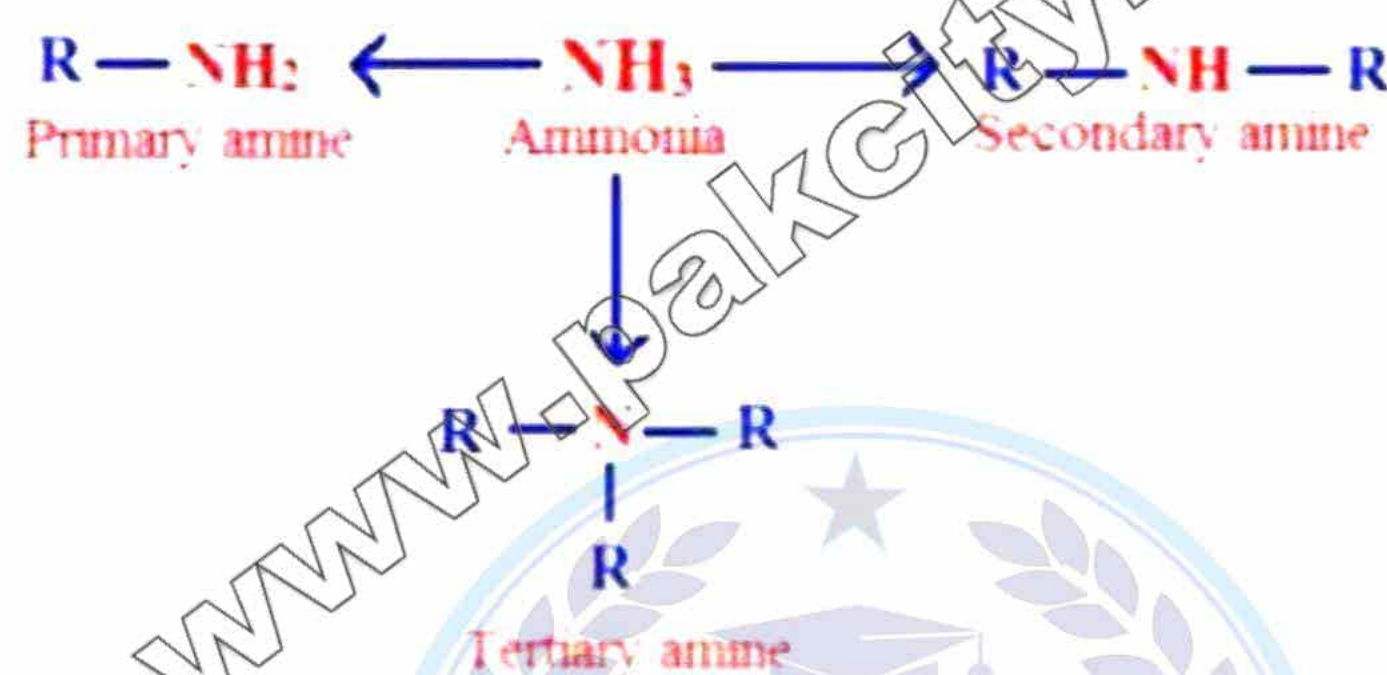


## AMINES

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

“Organic compounds that contain 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.



### Physical Properties

#### Physical state:

Lower members exist in gaseous states (i.e. Methylamine  $\text{CH}_3\text{NH}_2$ ) 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 colorless 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.

#### Solubility:

Amines are soluble in water, their solubility decreases with the increase in non-polar hydrocarbon chain.

**For example:** Methylamine ( $\text{CH}_3\text{NH}_2$ ) is soluble in water and Trimethylamine ( $\text{N}(\text{CH}_3)_3$ ) has limited solubility in water as the presence of three methyl groups hinders its interaction with water molecules.



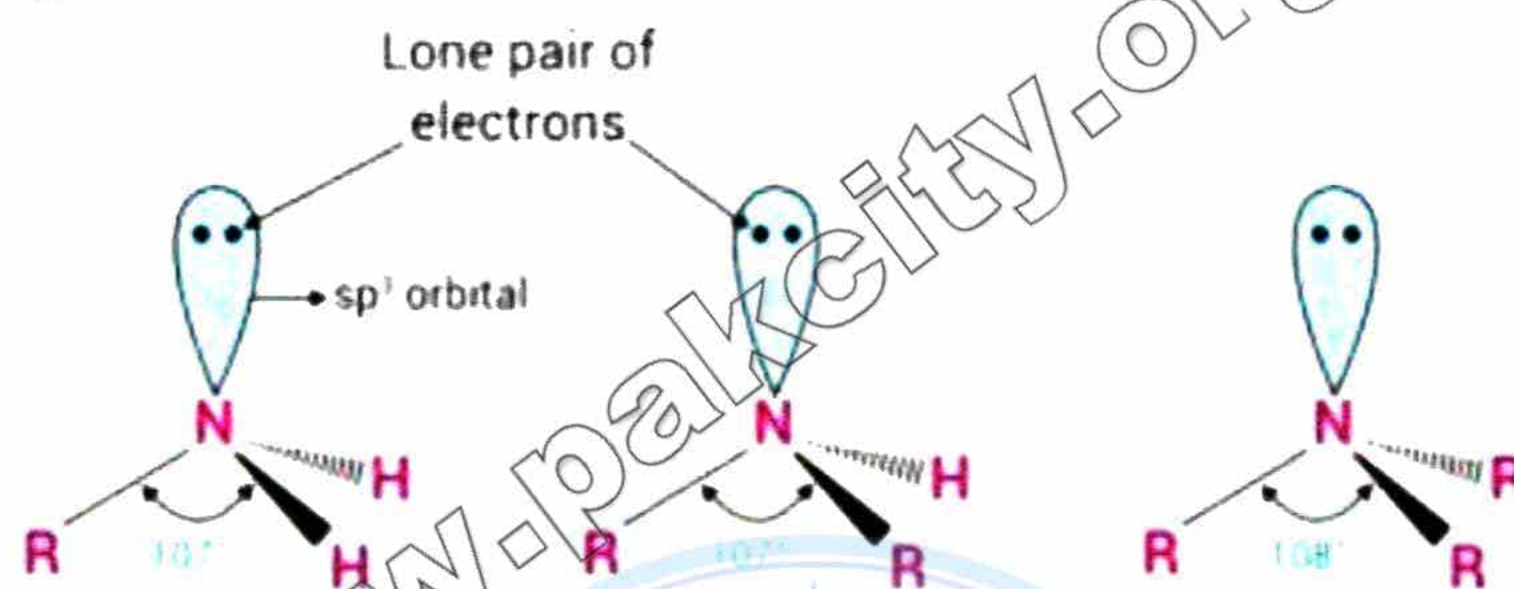
### Melting and Boiling Points:

Amines are polar in nature and form hydrogen bonds with each other that is why their melting and boiling points are relatively higher than those hydrocarbons of comparable molecular mass.

**For example:** Diethyl amine ( $\text{C}_2\text{H}_5$ ) $_2\text{NH}$  has a higher boiling point compared to ethylamine due to the presence of two ethyl groups.

### Structure

The nitrogen of amines is  $\text{sp}^3$  hybridized and contains four  $\text{sp}^3$  hybrid orbitals, out of which three  $\text{sp}^3$  hybrid orbitals are involved in the formation of sigma bonds whereas the fourth  $\text{sp}^3$  hybrid orbital contains a lone pair of electrons. These four  $\text{sp}^3$  hybrid orbitals are oriented in space in tetrahedral pyramidal geometry.



### Basicity of Amines

Compounds of all classes of amines are basic in nature.

"The basicity of amines is explained by the presence of non-bonding lone pair of electrons on nitrogen atom".



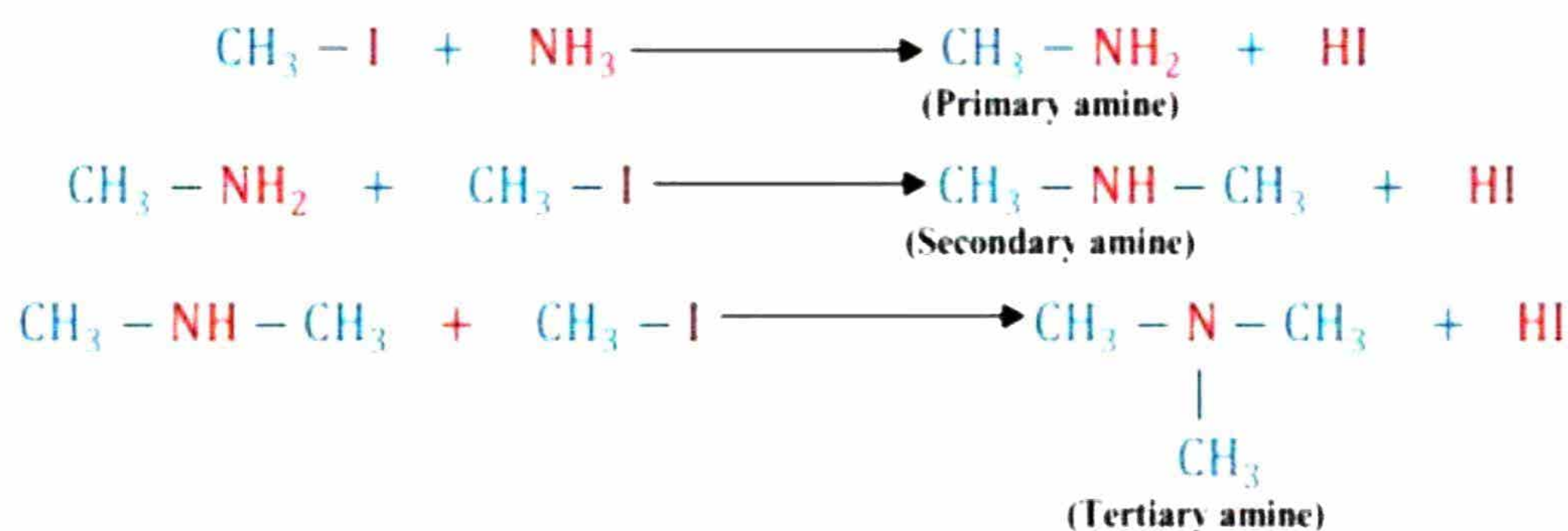
### Preparation of Amines

Amines are prepared by different methods:

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.





## Reduction of Nitrogen Containing Functional Group

### Reduction of Nitriles:

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



### Reduction of Amides:

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



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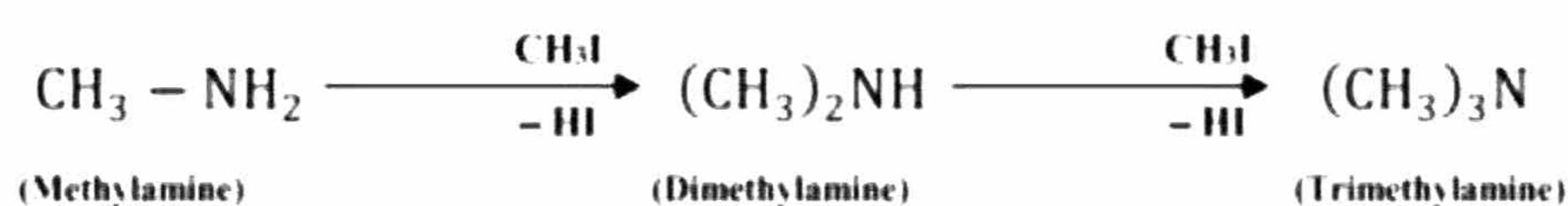
### Reactivity

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.

## Reactions of Amines

### Alkylation of Amines by Alkyl halides

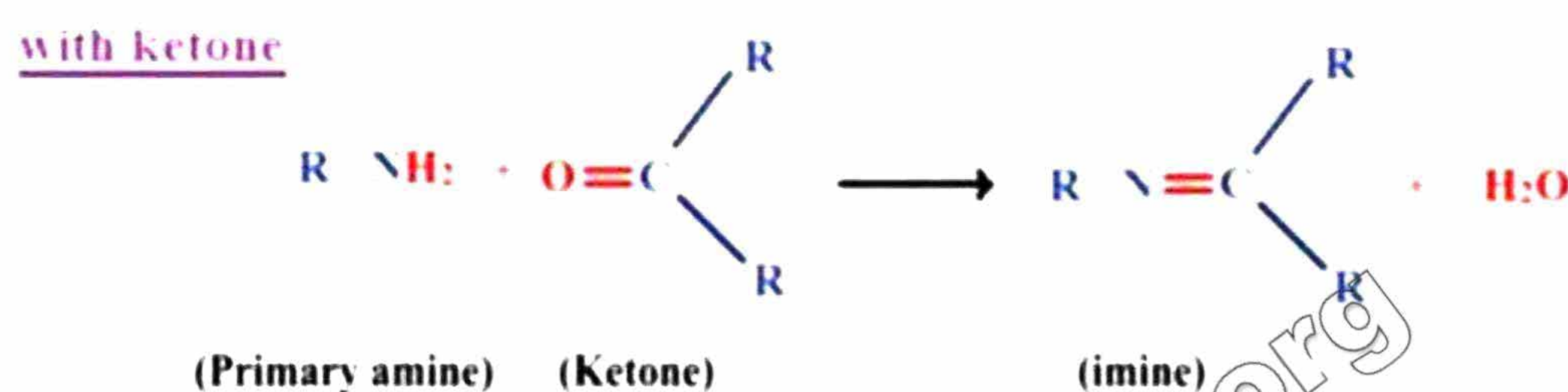
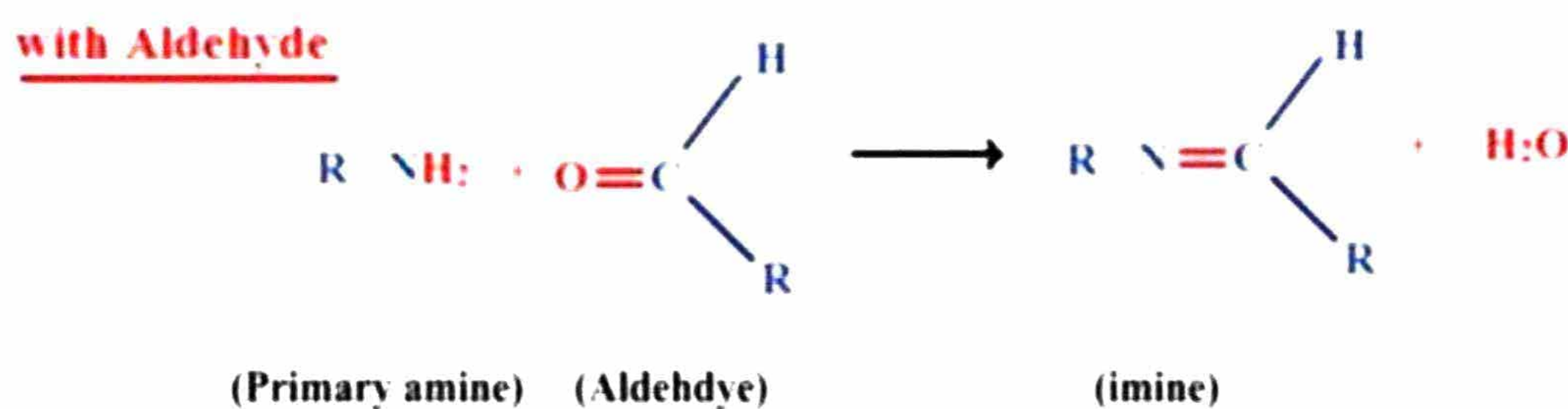
Primary amines react with alkyl halides to form secondary and tertiary amines. In this reaction hydrogen atoms of amines are replaced by alkyl groups.





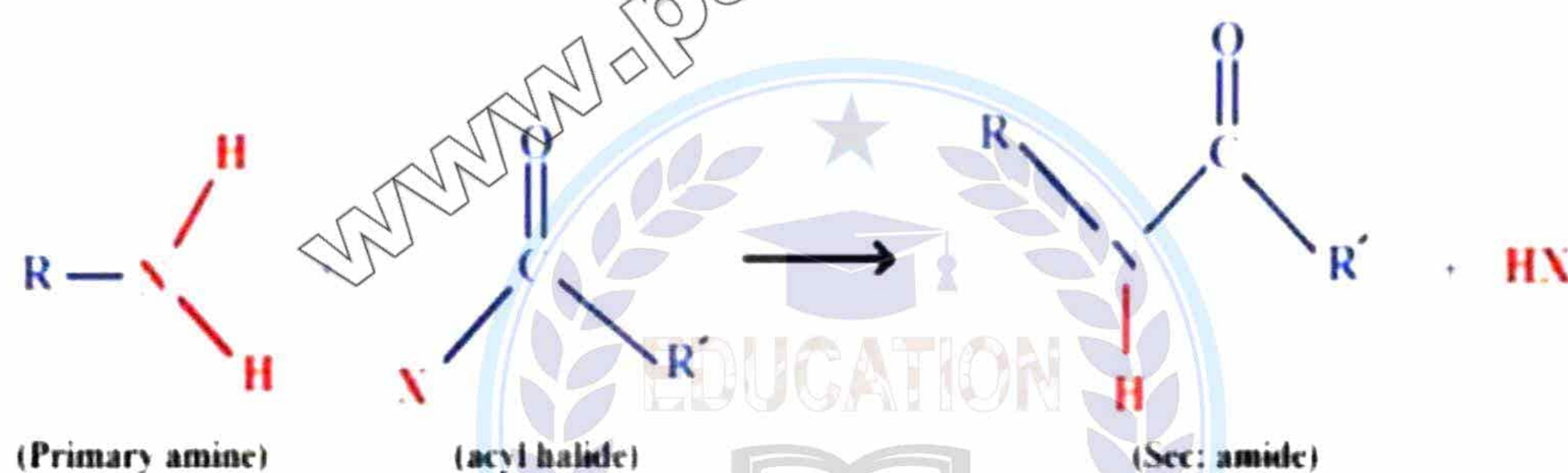
### Reactions of amine with Aldehydes & Ketones

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

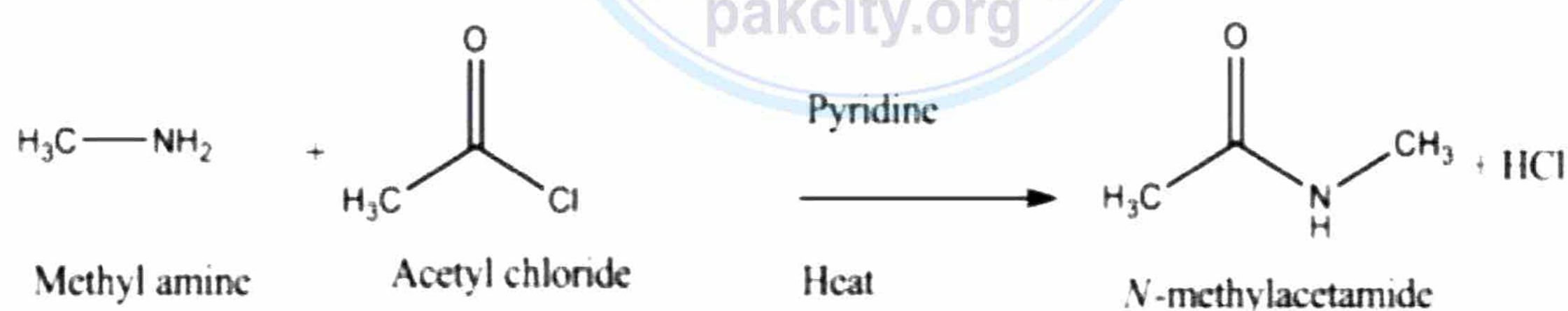


### Preparation of Amides

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

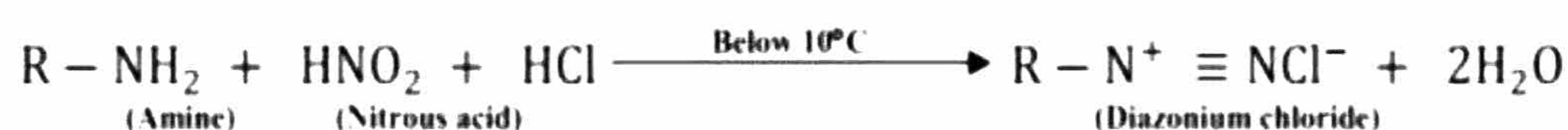


When methyl amine reacts with acetyl chloride to form:



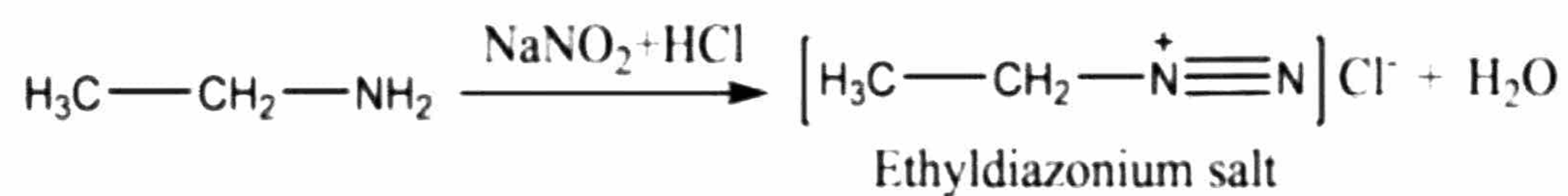
### Preparation of Diazonium Salt

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:



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### Short Questions

1. How are alkyl halides prepared by the reaction of alcohol with (i) HX (ii)  $PX_3$  (iii)  $SOCl_2$ . Give the equations.
2. How are amines prepared from nitriles, give the equations.
3. Why are secondary and tertiary amines more alkaline than primary amines?

#### 4. Why the alkyl part of Grignard reagent is nucleophilic in nature?

Despite not being a strong nucleophile on its own, the alkyl group in a Grignard reagent reacts with electrophiles due to several factors:

- **Strong basic character of the Grignard reagent:** The negative charge on the magnesium atom makes the Grignard reagent a strong base. It readily reacts with protic solvents like water ( $H_2O$ ) to form the corresponding alkane and a magnesium hydroxide byproduct.
- **Favorable thermodynamics of the reaction product:** When the alkyl group of the Grignard reagent reacts with an electrophile (often a carbonyl compound), a new carbon-carbon bond is formed. This C-C bond is typically much stronger than the C-Mg bond in the Grignard reagent. The formation of a stronger bond drives the reaction forward even though the alkyl carbon itself isn't a strong nucleophile.

#### 5. Convert the followings:

- (a) Methyl magnesium bromide into acetone
  - (b) Ethyl chloride into ethyl amine
  - (c) Ethyl chloride into ethyl alcohol
  - (d) Ethylamine into imine
6. How is primary amine converted into secondary and tertiary amines, give the equations.

#### 7. Give an account on the basicity of amines.

more hydrogen atoms with alkyl or aryl groups. They exhibit basic character due to the presence of a lone pair of electrons on the nitrogen atom. Here's a detailed look at factors affecting the basicity of amines:

##### Factors Influencing Basicity:

1. **Availability of the Lone Pair:**
  - The ability of the lone pair on nitrogen to donate electrons determines the basicity of an amine. This availability is influenced by surrounding atoms and electron-withdrawing/donating effects.
2. **Inductive Effect (-I or +I effect):**



- Substituent groups attached to the nitrogen atom can influence the electron density around nitrogen through inductive effects.
  - **Electron-withdrawing groups (-I effect):** Groups like carbonyl (C=O), nitro (NO<sub>2</sub>), or cyano (CN) withdraw electrons from the nitrogen atom, reducing its electron density and weakening its ability to donate electrons as a base. Thus, amines with electron-withdrawing groups are less basic.
  - **Electron-donating groups (+I effect):** Alkyl groups (like CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>) have a slight electron-donating effect. They slightly increase the electron density around nitrogen, making the lone pair more available for donation. However, the effect is relatively weak compared to electron-withdrawing groups.

### 3. **Steric Hindrance:**

- Bulky substituent groups around the nitrogen atom can create steric hindrance. This hindrance can interfere with the lone pair's ability to interact with a proton (H<sup>+</sup>) from an acid, thereby affecting basicity. As steric hindrance increases, the basicity of the amine may decrease

## 8. How can you justify the fact that alkyl halides are water insoluble?

Alkyl halides (RX, where R is an alkyl group and X is a halogen) are generally insoluble in water due to a fundamental difference in the intermolecular forces between the two:

- **Alkyl Halides:** Rely on weaker **dispersion forces** (also known as London dispersion forces) for intermolecular attraction. These forces arise from temporary fluctuations in electron distribution within the molecule, creating instantaneous dipoles that induce weak attractions with neighboring molecules.
- **Water:** Highly polar molecule due to the presence of a bent shape and electronegative oxygen atom. This polarity allows water molecules to participate in **strong hydrogen bonding** with each other. In hydrogen bonding, a hydrogen atom bonded to a highly electronegative atom (like oxygen in water) is attracted to the lone pair of electrons on another electronegative atom in a nearby molecule.

Here's a breakdown of why these differences lead to water insolubility:

1. **Energy Considerations:** Breaking the strong hydrogen bonds in water requires a significant amount of energy. When an alkyl halide dissolves in water, it would need to disrupt these hydrogen bonds to be surrounded by water molecules. The energy released by the dispersion forces between the alkyl halide and water molecules is insufficient to overcome the energy required to break the hydrogen bonds.



2. **Favorable Interactions:** Water molecules prefer to interact with each other through hydrogen bonding, forming a stable network. Alkyl halides, lacking the ability to participate in hydrogen bonding, offer a less favorable interaction for water molecules.

**9. How can you define a nucleophile? Write the names of four nucleophiles along with their typical reagents.**

A nucleophile is a chemical species that has an electron-rich center and can donate an electron pair to form a new covalent bond.

Here are four common nucleophiles and their typical reagents:

1. **Ammonia (NH<sub>3</sub>) and Amines (RNH<sub>2</sub>, R<sub>2</sub>NH, R<sub>3</sub>N):**
  - These Lewis bases possess a lone pair of electrons on the nitrogen atom readily available for donation.
  - **Typical reagents:** Ammonia is often used directly. Amines can be used directly or as their conjugate acid salts (e.g., ammonium chloride, NH<sub>4</sub>Cl).
2. **Hydroxide Ion (OH<sup>-</sup>):**
  - This negatively charged oxygen atom has a lone pair and readily acts as a nucleophile in many reactions.
  - **Typical reagents:** Aqueous solutions of sodium hydroxide (NaOH) or potassium hydroxide (KOH) are common sources of hydroxide ions.
3. **Alkoxide Anions (RO<sup>-</sup>):**
  - These negatively charged oxygen atoms in alkoxides (e.g., methoxide, CH<sub>3</sub>O<sup>-</sup>; ethoxide, C<sub>2</sub>H<sub>5</sub>O<sup>-</sup>) possess lone pairs and can act as nucleophiles.
  - **Typical reagents:** They are often generated in situ (at the reaction site) by reacting alcohols (ROH) with strong bases like sodium hydride (NaH) or lithium diisopropylamide (LDA).
4. **Grignard Reagents (RMgX):**
  - These organometallic compounds contain a carbon-magnesium bond (C-Mg) with a partial negative charge on the carbon due to the highly electronegative magnesium atom. While not strictly a classical nucleophile with a lone pair, the carbanion character of the carbon allows it to act as a nucleophile.
  - **Typical reagents:** Grignard reagents are prepared by reacting magnesium metal (Mg) with alkyl halides (RX) in an anhydrous ether solvent (e.g., diethyl ether)

10. Why the mechanism of SN<sup>2</sup> reaction completes in one step?

Notes



### Descriptive Questions

**1. How can you define nucleophilic substitution reactions? Describe the mechanisms of  $S_N^1$  and  $S_N^2$  reactions.**

Notes

**2. What is  $\beta$ -elimination? Discuss the mechanisms of  $E_1$  and  $E_2$  reactions.**

Notes

**3. What are organometallic compounds? How is Grignard reagent prepared? Write down the reactions of Grignard reagent with water, carbon dioxide, ester and amines.**

Notes

**4. What are alkyl halides? Define primary, secondary and tertiary alkyl halides.**

Notes

**5. Draw the orbital structure of methyl iodide and explain the type of hybridization in it.**

Notes

**6. Give a comparative study between nucleophilic substitution reactions and elimination reactions of alkyl halides.**

Notes

