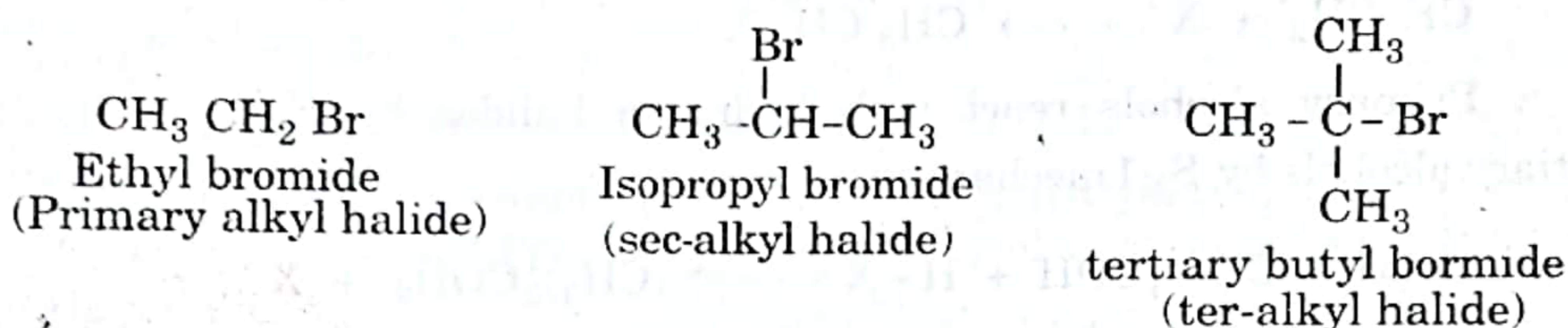# 8. ALKYL HALIDES

Monohaloderivatives of alkanes are called **alkyl halides**. They have the general formula R X, where R is an alkyl or substituted alkyl group and X is any halogen atom. They contain the halogen atom attached to a saturated carbon atom (– C – X) as their **functional group**. " A **functional group** is an atom or group of atoms that defines the structure of a particular family of organic compounds and also determines their properties".

Alkyl halides are classified as primary (I°), secondary (2°) or tertiary (3°) depending upon whether the halogen atom is attached to a primary, secondary or a tertiary carbon.

$$CH_3 CH_2 Br$$
Ethyl bromide
(Primary alkyl halide)

$$CH_3 - \overset{\overset{\displaystyle Br}{|}}{C}H - CH_3$$
Isopropyl bromide
(sec-alkyl halide)

$$CH_3 - \overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}} - Br$$
tertiary butyl bromide
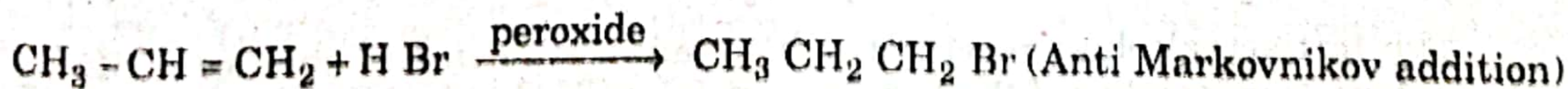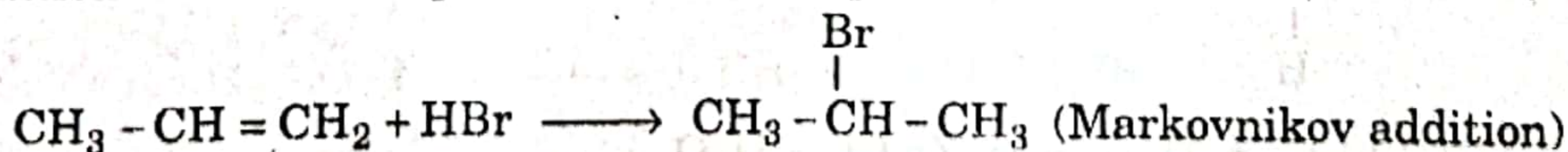(ter-alkyl halide)

8.1 Preparation of Alkyl Halides

1. Halogenation of alkanes. *A reaction in which an atom or a group in a molecule is replaced by another atom or a group is called* **substitution reaction,** *if the substituent is a halogen atom, the reaction is called* **halogenation.**

Alkanes react with Cl_2 or Br_2 in the presence of ultraviolet light or at 250 – 400°C to give alkyl halides along with polyhalogen derivatives. Therefore, halogenation of alkanes is not a useful method of preparation because of the difficulty of separating the products. Halogenation of alkanes proceeds by a free radical chain mechanism which has been discussed in chapter 4.

$$CH_4 + Cl_2 \xrightarrow{\text{UV light}} CH_3Cl + CH_2 Cl_2 + CHCl_3 + CCl_4$$
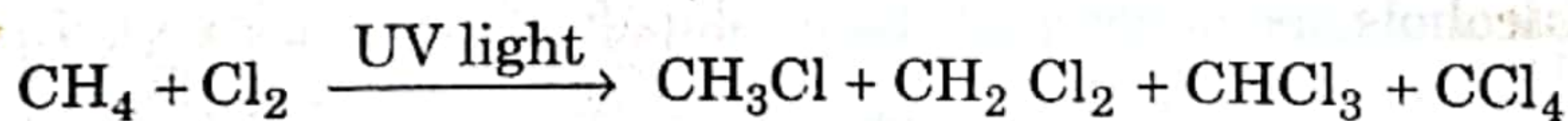
The reaction with F_2 is too violent to control and I_2 does not react at all.

2. Addition of Halogen acids to Alkenes. Halogen acids (HCl, HBr, HI) add to alkenes to form alkyl halides. The addition follows Markovnikov's rule, except for the addition of HBr in the presence of organic peroxides (R–O–O–R).

$$CH_3 - CH = CH_2 + HBr \longrightarrow CH_3 - \overset{\overset{\displaystyle Br}{|}}{C}H - CH_3 \text{ (Markovnikov addition)}$$

$$CH_3 - CH = CH_2 + H Br \xrightarrow{\text{peroxide}} CH_3 CH_2 CH_2 Br \text{ (Anti Markovnikov addition)}$$

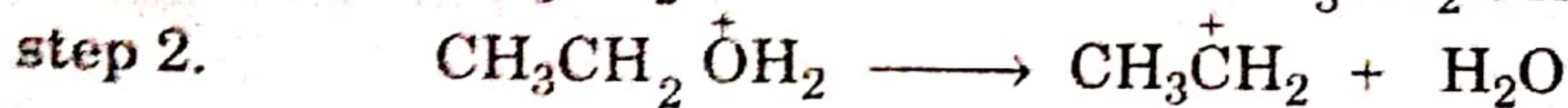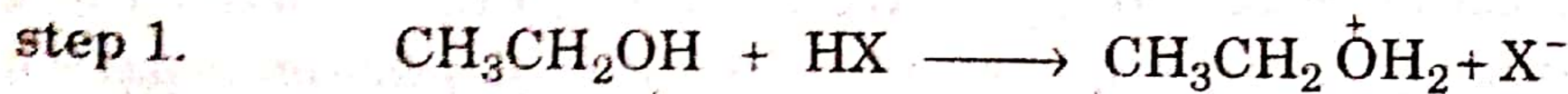The order of reactivity of halogen acid is HI > HBr > HCl.

3. From Alcohols. Alkyl halides are mostly prepared from alcohols, since alcohols are readily available. Alcohols react with halogen acids or with inorganic acid halides such as $SOCl_2$ (thionyl chloride), PCl_5, PBr_3 etc; to yield alkyl halides.

(i) Alkyl halides from the reaction of alcohols with halogen acids

$$ROH + HX \longrightarrow RX + H_2O$$

The reactivity of the halogen acids decreases in the order HI > HBr > HCl and the order of reactivity of alcohols is tertiary > secondary > primary.
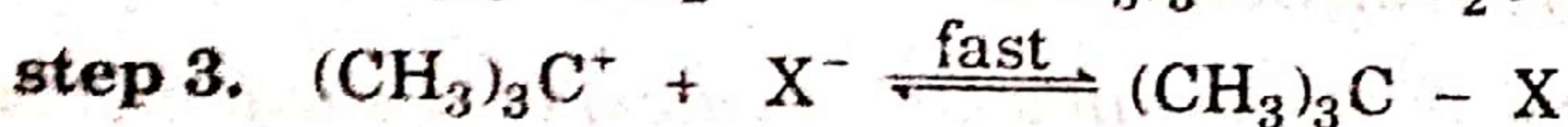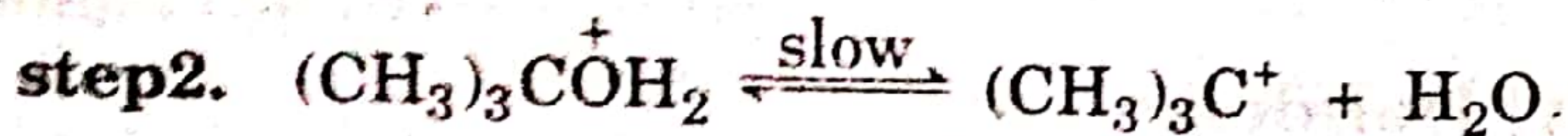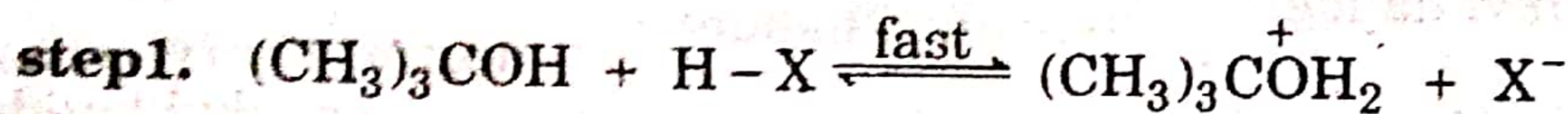
Mechanism. The alcohol accept a proton from the halogen acid and then the protonated alcohol dissociated to form a carbocation and water.

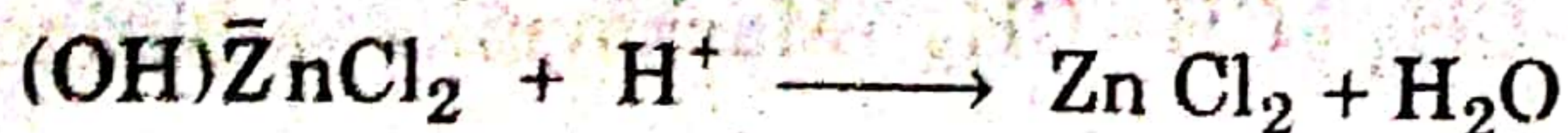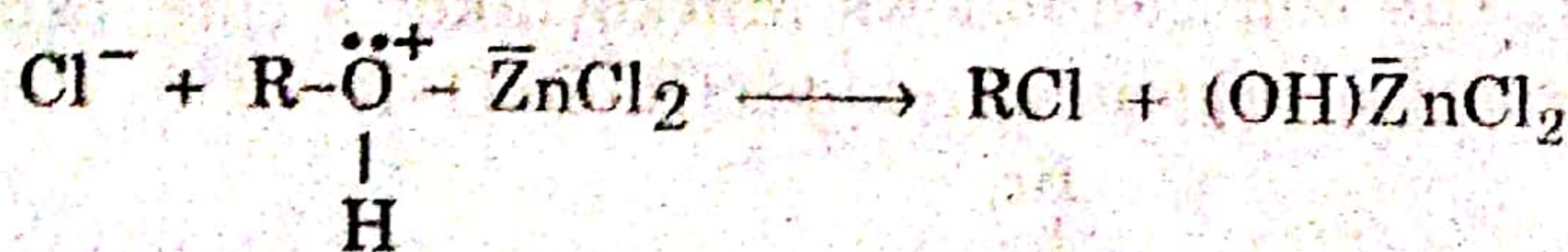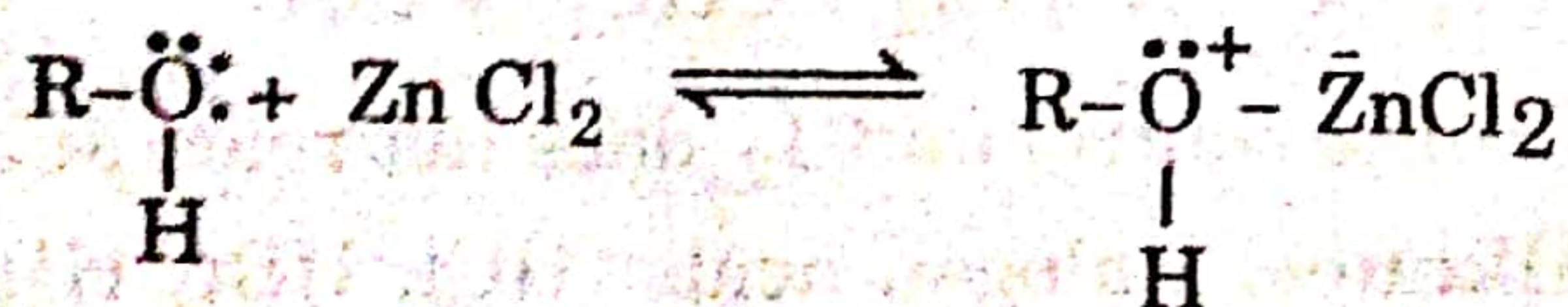step 1. $CH_3CH_2OH + HX \longrightarrow CH_3CH_2\overset{+}{O}H_2 + X^-$

step 2. $CH_3CH_2\overset{+}{O}H_2 \longrightarrow CH_3\overset{+}{C}H_2 + H_2O$

In step 3, the carbocation reacts with a nucleophile (as halide ion) to form an alkyl halide.

$$CH_3\overset{+}{C}H_2 + X^- \longrightarrow CH_3CH_2X$$

Primary alcohols react with hydrogen halides by S_N2 mechanism, and tertiary alcohols by S_N1 mechanism.

step1. $(CH_3)_3COH + H-X \underset{\longleftarrow}{\overset{fast}{\longrightarrow}} (CH_3)_3C\overset{+}{O}H_2 + X^-$

step2. $(CH_3)_3C\overset{+}{O}H_2 \underset{\longleftarrow}{\overset{slow}{\longrightarrow}} (CH_3)_3C^+ + H_2O$

step 3. $(CH_3)_3C^+ + X^- \underset{\longleftarrow}{\overset{fast}{\longrightarrow}} (CH_3)_3C - X$

The reaction depends on the nature of the alcohol and halogen acid. Hydrochloric acid, the least reactive of the halogen acids, does not react with primary alcohols unless $ZnCl_2$ or similar lewis acid is added to the reaction mixture as well. $ZnCl_2$, a good lewis acid forms a complex with the alcohol, which provides a better leaving group than $-\overset{+}{O}H_2$. A concentrated solution of zinc chloride in hydrochloric acid is often used for the preparation of primary or secondary alkyl halides from alcohols.

$$R-\overset{\cdot\cdot}{\underset{H}{O}} + ZnCl_2 \rightleftharpoons R-\overset{\cdot\cdot+}{\underset{H}{O}}-\bar{Z}nCl_2$$

$$Cl^- + R-\overset{\cdot\cdot+}{\underset{H}{O}}-\bar{Z}nCl_2 \longrightarrow RCl + (OH)\bar{Z}nCl_2$$

$$(OH)\bar{Z}nCl_2 + H^+ \longrightarrow ZnCl_2 + H_2O$$

The tertiary alcohols react with HCl readily even in the absence of $ZnCl_2$ because of relative stability of the tertiary carbonium ions.

Alkyl bromides are prepared by heating alcohols with constant boiling hydrogen bromide in presence of little conc. H_2SO_4. It is convenient to generate the HBr in *situ* by the reaction of KBr with conc. H_2SO_4. Sulphuric acid, however, is not

used in the preparation of secondary and tertiary bromides because in its presence they are dehydrated to form alkenes.

$$KBr + H_2SO_4 \longrightarrow KHSO_4 + HBr$$

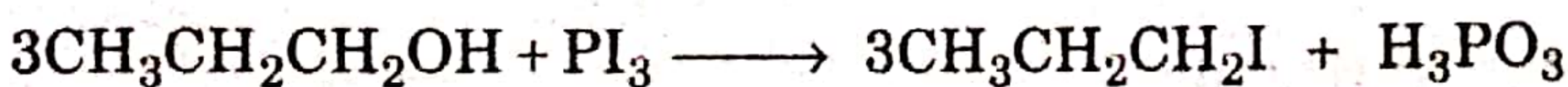$$ROH + HBr \longrightarrow RBr + H_2O$$

Alkyl iodides may be prepared by heating the alcohol with concentrated hydroiodic acid, but the yield of alkyl halide is very low due to its reduction to alkane by HI.

$$CH_3CH_2OH + HI \longrightarrow CH_3CH_2I + H_2O$$

$$CH_3CH_2I + HI \longrightarrow CH_3-CH_3 + I_2$$

This difficulty is overcome by heating alcohols with sodium or potassium iodide in 95% phosphoric acid.
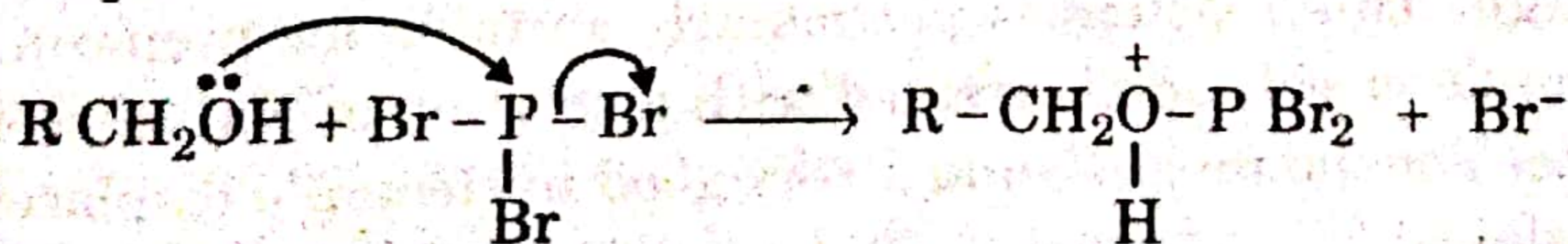
$$3ROH + 3KI + H_3PO_4 \longrightarrow 3RI + K_3PO_4 + 3H_2O$$

(ii) Alkyl halides from the reactions of alcohols with phosphorus halides (or $P + X_2$) or thionyl chloride. Primary and secondary alcohols react with PBr_3 or PI_3 to give alkyl halides.

$$3CH_3CH_2OH + PBr_3 \longrightarrow 3CH_3CH_2Br + H_3PO_3$$

$$3CH_3CH_2CH_2OH + PI_3 \longrightarrow 3CH_3CH_2CH_2I + H_3PO_3$$

PBr_3 or PI_3 are produced in *situ* by the addition of Br_2 and I_2 to red phosphorus. The reaction of an alcohol with PX_3 or $SOCl_2$ does not involve the formation of carbocation, hence occurs without the rearrangement of the carbon skeleton and elimination. For this reason PX_3 or $SOCl_2$ is preferred as a reagent for the conversion of an alcohol to the corresponding alkyl halide.

Mechanism. The reaction involves the initial formation of a protonated alkyl dibromophosphite by a nucleophilic displacement on phosphorus: the alcohol acts as the nucleophile.
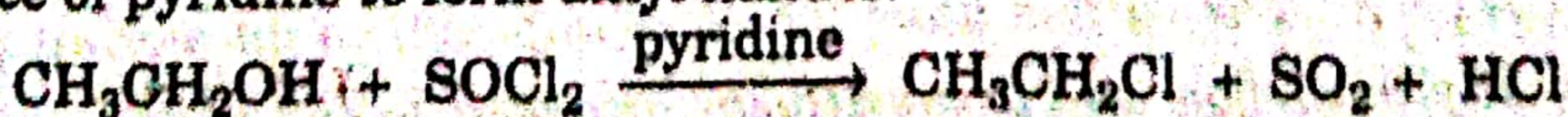
$$R\,CH_2\ddot{O}H + Br-P-Br \longrightarrow R-CH_2\overset{+}{O}-P\,Br_2 + Br^-$$
$$\qquad\qquad\qquad\;\; |\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\; Br\qquad\qquad\qquad\; H$$

Then a bromide ion acts as a nucleophile and displaces $HOPBr_2$.

$$Br^- + R\,CH_2\overset{+}{\underset{|}{O}}-P\,Br_2 \longrightarrow R\,CH_2\,Br + HO\,P\,Br_2$$
$$\qquad\qquad\qquad H$$
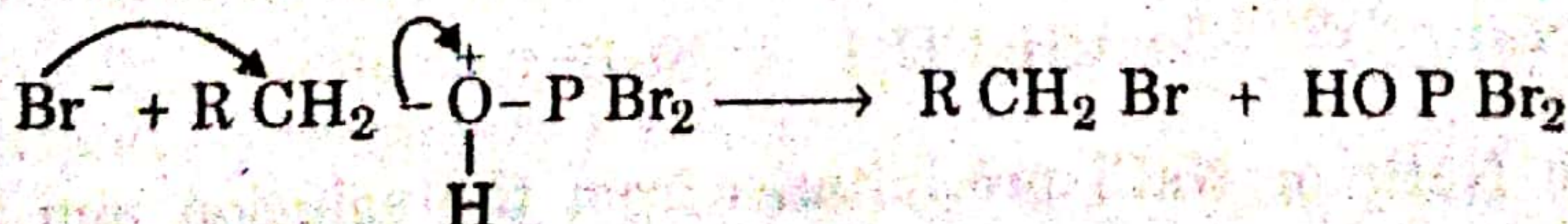
The $HOPBr_2$ can react with more alcohol so that the net result is the conversion of three moles of alcohols to alkyl bromide by 1 mole of PBr_3.

Primary and secondary alcohols react with thionyl chloride in the presence of pyridine to form alkyl halides.

$$CH_3CH_2OH + SOCl_2 \xrightarrow{\text{pyridine}} CH_3CH_2Cl + SO_2 + HCl$$

Mechanism:

$$RCH_2OH + \underset{\underset{Cl}{|}}{SOCl} \longrightarrow RCH_2 - \underset{\underset{H}{|}}{\overset{+}{O}} - SOCl + Cl$$

$$Cl^- + RCH_2\underset{\underset{H}{|}}{\overset{+}{O}} - SOCl \longrightarrow RCH_2Cl + \underset{\underset{H}{|}}{(O\ SOCl)} \longrightarrow SO_2 + HCl$$
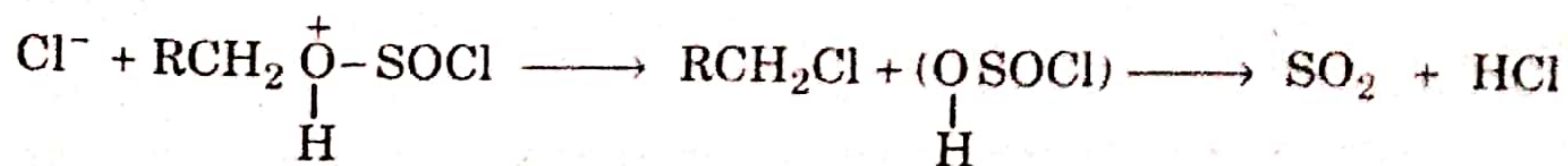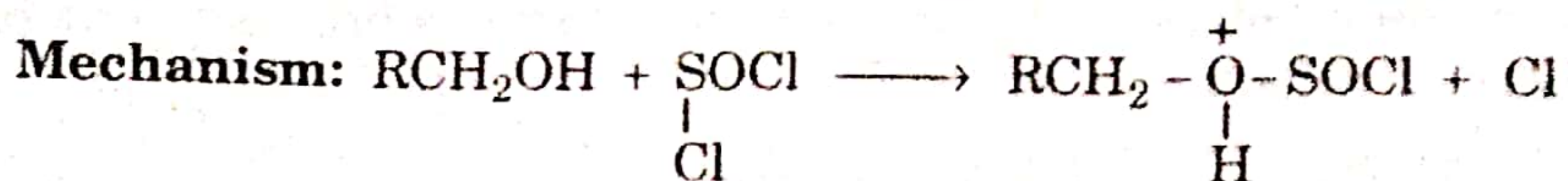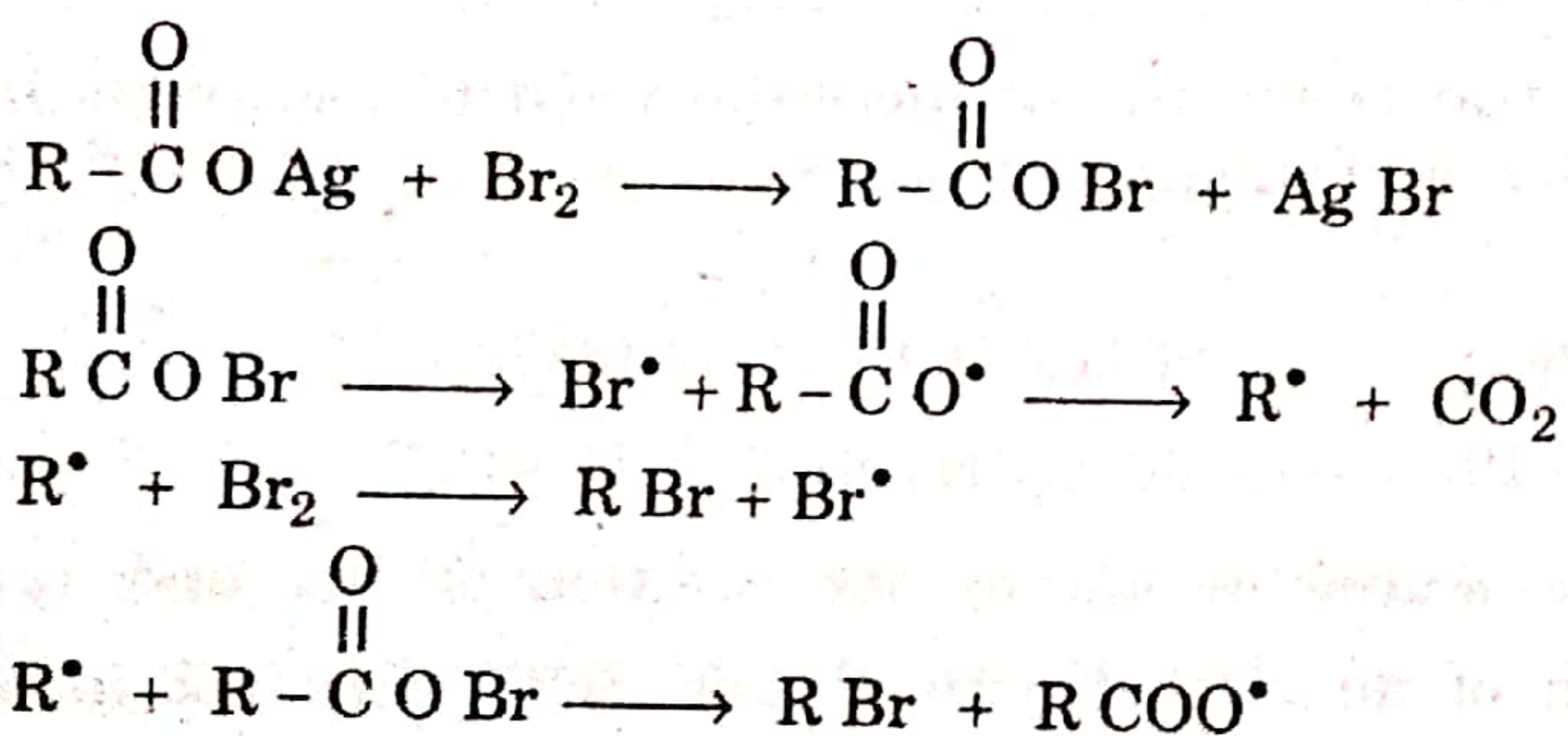
4. From carboxylic acids i.e., from silver salt of a carboxylic acid (Hunsdiecker reaction): Dry silver salts of a carboxylic acid upon refluxing with Br_2 in CCl_4 gives the corresponding alkyl chloride with the liberation of CO_2

$$RCOOAg + Br_2 \xrightarrow{CCl_4} RBr + CO_2 + AgBr$$
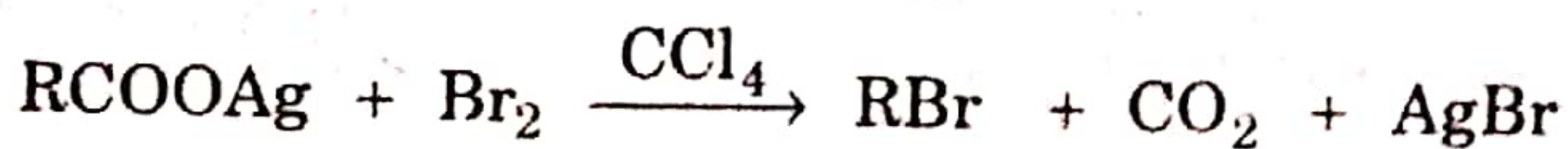
Mechanism: The reaction involves the initial formatiuon of an acyl hypohalide that decomposes into free-radicals which then lead to the products as shown below:

$$\underset{R-\overset{\overset{\displaystyle O}{\|}}{C}\,O\,Ag}{} + Br_2 \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}\,O\,Br + Ag\,Br$$

$$R\,\overset{\overset{\displaystyle O}{\|}}{C}\,O\,Br \longrightarrow Br^\bullet + R-\overset{\overset{\displaystyle O}{\|}}{C}\,O^\bullet \longrightarrow R^\bullet + CO_2$$

$$R^\bullet + Br_2 \longrightarrow R\,Br + Br^\bullet$$

$$R^\bullet + R-\overset{\overset{\displaystyle O}{\|}}{C}\,O\,Br \longrightarrow R\,Br + R\,COO^\bullet$$

Bromine gives good yield and is often used halogen, Cl_2 and iodine has also been used.

The synthetic utility of this method is limited, because only the primary alkyl halides are obtained in good yields where as the yields of secondary and tertiary alkyl bromides are quite low.
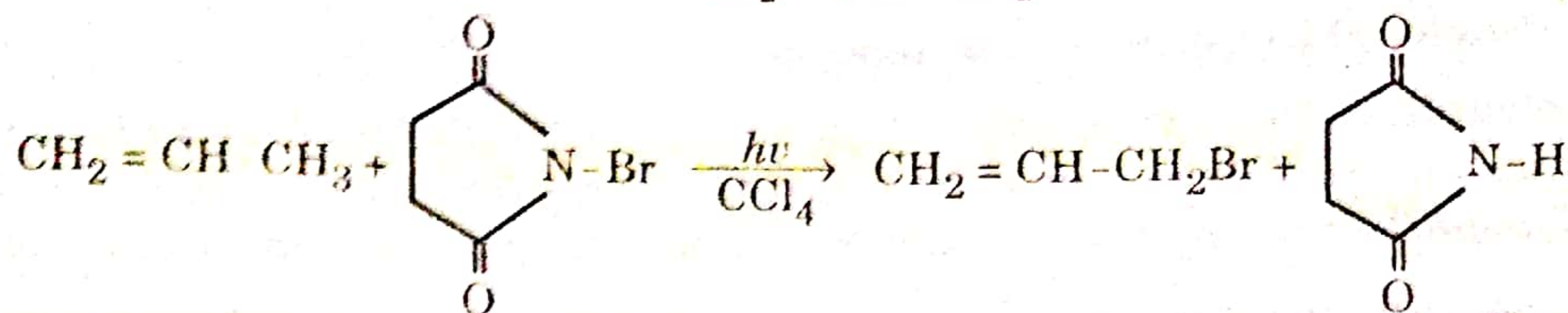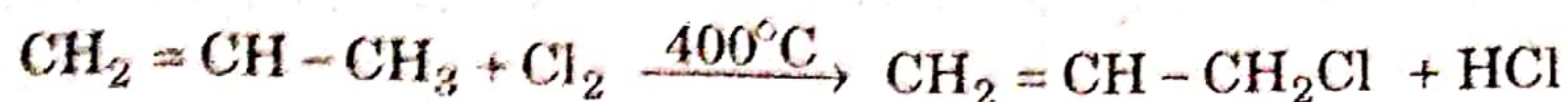
5. By halide exchange. This reaction is particularly suitable for preparing alkyl iodides. The alkyl bromide or chloride is treated with a solution of NaI in acetone to produce an alkyl iodide. The iodide ion being a very good nucleophile displaces other halogens from alkyl halides.

$$CH_3CH_2Br + NaI \xrightarrow{Acetone} CH_3CH_2I + NaBr$$
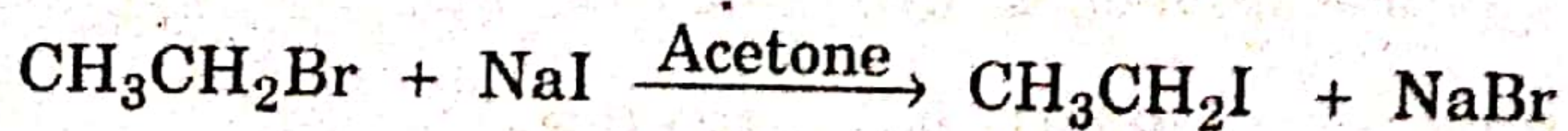
The less soluble NaBr or NaCl precipitates from the solution and can be removed by filtration.

6. Allylic Halogenation. *The halides in which the halogen atom is attached to a carbon atom which is adjacent to an olefinic double bond are called allylic halides, e.g., $CH_2 = CH - CH_2 - X$. The carbon atom which is adjacent to an olefinic double bond is called the allylic carbon and a substituent attached to the allylic carbon is*

called an allylic substituent. Allylic halides (chlorides and bromides) can be prepared by treating alkenes with chlorine or bromine at high temperatures or with N-bromosuccinimide (NBS) in CCl_4.

$$CH_2 = CH - CH_3 + Cl_2 \xrightarrow{400°C} CH_2 = CH - CH_2Cl + HCl$$

$$CH_2 = CH \ CH_3 + \begin{array}{c} O \\ \parallel \\ \\ N-Br \\ \\ \parallel \\ O \end{array} \xrightarrow[CCl_4]{hv} CH_2 = CH - CH_2Br + \begin{array}{c} O \\ \parallel \\ \\ N-H \\ \\ \parallel \\ O \end{array}$$

Benzylic halides can be prepared in a similar way.

$$\bigcirc\!\!\!-CH_3 + X_2 \xrightarrow{hv} \bigcirc\!\!\!-CH_2X \quad (X = Cl \ or. \ Br)$$
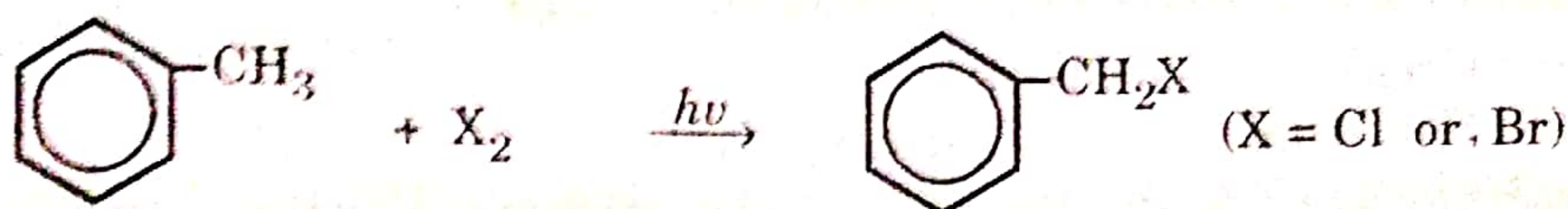
7. Chloromethylation.
*A hydrogen atom of a certain aromatic ring can be replaced by the chloromethyl group – CH_2Cl. The reaction is called **chloromethylation**.* When benzene is treated with formaldehyde and HCl in the presence of a catalyst such as $SnCl_2$, H_2SO_4 or H_3PO_4, benzyl chloride is formed.

$$\bigcirc + HCHO + HCl \xrightarrow[60°C]{ZnCl_2} \bigcirc\!\!\!-CH_2Cl$$
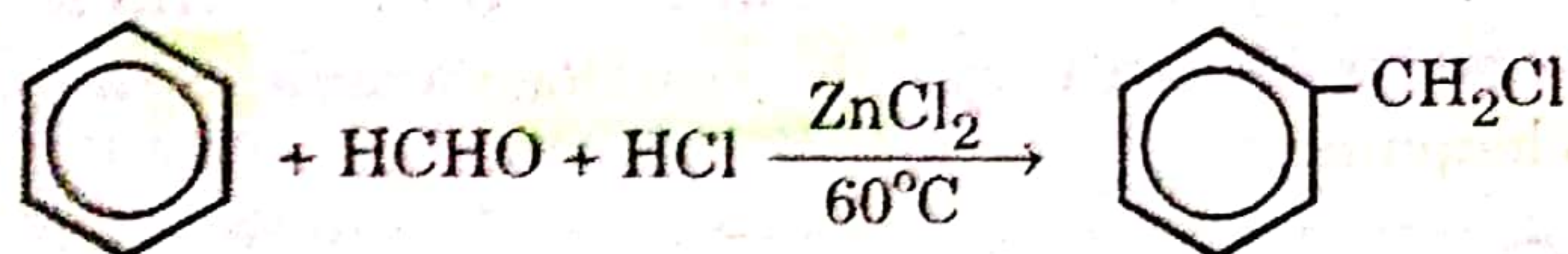
8.2 Physical properties of Alkyl Halides

1. CH_3Cl, CH_3Br and CH_3CH_2Cl are gases at room temperature, whereas other alkyl halides up to C_{18} are colourless liquids and above C_{18} are colourless solids.

2. Alkyl halides are usually insoluble in water but soluble in organic solvents. They are miscible with each other. CH_2Cl_2, $CHCl_3$ and CCl_4 are often used as solvents for nonpolar and moderately polar organic compounds.

3. The boiling and melting points of alkyl halides are higher than those of alkanes with the same number of carbon atoms. This is because of their higher molecular masses which result in greater van der Waals attractions. In a series of alkyl halides having the same alkyl group, the boiling and melting points increase with the increase in atomic mass of halogen. Further, in a group of isomeric alkyl halides, the order of boiling point is: primary > secondary > tertiary.

4. Alkyl halides are more dense than hydrocarbons, the order being hydrocarbons < alkyl chlorides < bromides < iodies, if compounds with the same number of carbon atoms are compared.

5. Many chlorohydrocarbons including $CHCl_3$ and CCl_4 have a coinulative toxicity, therefor, they should be used in fume hoods and with great care.

8.3 Reactions of Alkyl Halides

Alkyl halides are extremely useful compounds because they undergo a wide variety of organic reactions leading to the synthesis of a large number of organic compounds. Some of the important reactions of alkyl halides are described below.

8.4 Nucleophilic substituion Reactions

Nucleophile. "*A negative ion or a molecule with an unshared electron pair which can donate an electron pair to an electron-deficient centre in a reaction is called a* **nucleophilic reagent** or simply a nucleophile (means "nucleus loving"). For example, $Cl^-, Br^-, OH^-, CN^-, \overset{..}{N}H_3, H_2\overset{..}{O}:$ etc. *A species that accepts an electron-pair in a reaction is called an electrophile, i.e., (electron loving).*

$$OH^- + CH_3Br \longrightarrow CH_3OH + Br^-$$

Nuclcophile   Substrate   leaving group
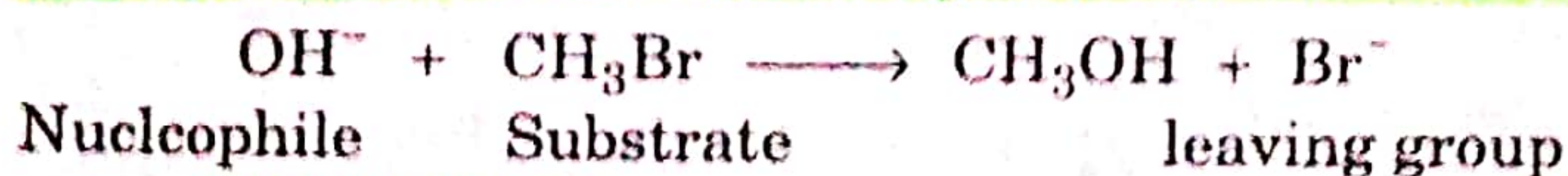
The molecule like CH_3Br that is attacked by a reagent is called a substrate, and the part of the substrate that departs along with the electron pair, like bromide, is called the **leaving group** (or **nucleofuge**),

A reaction in which one nucleophile ($N\overset{..}{u}:$) displaces another nucleophile (X^-) from combination with an electrophilic carbon atom is called a **nucleophilic substitution reaction** and is denoted by SN reaction where S stands for substitution and N for nucleuphilic.

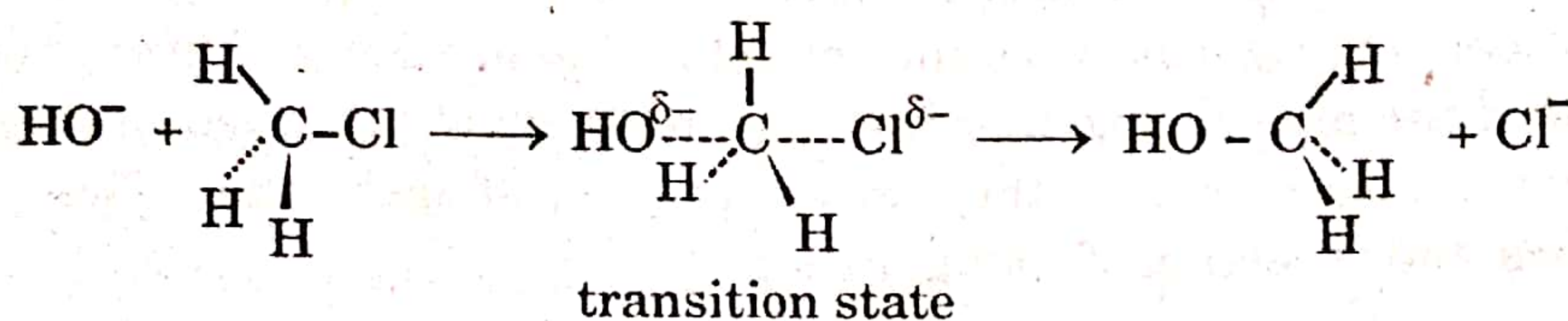$$Nu:^- + R-CH_2-X \longrightarrow R-CH_2-Nu + X:^-$$

The C – X bond in alkyl halides is polar because of the high electronegativity of the halogen atom relative to carbon. Thus the carbon atom attached to halogen carries a partial positive charge and is therefore, electrophilic in nature. It has a tendency to accept an electron pair from a nucleophilic reagent to form a new bond. In doing so the electrophilic carbon breaks its old bond with the halogen atom. The net result of this reaction is that one nucleophile ($Nu:^-$) displaces an other nucleophile (X^-) from combination with an electrophilic carbon atom. Such displacement reactions are called **nucleophilic substitution reactions**.

The reagent $Nu:^-$ is called the **attacking nucleophile**, $R-CH_2-X$ which contains the electrophilic carbon atom is called the **substrate** and X^- (the **halide** ion) is called the **leaving nucleophile.**

Mechanism

The **mechanism** of a reaction is the actual process by which a reaction takes place, i.e., which bonds are broken, which are formed, and in what order, how many steps are involved and what is the relative rate of each step, etc. Alkyl halides can undergo nucleophilic substitution by two mechansims: $S_N 1$ and $S_N 2$ mechanism.

S_N2 Mechanism. S_N2 stands for bimolecular nucleophilic substitution. In this mechanism the nucleophile attacks the substrate from the back side i.e. from the side directly opposite the leaving group. As the reaction progresses the bond between the nucleophile and the electrophilic carbon atom grows and the bond between the carbon atom and the leaving group weakens. In the transition state both the nucleophile and the leaving group are partially bonded to the carbon undergoing attack. The hybridization of this carbon atom changes from sp^3 in the substrate to sp^2 in the transition state and again to sp^3 in the product. Thus the carbon atom and three non-reacting groups are approximately coplanar in the transition state, with the unhybridized p orbital perpendicular to the plane and having one lobe on either side of the plane; one lobe of the p orbital overlaps with the nucleophile and the other with the leaving group.
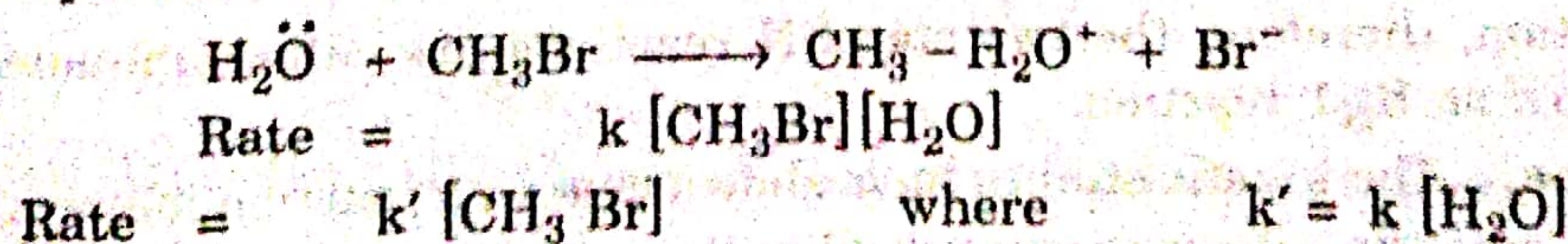
$$HO^- + \underset{H}{\overset{H}{C}}{-}Cl \longrightarrow HO^{\delta-}{\cdots}\underset{H}{\overset{H}{C}}{\cdots}Cl^{\delta-} \longrightarrow HO-\underset{H}{\overset{H}{C}}{\overset{H}{} + Cl^-}$$

transition state

Since two molecules, i.e., the nucleophile (e.g., OH^- ion) and the substrate (e.g., a molecule of CH_3Cl) are involved in the formation of transition state in the rate determining step (the only step of the reaction), thus the reaction is said to be **bimolecular.**

Kinetic Evidence. The S_N2 mechanism involves only one step and this is the rate determining step. In this step both the substrate and attacking nucleophile are involved. The reaction rate is, therefore, directly proportional to the concentration of the substrate and to the concentration of the attacking nucleophile and follows the second order kinetics. According to the rate expression:

Rate $\propto$ $[CH_3Cl]\,[OH^-]$

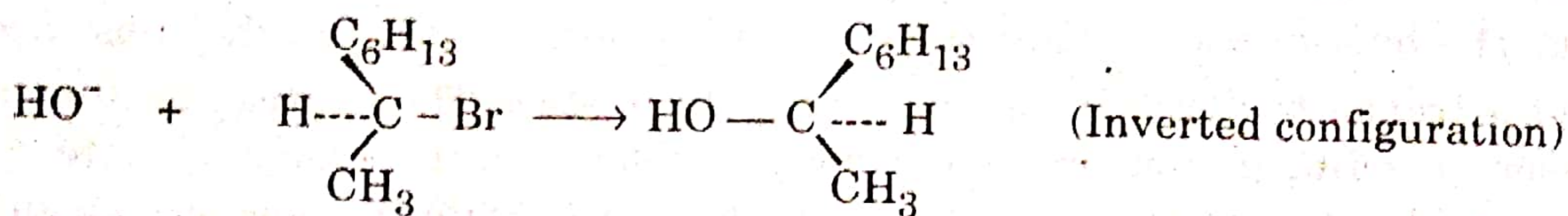Rate $=$ $k\,[CH_3Cl]\,[OH^-]$

Where k is the specific rate constant and brackets denote the concentrations of the species enclosed within them. Concentrations are usually expressed in $mol\,dm^{-3}$.

However, if the solvent itself acts as a nucleophile, the mechanism may still be bimolecular but the experimentally determined kinetic will be first order. This is because the concentration of the solvent remains constant due to its large quantities and the rate will depend only on the concentration of the substrate. Such a reaction is called pseudo-first order. For example

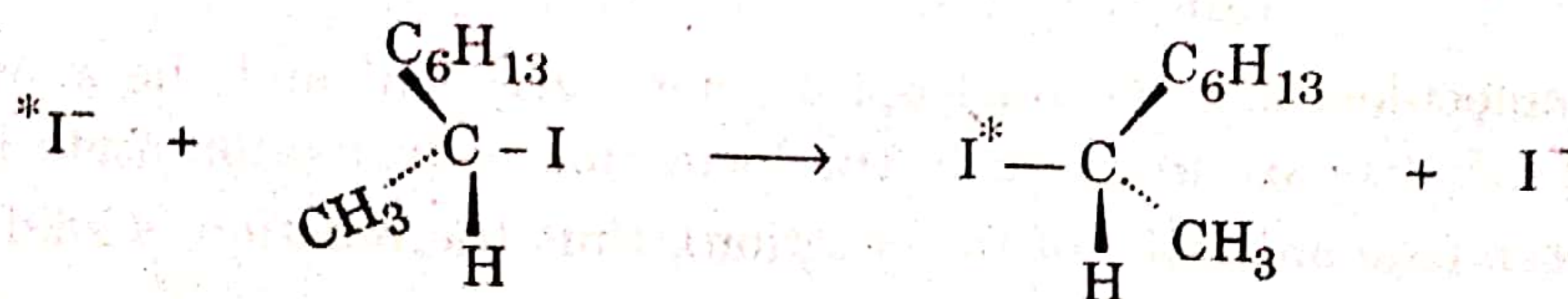$$H_2\ddot{O} + CH_3Br \longrightarrow CH_3-H_2O^+ + Br^-$$

Rate $=$ $k\,[CH_3Br][H_2O]$

Rate $=$ $k'\,[CH_3Br]$ where $k' = k\,[H_2O]$

Stereochemical evidence. Much more convincing evidence for S_N2 mechanism

comes from the Stereochemical study of the reaction. The S_N2 mechanism predicts inversion of configuration when substitution occurs at a chiral carbon. This **inversion of configuration** is called the **Walden inversion.** Since the nucleophile attacks the substrate from the backside, inversion of configuration should take place. This has been actually observed that the hydrolysis of optically active 2-bromooctane with NaOH gives active 2-octanol with inverted configuration.

$$HO^- \quad + \quad \overset{\overset{\displaystyle C_6H_{13}}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{H\text{----}C}} - Br \quad \longrightarrow \quad HO - \overset{\overset{\displaystyle C_6H_{13}}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}\text{----}H \qquad \text{(Inverted configuration)}$$
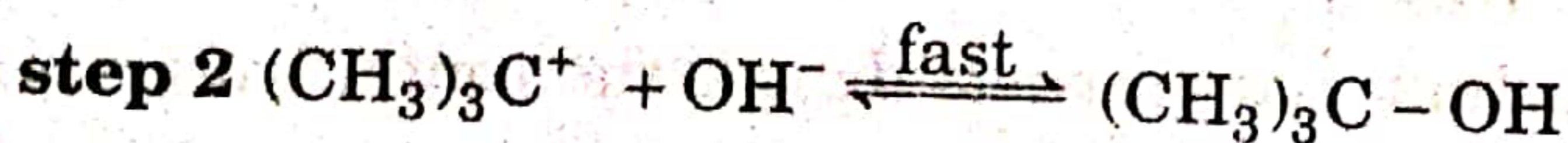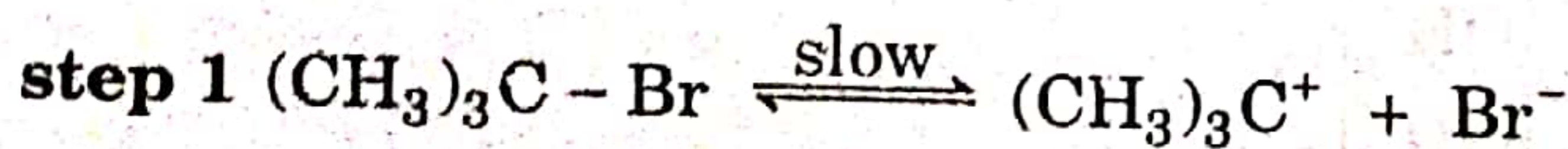
When optically active 2-iodooctane is treated with NaI having radioactive iodine in acetone. The iodine exchange was accompanied by loss of optical activity and the rate of loss of optical activity was twice the rate of iodine exchange. This is because that one molecule of the product together with one molecule of the starting substrate will form a racemic mixture because they are enantiomer of each other. This proves the backside attack and inversion of configuration.

$$^*I^- \quad + \quad \overset{\overset{\displaystyle C_6H_{13}}{\diagup}}{\underset{\underset{\displaystyle H}{|}}{\underset{CH_3}{\diagdown}C - I}} \quad \longrightarrow \quad I^* - \overset{\overset{\displaystyle C_6H_{13}}{\diagup}}{\underset{\underset{\displaystyle H}{|}}{C\underset{CH_3}{\diagdown}}} \quad + \quad I^-$$

The S_N1 Mechanism

The S_N1 (substitution nucleophilic unimolecular) mechanism consists of two steps. In the first step, the substrate ionizes reversibly to form a carbonium ion and a halide ion. In the second step, the intermediate carbonium ion rapidly combines with the attacking nucleophile to form the product.

step 1 $(CH_3)_3C - Br \xrightleftharpoons{\text{slow}} (CH_3)_3C^+ + Br^-$

step 2 $(CH_3)_3C^+ + OH^- \xrightleftharpoons{\text{fast}} (CH_3)_3C - OH$

In a reaction involving more than one step the slowest step determines the rate of the reaction, and is therefore called the **rate-determining step.** In the S_N1 reaction, the first step, i.e., the ionization of the substrate, is usually very slow as compared to the second step, so the first step is the rate determining step. Since in the rate determining step only one molecule $((CH_3)_3C - Br$ i.e., substrate) takes part in the reaction, therefore, the two step SN reactions are called unimolecular and are symbolized as S_N1 reaction.

Kinetic evidence. The kinetic studies have shown that in a reaction following the S_N1 mechanism, only the substrate is involved in the rate determining step, and the reaction is called a **unimolecular reaction.** The rate of a reaction, therefore,

depends only on the concentration of the substrate, but is independent on the concentration of the attacking nucleophile and S_N1 reaction should be a **first order** with the following rate law:
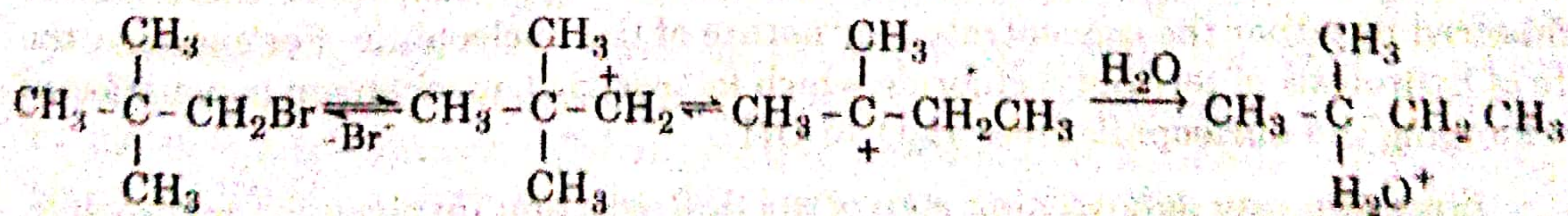
Rate $=$ k [substrate]

Rate $=$ k [$(CH_3)_3C-Br$]

Solvents play a very important role in S_N1 reactions, since the ionization is always assisted by the solvent, it does not enter the rate expression, since it is present in large excess. Mostly the solvent itself acts as a nucleophile and the reaction is generlly called **solvolysis**.

Stereochemical evidence. Another strong evidence in favour of S_N1 mechanism comes form the Stereochemical studies. The mechanism involves the formation of carbonium ion as an intermediate Since the trivalent carbon atom of the carbonium ion is sp² hybridized, it is a planar molecule. The unhybridized p orbital on carbon is perpendicular to the plane of the sp² orbitals with one lobe on each side of the plane. The nucleophile can therefore attack from either side of the plane with equal facility to form a bond with the carbonium ion. If we take optically active substrate, we are expected to get a racemic mixture of the product. SN reactions is generally expected to be accompanied by racemization if it proceeds by S_N1 mechanism

Racemate (optically active)
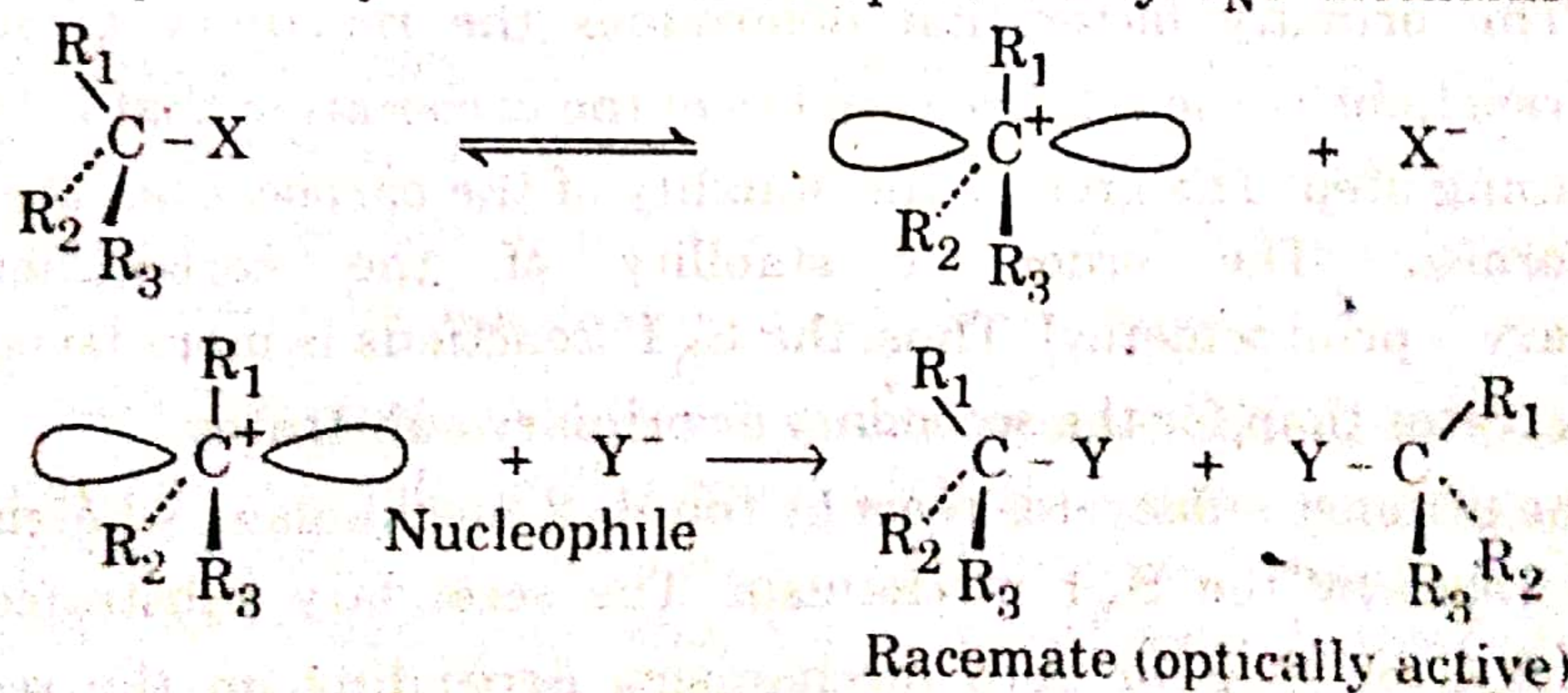
The formation of a carbonium ion as an intermediate is also supported by the fact that it can undergo rearrangement to a more stable carbonium ion before it combines with the nucleophile.

8.5 Factors Affecting the Rates of S_N1 and S_N2 Reactions

A number of factors affect the relative rates of S_N1 and S_N2 reactions. The most important factors are:

1. The effect of the structure of the substrate.
2. The effect of attacking nucleophile (for S_N2 reactions only).
3. The effect of the solvent.
4. The effect of leaving group

1. The effect of the structure of the substrate. In S_N2 reactions the order of reactivity of various alkyl halides is methyl > primary > secondary > tertiary. The important factor behind this order of reactivity is **a steric effect** (i.e. steric hindrance). As the hydrogen atoms of the methyl halides are replaced by other bulky groups, the nucleophile finds it more and more difficult to push in among the carbon bulky substituents in order to reach the transition state. Moreover, if the substituents are bulky the transition state will be heavily crowded and the nonbonding interactions between various substituents would raise its energy. Also, the approach of a nucleophile from the backside to a tertiary carbon atom is sterically more hindered than to a primary carbon. Thus, the S_N2 reactions are more favourable for the primary substrates and less favourable for tertiary substrates. Tertiary halides seldom react by the S_N2 mechanism; even the neopentyl halides which are primary halides, are very unreactive, in S_N2 reactions because of the steric crowding in the transition state by the methyl groups of the β – carbon.

S_N1 reactions. The primary factor that determines the reactivity of organic substrates in S_N1 reactions is the relative stability of the carbocation that is formed in the rate determining step. The greater the stability of the carbocation, the more rapidly it is formed. The order of stability of the carbocation is: tertiary > > secondary > prim > methyl. Thus, the S_N1 reactions is more favourable for the tertiary substrates than for the secondary or primary substrates.

Generally, the primary substrates react by the S_N2 mechanism, whereas the tertiary substrates react by the S_N1 mechanism. The secondary substrates may proceed either by S_N1 or S_N2 or both mechanisms depending on the reaction conditions, mostly they follow S_N2 mechanism.

2. The effect of the nucleophile. Since the nucleophile is not involved in the rate determining step of S_N1 reaction, the rate of the S_N1 reaction is therefore not influenced by either the concentration or nature of the nucleophile. For example, the rate of hydrolysis of tert-butyl chloride which follows S_N1 mechanism is not affected by changing the nucleophile from H_2O to OH^-.

Since the rate determining step of an S_N2 reaction involves the nucleophile, the rates of S_N2 reactions depend on the concentration as well as the nature of the nucleophile. The rate of S_N2 reaction is directly proportional to the concentration of the attacking nucleophile. When one doubles the concentration of attacking

nucleophile, the rate of reaction doubles.

The rate of S_N2 reaction depends upon the reactivity of the nucleophile which is called **nucleophilicity.** The nucleophilicity of a nucleophile (i.e., reagent) may be defined as its ability to donate an electron pair to carbon. Thus all the nucleophiles should be basic in nature. However, their nucleophilicity does not always parallel their basicity. The relative strengths of nucleophiles can be correlated with structural features.

1.   A negatively charged nucleophile is always a stronger nucleophile than its conjugated acid. Thus OH^- is a stronger nucleophile than H_2O.

2.   In a group of nucleophiles in which the nucleophilic atom is the same, nucleophilicities parallel basicities. For example, the order of nucleophilicity of $RO^- > HO^- \gg RCOO^- > ROH > H_2O$.

3.   In comparing nucleophiles whose attacking atom is in the same row of periodic table, nucleophilicities is roughly in the order of basicity. So an approximate order of nucleophilicity is $NH_2^- > RO^- > OH^- > R_2 NH > NH_3 > F^- > H_2O > ClO_4^-$ and another is $R_3 C^- > R_2 N^- > RO^- > F^-$.

However, in a series of nucleophiles belonging to the same family in the periodic table, the nucleophilicity increases with increase in atomic number, though the basicity decreases. Thus the order of halide nucleophilicity is $I^- > Br^- > Cl^- > F^-$ which is opposite to the order of their basicity. Similarly, RS^- is a better nucleophile than RO^-, though RO^- is a better base than RS^-. This is because that larger atoms are more polarizable and hence better nucleophiles.

Steric factors in the attacking nucleophile also affect the rate of S_N2 reaction. For example, methoxide ion (O^-CH_3) can easily approach the carbon atom during SN reaction, tert-butoxide ion, being very bulky, is sterically hindered to approach the carbon atom. Thus the ability of tert - butoxide ion is greatly reduced to act as a nucleophile, although its basicity is similar to that of methoxide ion.

3. The Effect of the Solvent. Solvents play an important role in determining the rate and mechanism of nucleophilic substitution reactions. The solvent effects can be anticipated by considering whether ions are formed or destroyed, or neither, in the rate determining step of the reaction. **Good ionizig (polar) solvents** are those in which ions are stabilized by solvation. The polarity of a solvent, is usually measured by its dielectric constant. The **dielectric constant** is a measure of the solvent's ability to insulate opposite charges from each other. The greater the dielectric constant, the higher is the polarity of the solvent. The greater the polarity of a solvent, the greater is its ability to stabilize a charged species. Reactions which produce ions from neutral species are accelerated by polar solvent. Thus S_N1 reactions in which carbocations are formed in the rate determining step. are

accelerated by polar solvents. For example, the rate of hydrolysis of tert-butyl bromide increases more than 100 times when solvent is changed from ethanol to water because water is more polar than ethanol.

For S_N2 reactions, the effect of the solvent depends on whether the initial charge is dispersed or decreased or increased in the rate controlling transition state. The reactions in which the initial charges are increased in the transition state, are favoured by increasing the polarity of the solvent, whereas the reactions in which the initial charges are either dispersed or decreased in the transition state, are favoured by decreasing the polarity of the solvent, (i.e., are favoured in nonpolar solvents).

Generally, the influence of a solvent is large when the charge is either increased or decreased, but the effects are small when there is a dispersal of charges.
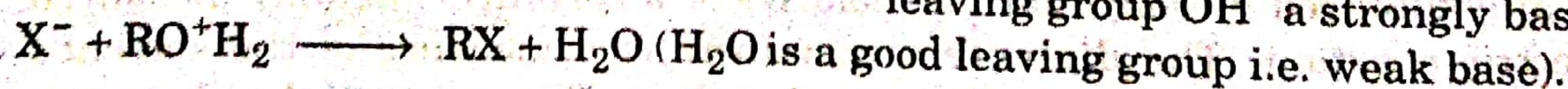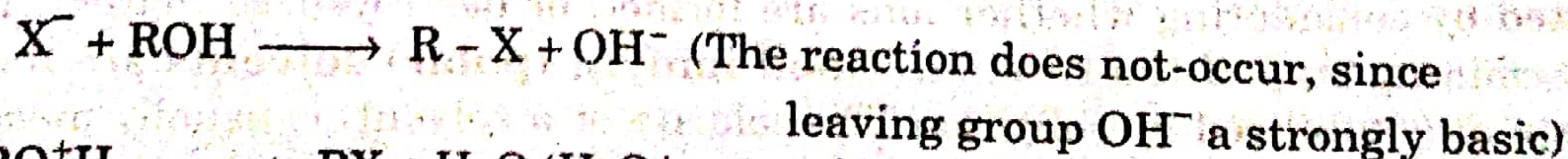
Aprotic solvent may also decrease the nucleophilicity of a nucleophile through solvation. However, the solvation is less in aprotic solvents like dimethyl sulphoxide (DMSO), dimethylacetamide (DMA), dimethylformamide (DMF) than in protic solvents like H_2O, C_2H_5OH which solvate the nucleophile through hydrogen bonding.

Aprotic solvents *are those solvents whose molecules do not have a hydrogen that is attached to a strongly electronegative element.*

4. The Effect of Leaving Group.

The best leaving groups are those that become the most stable molecules or ions after they depart. In general, the best leaving groups are the ions or molecules that are the weakest bases. The ability of a group to act as a leaving group is usually inverse of its basicity. Thus, among the halides, iodide is the best leaving group and a fluoride ion is the poorest.

Other weak bases that are good leaving groups are alkanesulphonate ions RSO_3^- and alkyl sulphate ions RSO_4^-.

Since in both S_N1 and S_N2 reactions, the leaving group comes off along with its bonding electron pair. So the groups that can better accommodate the electron pair (or negative charge) are better leaving groups. For example, phenoxide ion, PhO^- is a better leaving group than RO^- because the negative charge of. phenoxide ion is delocalized over to the ring, whereas delocalization is not possible in RO^-. However, a poor leaving group like RO^- (or HO^-) may be converted to a good leaving group by protonation, e.g., H_2O is a better leaving group than HO^- because H_2O is a weaker base than HO^-. Thus

$$X^- + ROH \longrightarrow R-X + OH^-$$ (The reaction does not-occur, since leaving group OH^- a strongly basic)

$$X^- + RO^+H_2 \longrightarrow RX + H_2O$$ (H_2O is a good leaving group i.e. weak base).

S_N1 reactions do not require powerful nucleophiles but do require good leaving groups, most of them take place under acidic (or neutral) conditions. The S_N2 reactions which do require powerful nucleophiles, mostly take place under basic (or neutral) conditi ns.

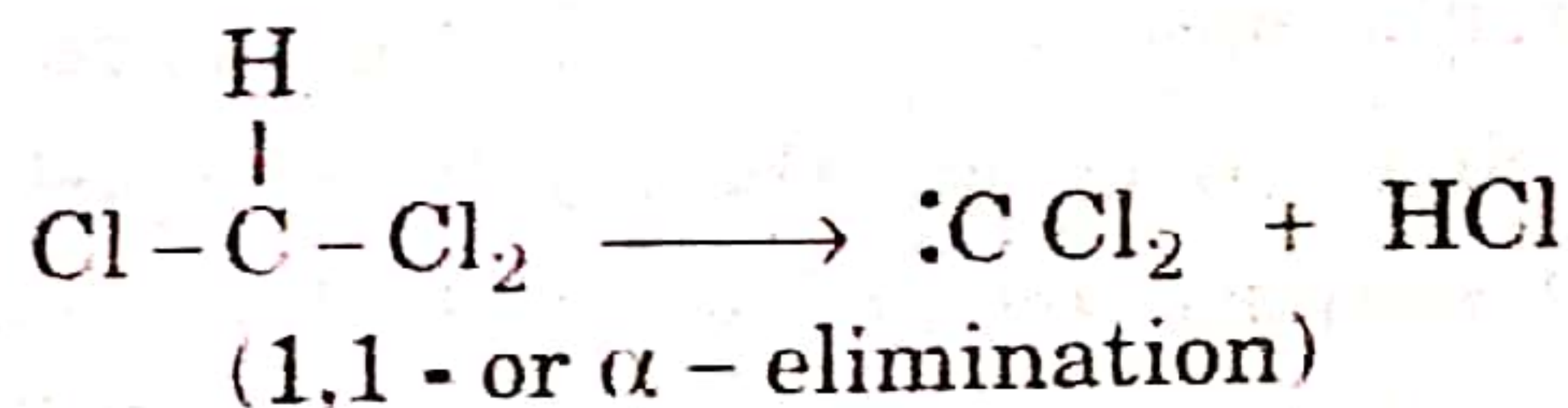## 8.6 Main Features that Differentiate between S_N1 and S_N2 Reactions

S_N1 Reaction	S_N2 Reaction
1. S_N1 stands for substitution nucleophilic unimolecular.	1. S_N2 stands for substitution nucleophilic bimolecular.
2. S_N1 is a two step mechanism.	2. S_N2 is one step mechanism.
3. In the two step S_N1 reaction, the substrate, R – X, first ionizes reversibly into R^+ and X^- and then the intermediate carbocation combines with the attacking nucleophile, Nu^- to form the product. $$R - X \xrightleftharpoons{slow} R^+ + X^-$$ $$R^+ + Nu^- \xrightarrow{fast} R - Nu$$	3. The attack of nucleophile on carbon and deparature of halide ion takes place simultaneously in a single step. $$Nu^- + R - X \longrightarrow R - Nu + X^-$$
4. Rate depends only on the concentration of the substrate. $$Rate = k~[R - X]$$	4. Rate depends on the concentration of substrate as well as on the concentration of attacking nucleophile. $$Rate = k~[R - X]~[Nu^-]$$
5. The nucleophile can attack the electrophilic carbon from either side (front or backside).	5. The nucleophile attacks the electrophilic carbon from the backside.
6.It is expected to first order kinetics.	6. It is expected to be second order kinetics. If however one of the reactants is the solvent, the S_N2 mechanism will lead to first order kinetics.
7. In S_N1 reaction, the product may be partially inverted with respect to that of starting substrate, largely inverted or inverted to a very small extent. The product is racemate usually.	7. S_N2 Reactions always proceed with complete inversion of configuration (backside attack).
8. Reaction is favoured by polar solvents.	8. Reaction is favoured by nonpolar solvents.
9.Reaction can occur with weak base.	9. Reaction requires strong bases.
10. S_N1 reactions are generally given by tert-alkyl halides; $3° > 2° > I° > CH_3$	10. S_N2 are generally given by primary alkyl halides. $CH_3 > 1 > 2° > 3°$

8.7 ELIMINATION REACTIONS

Reactions in which two atoms or groups are removed from two adjacent carbon atoms of the substrate molecule to form a multiple bond are call'd β-elimination reactions. In these reactions, one atom is removed from the α- and the other from the β-carbon atom, two σ bonds are lost and a new π bond is formed

$$HO^- + H - CH_2 - CH_2 - Br \longrightarrow CH_2 = CH_2 + H_2O + Br^-$$
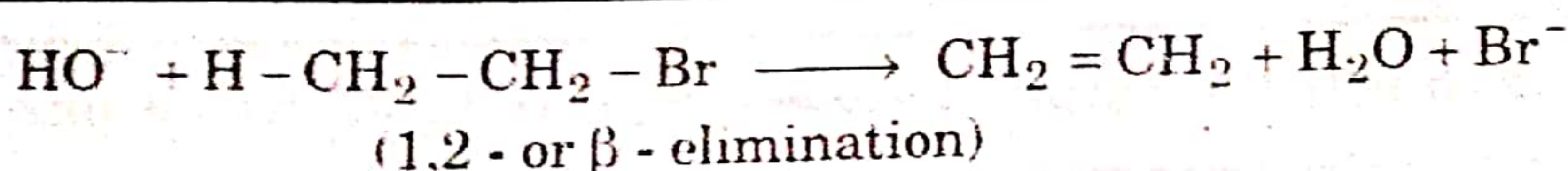
<center>(1.2 - or β - elimination)</center>

If two atoms or groups are removed from the same carbon atom of a molecule forming a highly reactive species known as **carbene,** the reaction is called 1, 1- or **α - elimination reaction.**

$$Cl - \overset{\overset{\displaystyle H}{|}}{C} - Cl_2 \longrightarrow :CCl_2 + HCl$$

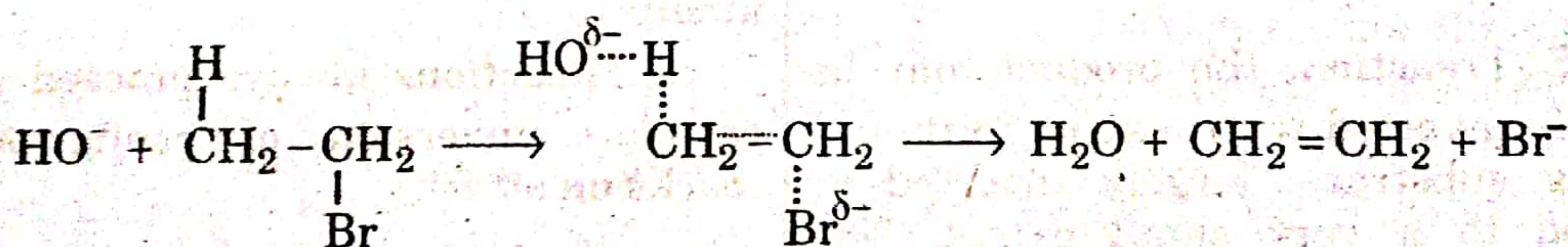<center>(1,1 - or α – elimination)</center>

We shall describe β-elimination which is more important and is mechanistically closely related to nucleophilic substitution.

Mechanism

In the β - eliminations one group leaves with its electron pair and is referred to as the **leaving group** (or nucleofuge) and the other group leaves without electrons, mostly hydrogen. Elimination reactions occur by a variety of mechansims. With alkyl halides, two mechanisms E2 and El that are closely related to the S_N2 and S_N1 are especially important:

The E 2 mechanism. In the E2 (elimination bimolecular) mechanism, pulling off the proton from the β-carbon atom by a base and the departure of the halide ion(the leaving group) from the α-carbon occurs simultaneously. Thus the E2 reaction is a one step process in which both the substrate and the base are involved in the formation of transition state. In the transition state partial bond exist between the hydroxide ion and the β-hydrogen, between the β-hydrogen and β-carbon and between the α-carbon and the bromine. The C–C bond has also begun to develop some double bond character.
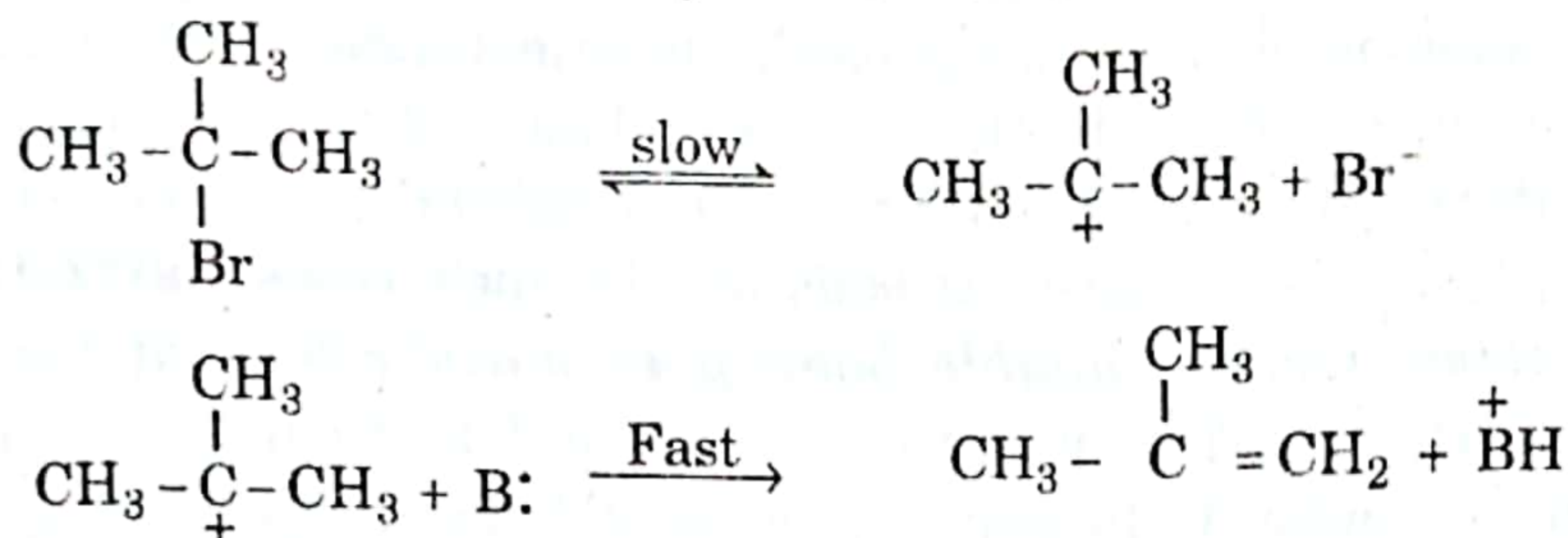
$$HO^- + \overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle Br}{|}}{CH_2}} - CH_2 \longrightarrow \overset{HO^{\delta-} \cdots H}{\underset{\underset{\displaystyle Br^{\delta-}}{\vdots}}{CH_2 = CH_2}} \longrightarrow H_2O + CH_2 = CH_2 + Br^-$$

The E2 mechanism is supported by a typical second-order kinetics, first -order in substrate and first- order in base. The rate equation is:

<center>Rate = k $[CH_3 CH_2 Br] [OH^-]$</center>

The E2 mechanism is analogous to the S_N2 mechanism and often competes with it. The difference between the two pathways is whether the reagent with an unshared electron pair attacks the hydrogen atom (acts as a base) or the carbon atom (acts as a nucleophile) of the substrate. Any species (neutral or negatively charged) that carries a lone pair of electrons can act as both base and nucleophile. A base attacks hydrogen atom in elimination reactions while a nucleophile attacks carbon atom in substitution reactions.

The E1 mechanism. The E1 (elimination unimolecular) like S_N1 is a two step

process. In the first step, the substrate ionizes slowly to form a carbocation that rapidly loses a proton from a β – carbon atom to a base, usually the solvent, in the second step. E1 reaction normally occurs without an added base.
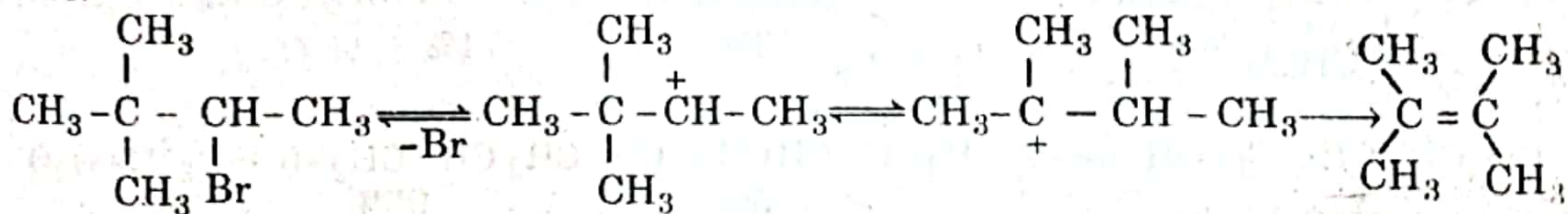
$$CH_3-\underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_3 \quad \underset{\longleftarrow}{\xrightarrow{\text{slow}}} \quad CH_3-\underset{\underset{+}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_3 + Br^-$$

$$CH_3-\underset{\underset{+}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_3 + B: \quad \xrightarrow{\text{Fast}} \quad CH_3-\overset{\overset{CH_3}{|}}{C}=CH_2 + \overset{+}{B}H$$

The E1 reaction is analogous to the S_N1 reaction and often competes with it. In fact, the first step (i.e., rate determining step) of the E1 reaction is exactly the same as that of the S_N1 reaction. The second step differs in that the solvent pulls a proton from the β-carbon of the carbocation to form an alkene rather than attacking it at the positively charged carbon to form the substitution product as in the S_N1 process. E1 reactions always accompany S_N1 reactions.

$$(CH_3)_3\,CBr \xrightarrow{C_2H_5OH,\ H_2O} (CH_3)_3COH + (CH_3)_2C=CH_2$$
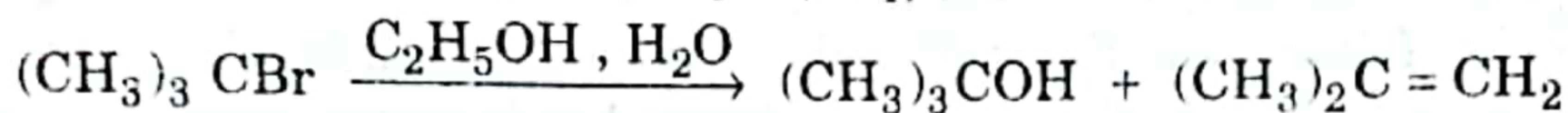
The E1 mechanism is supported by the kinetic studies of the reaction. It follows first-order kinetic, the rate depends on the concentration of the substrate only.
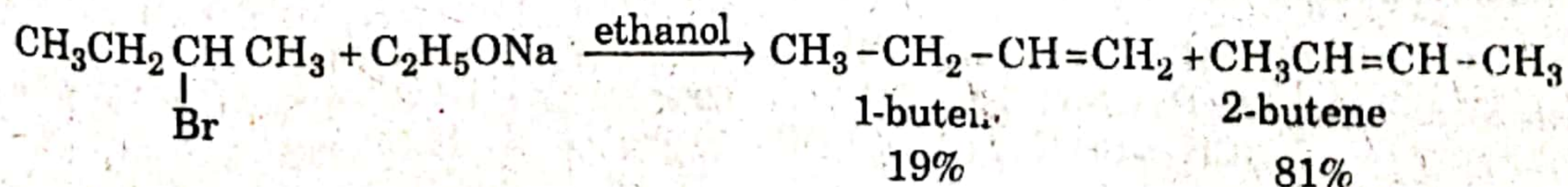
Rate $=$ $k\,[CH_3)_3\,C\,Br]$

The formation of a carbocation as an intermediate is also supported by the fact that it can rearrange itself to a more stable carbocation before losing a β– proton to the base.

$$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\underset{\underset{Br}{|}}{CH}-CH_3 \underset{-Br}{\rightleftharpoons} CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\overset{+}{CH}-CH_3 \rightleftharpoons CH_3-\underset{\underset{+}{|}}{\overset{\overset{CH_3}{|}}{C}}-\underset{\underset{}{|}}{\overset{\overset{CH_3}{|}}{CH}}-CH_3 \longrightarrow \underset{\underset{CH_3}{\diagdown}}{\overset{\overset{CH_3}{\diagup}}{C}}=\underset{\underset{CH_3}{\diagup}}{\overset{\overset{CH_3}{\diagdown}}{C}}$$

8.8 Orientation in Elimination-Orientation of Double Bond

If a substrate has a β – hydrogen on only one carbon, there is no doubt about the position of the new double bond. For example, $CH_3CH_2CH_2Br$ gives only $CH_3CH=CH_2$. However, many substrates have β – hydrogens at more than one position that can be lost in the elimination reaction and more than one alkenic product are possible. For example, dehydrohalogenation of 2-bromobutane can yield two products: 2-butene or 1-butene. In fact, a mixture of both alkenes is formed.

$$CH_3CH_2\underset{\underset{Br}{|}}{CH}CH_3 + C_2H_5ONa \xrightarrow{\text{ethanol}} CH_3-CH_2-CH=CH_2 + CH_3CH=CH-CH_3$$

<div align="center">

1-butene   2-butene

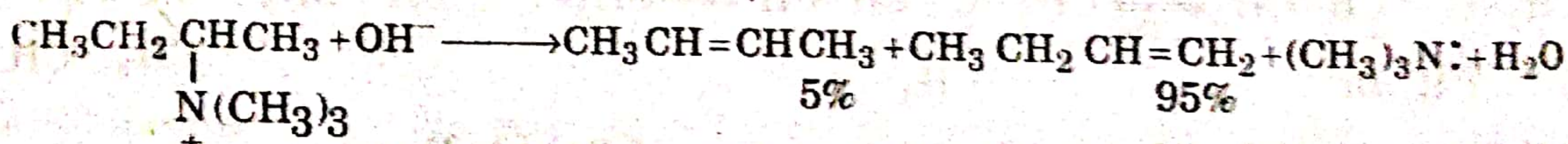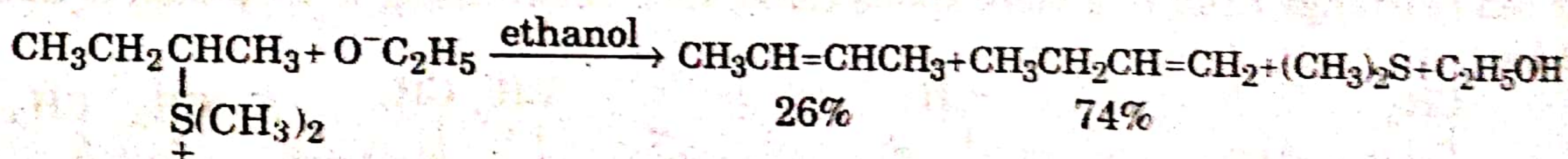19%   81%

</div>

The question arises which alkenic product predominates. There are a number of rules that enable us to predict which product will predominantly form.

In the E1 mechanism the leaving group is gone before the choice is made as to which direction is taken by the new double bond. The orientation of the double bond in this case is determined entirely by the relative stabilites of the possible alkenes. In general, *the greater the number of alkyl groups attached to the carbon atoms of the double bond, the greater is the alkenes stability*. In such cases **Saytzeff rule operates** which states that *the double bond goes mainly toward the more highly substituted alkene*. Thus, in the elimination of HBr from 2-bromobutane, 2-butene is the major product. In general, *in an E1 reaction the most highly substituted alkene is formed through the most stable carbocation*.
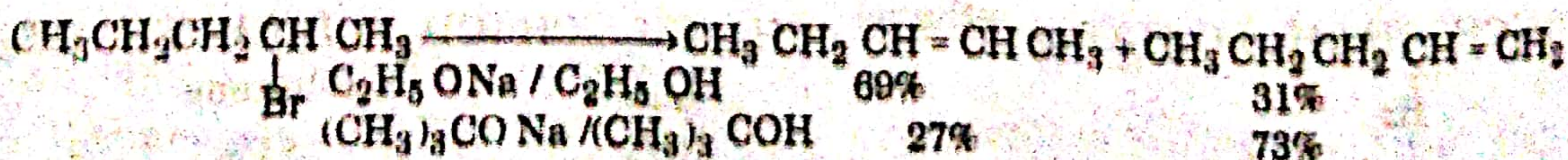
In the case of E2 mechanism, the presence of a trans β-hydrogen is necessary. If trans β-hydrogen is available at only one position then that is the direction of the double bond. However, if trans β-hydrogens are available on two or three carbons, two types of behaviour are observed depending on the structure of the substrate and the nature of the leaving group. Most eliminations involving neutral substrates tend to follow the Saytzeff rule and yield mainly the more highly substituted alkene, while eliminations with charged substrates tend to follow the Hofmann rule and yield mainly the least substituted alkene. *The Hofmann rule states that the double bond goes mainly toward the least highly substituted alkene.*

Substrates containing charged leaving groups like $-NR_3^+$, $-SR_2^+$, (that comes off as a neutral molecule) follow Hofmann rule if the substrate is acylic and the product formed is called the Hofmann product.

$$CH_3CH_2\underset{\underset{+}{S(CH_3)_2}}{CHCH_3} + O^-C_2H_5 \xrightarrow{\text{ethanol}} \underset{26\%}{CH_3CH=CHCH_3} + \underset{74\%}{CH_3CH_2CH=CH_2} + (CH_3)_2S + C_2H_5OH$$

$$CH_3CH_2\underset{\underset{+}{N(CH_3)_3}}{CHCH_3} + OH^- \longrightarrow \underset{5\%}{CH_3CH=CHCH_3} + \underset{95\%}{CH_3CH_2CH=CH_2} + (CH_3)_3N: + H_2O$$

With a charged substrate, the base attacks the more acidic hydrogen Primary hydrogens are more acidic because their carbon bears only one electron-releasing group.

The Hofmann product appears to be formed because of steric effects, since the formation of a less substituted alkene is favoured even when the leaving group is a halide, if a large base is used.

$$CH_3CH_2CH_2\underset{\underset{C_2H_5ONa / C_2H_5OH}{\overset{|}{Br}}}{CH}CH_3 \longrightarrow \underset{\underset{27\%}{69\%}}{CH_3CH_2CH=CHCH_3} + \underset{\underset{73\%}{31\%}}{CH_3CH_2CH_2CH=CH_2}$$
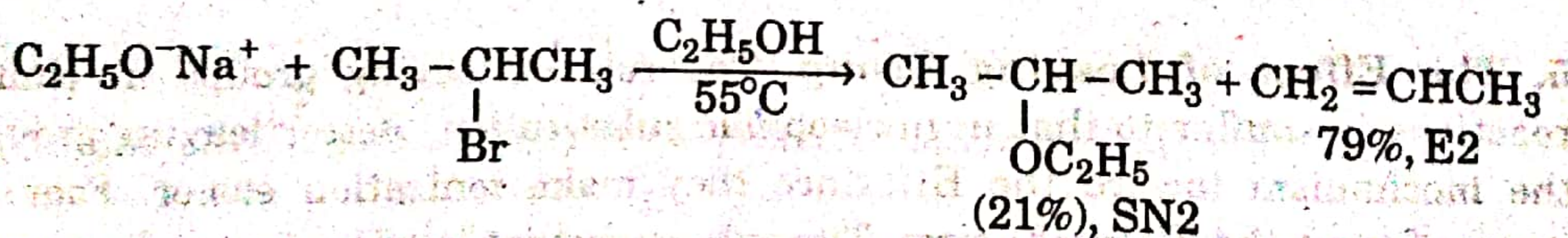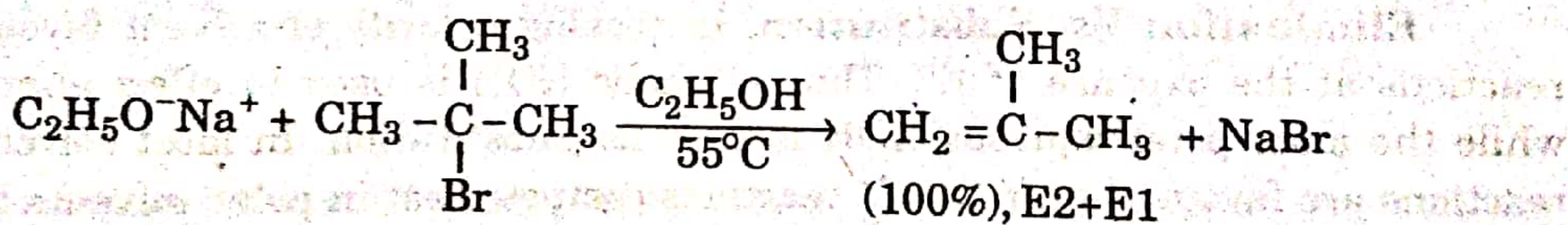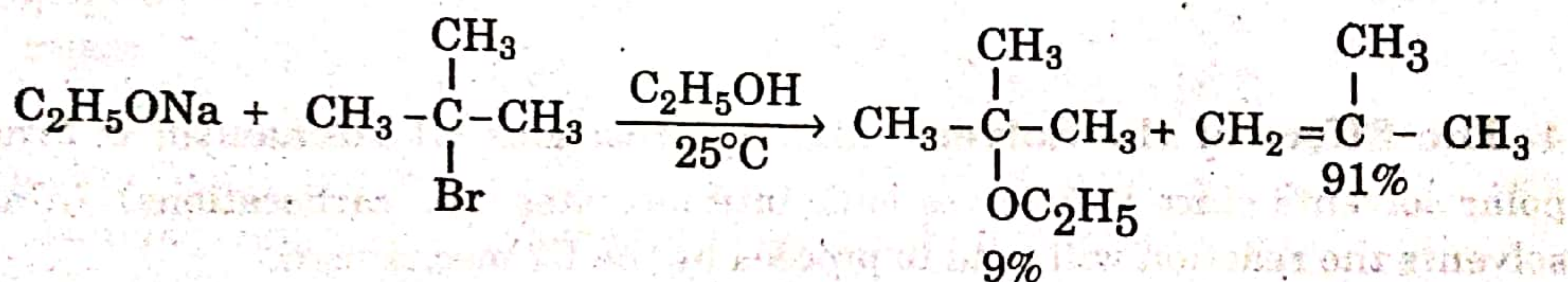$$(CH_3)_3CONa /(CH_3)_3COH$$

8.9 Factors Affecting Reactivity of Elimination Reactions:- Reactivity

Like substitution reactions, the mechanism and the relative rates of E1 and E2 reactions depend on various factors. Though substitution and, elimination reactions lead to different products, since they are closely related in mechanism, thus there is often a competition between them.

1. The effect of substrate structure. Like substitution reactions, tertiary substrates (i.e., tertiary halides) usually proceed by the E1 mechanism, since they can form stable carbocations readily. Primary substrates usually follow E2 mechanism. Secondary substrates proceed either by E1 mechanism or by E2 mechanism depending on the reaction conditions. However in contrast to the substitution reactions the E2 mechanism is often observed with tertiary substrate because the base can easily abstract a proton from a β-carbon atom where the steric hindrance is not as significant as when the nucleophile must directly approach the α-carbon from which the leaving group departs for S_N2 reaction.

Elimination Vs. Substitution. Crowding within the substrate generally favours elimination over substitution because the approach of the nucleophile to the β-carbon is usually subjected to much more steric hindrance than is abstraction of a β-hydrogen atom by the base. The increased number of alkyl groups on the substrate favours elimination over substitution since they stabilize the elimination product, i.e., alkene more than the substitution.
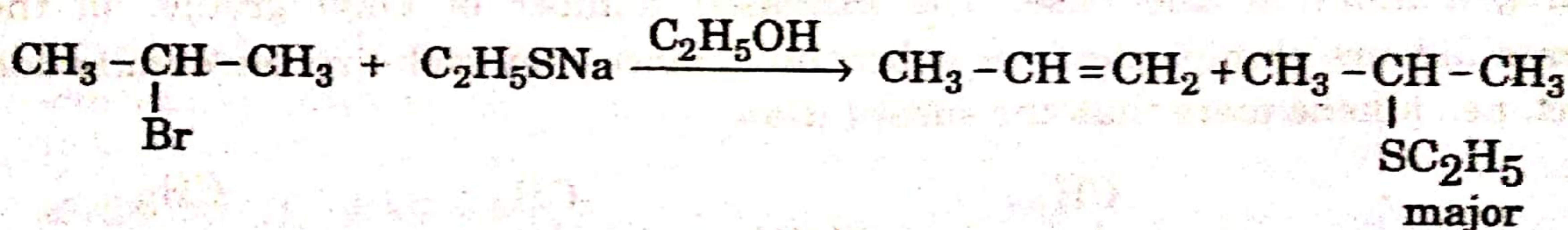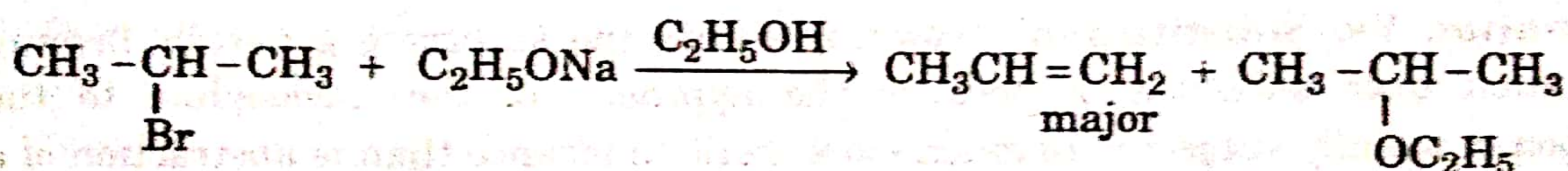
$$C_2H_5ONa + \underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{CH_3-C-CH_3}} \xrightarrow[25°C]{C_2H_5OH} \underset{\underset{OC_2H_5}{|}}{\overset{\overset{CH_3}{|}}{CH_3-C-CH_3}} + \underset{91\%}{CH_2=\overset{\overset{CH_3}{|}}{C}-CH_3}$$

9%

$$C_2H_5O^-Na^+ + \underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{CH_3-C-CH_3}} \xrightarrow[55°C]{C_2H_5OH} \underset{(100\%),\ E2+E1}{CH_2=\overset{\overset{CH_3}{|}}{C}-CH_3} + NaBr$$

$$C_2H_5O^-Na^+ + \underset{\underset{Br}{|}}{CH_3-CHCH_3} \xrightarrow[55°C]{C_2H_5OH} \underset{\underset{OC_2H_5}{|}}{CH_3-CH-CH_3} + \underset{79\%,\ E2}{CH_2=CHCH_3}$$

(21%), SN2

2. The Effect of temperature. Elimination is favoured over substitution by increasing temperature, whether the mechanism is unimolecular or bimolecular. The reason is that the activation energies of elimination are higher than those of substitutions, therefore at higher temperature elimination is favoured.

3. Effect of the Attacking Base. In the E1 mechanism, an external base is generally not required; the solvent itself acts as the base. Hence when external

bases are added, the mechanism is shifted toward E2. A strong base favours the E2 mechanism even with a tertiary substrate. E1 reactions are favoured by the use of weak bases with tertiary and, in some cases, secondary substrates. -

Elimination Vs. Substitution. Strong bases not only favour E2 over El, but also favour elimination over substitution. With a high concentration of strong base in a nonionizing solvent, bimolecular mechanisms are favoured and E2 predominates over S_N2. At low high concentration, or in the absence of base altogether, in ionizing solvents, unimolecular mechanisms are favoured, and the S_N1 mechanism predominates over the E1. For example, 2-bromopropane with ethoxide ion (a strong base) gives alkene as the major product, and with an anion of the same corresponding thioalcohol $(C_2H_5S^-)$ substitution is the predominant reaction because $C_2H_5S^-$ is more nucleophilic but less basic than $O^-C_2H_5$.
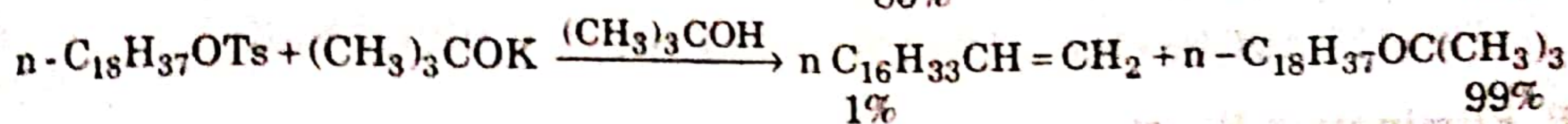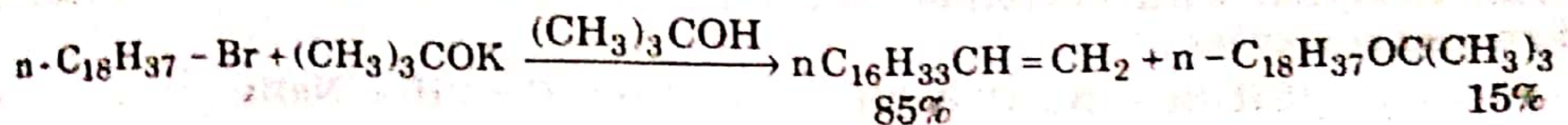
$$CH_3-CH-CH_3 + C_2H_5ONa \xrightarrow{C_2H_5OH} CH_3CH=CH_2 + CH_3-CH-CH_3$$

(Br below first structure; major; OC_2H_5 below last structure)

$$CH_3-CH-CH_3 + C_2H_5SNa \xrightarrow{C_2H_5OH} CH_3-CH=CH_2 + CH_3-CH-CH_3$$

(Br below first structure; SC_2H_5 below last structure; major)

4. The Effect of the Solvent. Like S_N1 reactions E1 mechanism is favoured by polar solvents since it involves ionic intermediates (i.e., carbocations). In non-polar solvents the reaction will tend to proceed by the E2 mechanism.

Elimination Vs. Substitution. Increasing polarity of solvent favours SN2 reactions at the expense of E2. Thus alcoholic KOH is used to effect elimination, while the more polar aqueous KOH is used for substitution. In most solvents SN1 reactions are favoured over E1. E1 reactions compete best in polar solvents that are poor nucleophiles.

5. The Effect of Leaving Group. The role of leaving groups in elimination reactions is similar to that in nucleophilic substitution. Better leaving groups shift the mechanism toward the E1, since they make ionization easier. Poor leaving groups favour the E2 mechanism. The only important leaving groups for preparative purposes are OH_2^+ (always by E1) and Cl, Br, I and NR_3^+ (usually by E2).

Elimination Vs. Substitution. For the unimolecular reactions the leaving group has nothing to do with the competition between elimination and substitution, since it is gone before the decision is made as to which path to take. In the bimolecular reactions, the elimination substitution ratio is not greatly dependent on a halide

leaving group, though there is a slight increase in elimination in the order $1 > Br >$ Cl. When OTs is the leaving group there is usually much more substitution. It means that in the bimolecular reactions the nature of the product greatly depends on the nature of the leaving group as shown below.

$$n\text{-}C_{18}H_{37}-Br+(CH_3)_3COK \xrightarrow{(CH_3)_3COH} \underset{85\%}{nC_{16}H_{33}CH=CH_2} + \underset{15\%}{n-C_{18}H_{37}OC(CH_3)_3}$$

$$n\text{-}C_{18}H_{37}OTs+(CH_3)_3COK \xrightarrow{(CH_3)_3COH} \underset{1\%}{nC_{16}H_{33}CH=CH_2} + \underset{99\%}{n-C_{18}H_{37}OC(CH_3)_3}$$

8.10 Alkyl Halides in Organic Synthesis (Chemical properties)

The alkyl halides are extremely useful compounds because they undergo a large variety of reactions that make them valuable in organic synthesis.

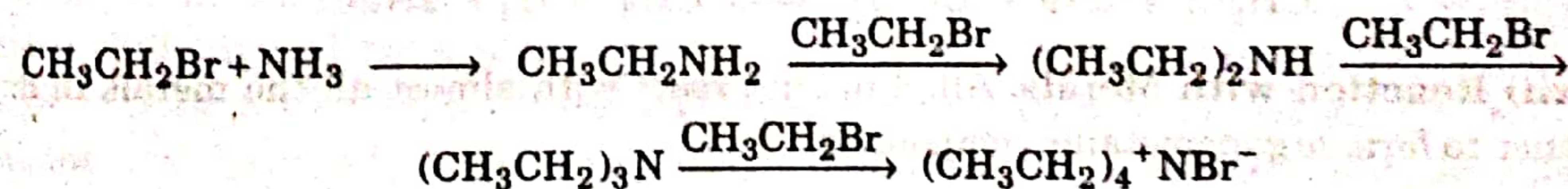**A.** Some of the important nucleophilic substitution reactions of alkyl halides are described below:

(i) Reaction with aqueous KOH. Alkyl halides react with aqueous KOH to form alcohols.

$$CH_3CH_2\,Br + aq.\,KOH \longrightarrow CH_3CH_2OH + KBr$$
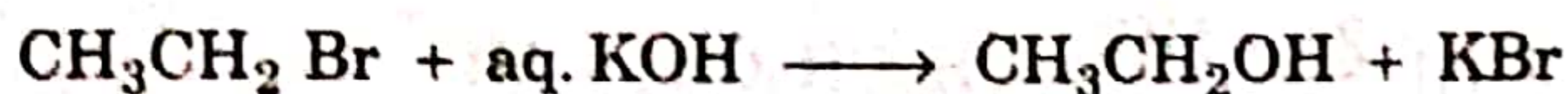
(ii) Reaction with Sodium alkoxides. Alkyl halides react with sodium alkoxides (RONa) to form ethers.

$$CH_3CH_2Br + {}^+Na\,{}^-OH_2CCH_3 \longrightarrow CH_3CH_2OCH_2CH_3 + NaBr$$

(iii) Reaction with ammonia. The alkyl halides react with ammonia to form primary, secondary and tertiary amines and quaternary ammonium salts.

$$CH_3CH_2Br + NH_3 \longrightarrow CH_3CH_2NH_2 \xrightarrow{CH_3CH_2Br} (CH_3CH_2)_2NH \xrightarrow{CH_3CH_2Br}$$

$$(CH_3CH_2)_3N \xrightarrow{CH_3CH_2Br} (CH_3CH_2)_4{}^+NBr^-$$

(iv) Reaction with NaCN. Alkyl halides react with sodium cyanide in a suitable reagent (generally aqueous ethanol) to form alkyl cyanides or nitriles.

$$CH_3CH_2Br + NaCN \longrightarrow CH_3CH_2CN + NaBr$$

Tertiary alkyl cyanides cannot be prepared since they undergo elimination reaction.

(v) Reaction with KSH. Alkyl halides react with alcoholic potassium hydrosulphide to form Thiols.

$$CH_3CH_2-I + KSH \xrightarrow{ethanol} CH_3CH_2SH + KI$$
$$\text{Ethanethiol}$$
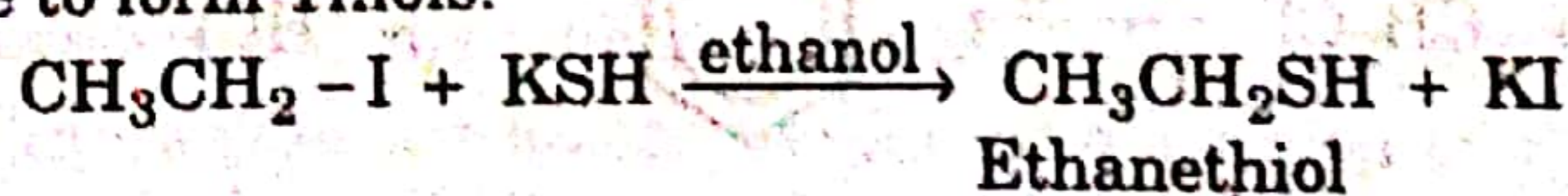
(vi) Reaction with mercaptides. Alkyl halides on treatment with mercaptides form alkyl sulphides.

$$C_2H_5-I + C_2H_5SNa \longrightarrow C_2H_5SC_2H_5 + NaI$$
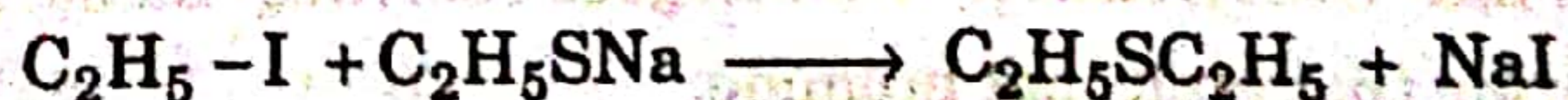
(vii) Reaction with RCOOAg. Alkyl halides on treatment with an alcoholic solution of silver salt of a carboxylic acid yield esters.

$$CH_3COOAg + CH_3CH_2Br \longrightarrow CH_3COOCH_2CH_3 + AgBr$$

(viii) Reaction with Acetylides. Alkyl halides react with sodium acetylides to form higher alkynes.

$$CH_3Br + Na^+C^- \equiv CH \longrightarrow CH_3-C \equiv CH + NaBr$$

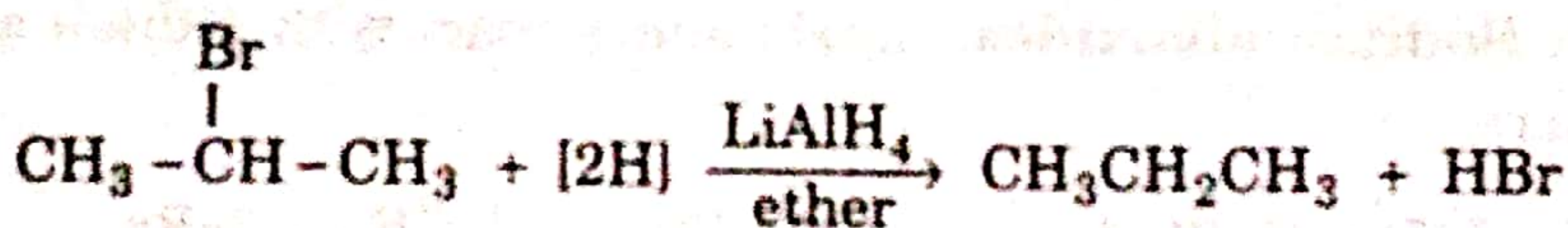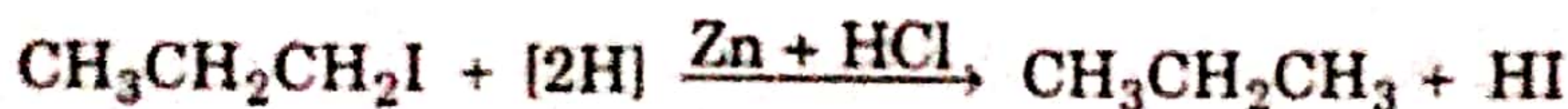$$CH_3Br + Na^+C^- \equiv CCH_3 \longrightarrow CH_3C \equiv CCH_3 + NaBr$$

B. Elimination Reactions

(ix) Reaction with Alcoholic KOH. Alkyl halides on boiling with alcoholic KOH undergo dehydrohalogenation to form alkenes.
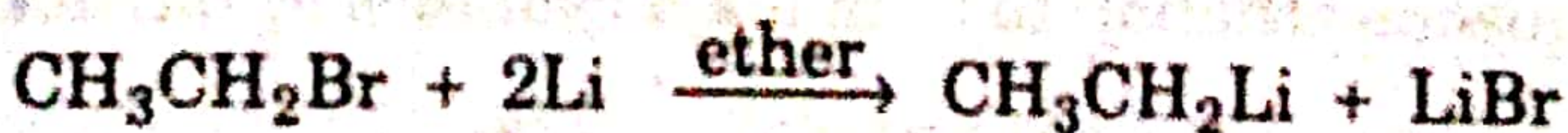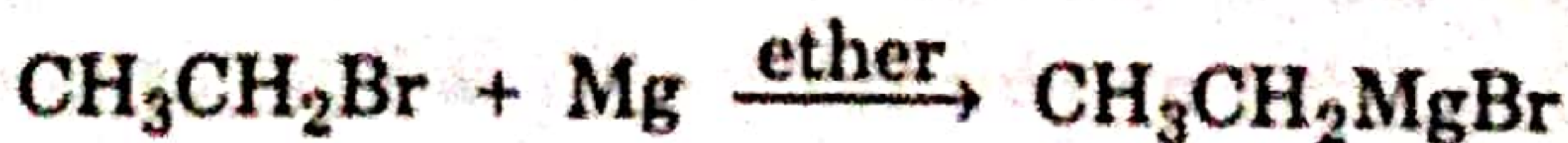
$$CH_3CH_2Br + KOH \xrightarrow{\text{ethanol}} CH_2 = CH_2 + KBr + H_2O$$
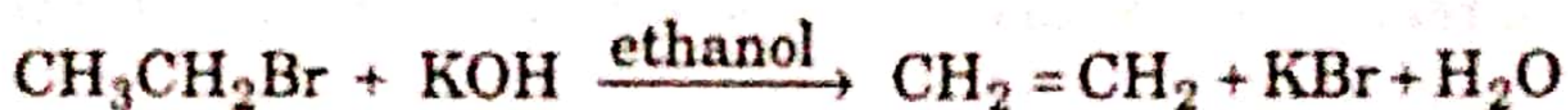
(C) Miscellaneous Reactions

(x) Reduction. Alkyl halides are reduced to alkanes by (i) Zn+ HI; (ii) LiAlH$_4$; and (iii) H$_2$ in the presence of Ni or Pd.

$$CH_3CH_2CH_2I + [2H] \xrightarrow{Zn + HCl} CH_3CH_2CH_3 + HI$$

$$\overset{\displaystyle Br}{\underset{}{CH_3-CH-CH_3}} + [2H] \xrightarrow[\text{ether}]{LiAlH_4} CH_3CH_2CH_3 + HBr$$

(xi) Wurtz Reaction. Alkyl halides react with metallic sodium in dry ether to form higher alkanes.
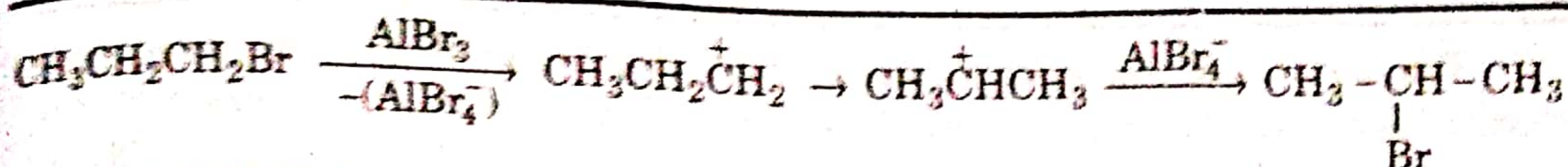
$$CH_3Cl + 2Na + ClCH_3 \longrightarrow CH_3-CH_3 + 2NaCl$$

(xii) Reaction with Metals. Alkyl halides react with almost all the metals in dry ether to form organometallic compounds.

$$CH_3CH_2Br + Mg \xrightarrow{\text{ether}} CH_3CH_2MgBr$$

$$CH_3CH_2Br + 2Li \xrightarrow{\text{ether}} CH_3CH_2Li + LiBr$$

(xiii) Friedel- Crafts Reaction. Alkyl halides react with benzene in the presence of anyhydrous AlCl$_3$ to form alkyl benzenes.
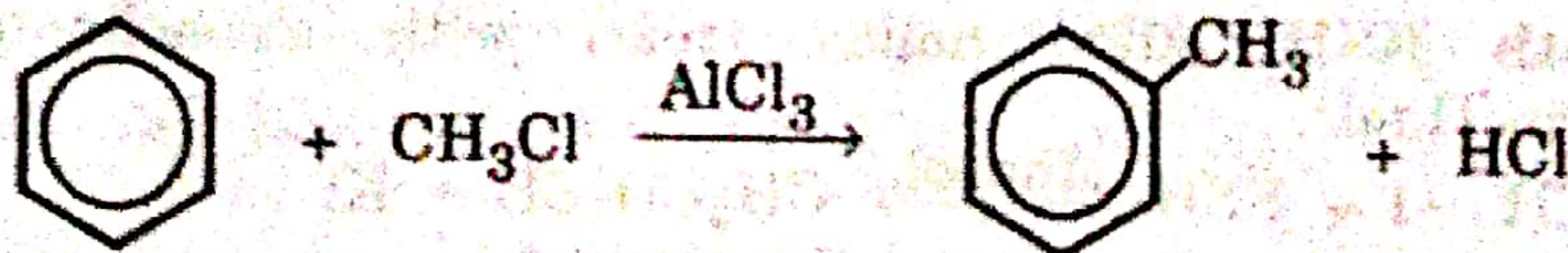
(xiv) Rearrangement. When an alkyl halide is heated at about 300°C, or in the presence of catalyst like AlCl$_3$, AlBr$_3$, it undergoes rearrangement. Hydride ion can migrate. It was hydride that shift, not bromide.

$$CH_3CH_2CH_2Br \xrightarrow[-(AlBr_4^-)]{AlBr_3} CH_3CH_2\overset{+}{C}H_2 \rightarrow CH_3\overset{+}{C}HCH_3 \xrightarrow{AlBr_4^-} CH_3-CH-CH_3$$
$$\underset{Br}{|}$$

8.11 ORGANOMAGNESIUM COMPOUNDS: GRIGNARD REAGENTS

The alkyl - or arylmagnesium halides, R (or Ar) - Mg - X, are commonly known as **Grignard reagents** after the name of Victor Grignard who introduced them as synthetic reagents in organic chemistry, and Grignard was awarded the Nobel prize for his work in 1912.

Preparation of Grignard Reagents

A Grignard reagent is prepared by refluxing an alkyl or aryl halide, dissolved in dry ether, with small magnesium turnings. A reaction takes place at the surface of magnesium which slows down during the course of the reaction.

$$R - X + Mg \xrightarrow{ether} R - Mg - X$$
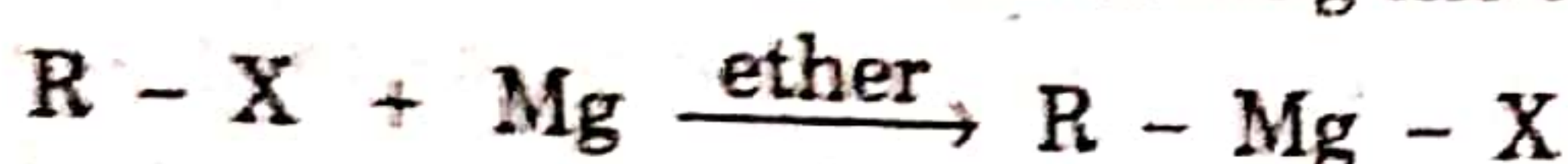
The reaction takes place in two steps. In the first step, alkyl halide reacts at the surface of magnesium to produce an alkyl radical and a $^\bullet MgX$ sepecies (probably still associated with the metal surface). The alkyl radical then reacts with $^\bullet MgX$ to form the Grignard reagent.

$$RX + Mg \longrightarrow R^\bullet + {^\bullet MgX} \longrightarrow RMgX$$
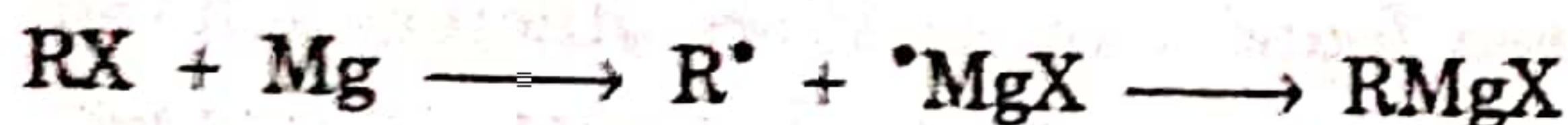
Grignard reagents cannot be isolated. The ethereal solution of the Grignard reagent is used directly for further reactions.
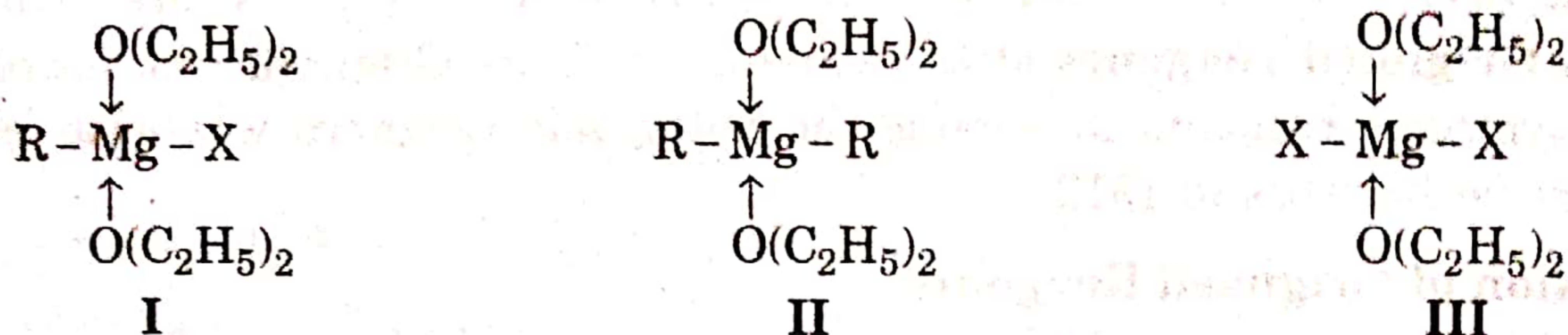
The ease of the formation of Grignard reagents depends upon many factors including the nature of alkyl (or aryl) group and the halogen atom. Increase in the number of carbon atoms in the alkyl group makes the formation of the reagent rather difficult and for a particular alkyl group the ease of formation follows the order: I > Br > Cl. The alkyl (or aryl) magnesium fluorides are not known. Alkyl iodides are generally expensive. Alkyl bromides are most suitable for the preparation of Grignard reagents.

Besides ether, a number of other solvents such as tetrahydrofuran (THF), and tertiary amines may also be used as solvent. The best solvent, however, is THF as it increases the reactivity of organic halides towards magnesium.

Structure of Grignard Reagents: It is fairly certain that the C - Mg bond in Grignard reagents is covalent and not ionic. The actual structure of Grignard reagents in solution has been the subject of much controversy over the years. In 1929 it was discovered that the addition of dioxane to an ethereal Grignard solution precipitates all the magnesium halide and leaves a solution of R_2Mg in ether. The following equilibrium, now called the **schlenk equilibrium,** was proposed to represent the composition of the Grignard solution.

$$2RMgX \rightleftharpoons R_2Mg + MgX_2 \rightleftharpoons R_2Mg \cdot MgX_2$$
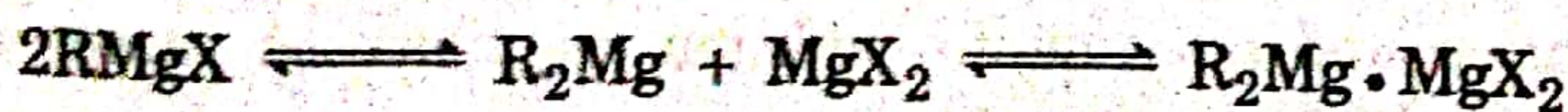
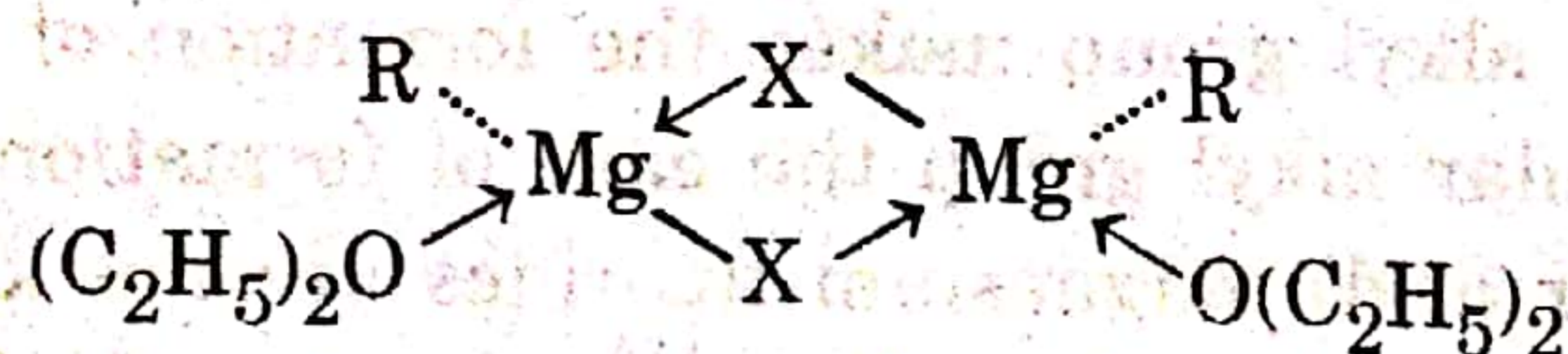The position of the equilibrium depends on the identity of R, X, the solvent, concentration and the temperature. It has been known for many years that the magnesium in a Grignard solution, no matter whether it is R MgX, R_2Mg or MgX_2 can coordinate with two molecules of ether in addition to the two covalent bonds.

$$
\begin{array}{ccc}
O(C_2H_5)_2 & O(C_2H_5)_2 & O(C_2H_5)_2 \\
\downarrow & \downarrow & \downarrow \\
R-Mg-X & R-Mg-R & X-Mg-X \\
\uparrow & \uparrow & \uparrow \\
O(C_2H_5)_2 & O(C_2H_5)_2 & O(C_2H_5)_2 \\
\mathbf{I} & \mathbf{II} & \mathbf{III}
\end{array}
$$

The crystalline Grignard reagents have been obtained by cooling ordinary ethereal Grigard solution and their structures have been determined by X - ray diffraction technique. This study shows that these compounds exist as dietherate of the monomer in which four groups are tetrahedrally arranged around magnesium atom.

$$
\begin{array}{c}
R \diagdown \quad \diagup O(C_2H_5)_2 \\
\quad \ \text{Mg} \\
X \diagup \quad \diagdown O(C_2H_5)_2
\end{array}
$$
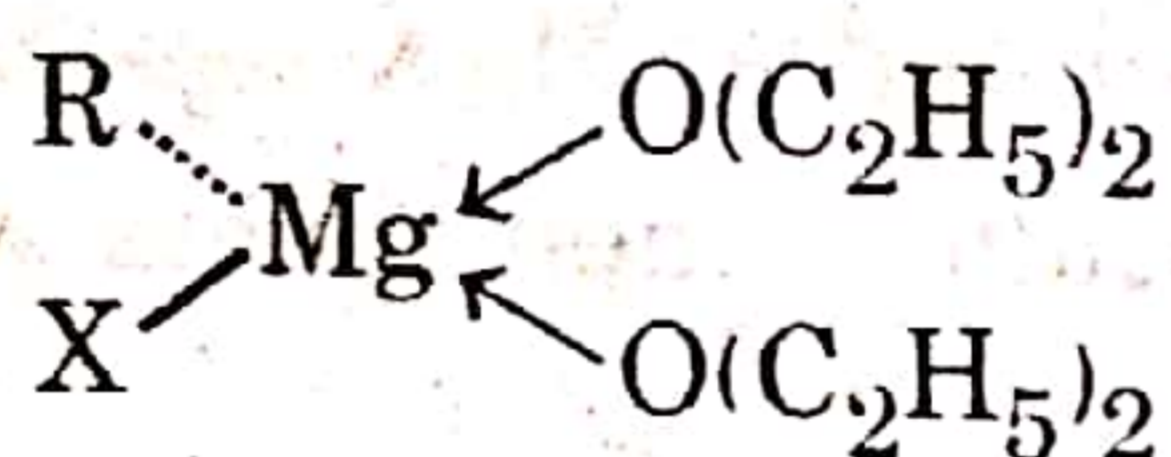
In general, it has been found that in dilute ethereal solution (upto about 0.1M) Grignard reagents exist as monomers. However, in higher concentrated solution (0.5 to 1M) the principal species is a dimer in which two magnesium atoms are bridged by two halogens. In this structure each magnesium acquires its octet by additional coordination, one with halogen of the other RMgX and one with oxygen of the ether molecule.

$$
\begin{array}{ccccc}
R \diagdown & & X & & R \\
& \text{Mg} & & \text{Mg} & \\
(C_2H_5)_2O \diagup & & X & & \diagdown O(C_2H_5)_2
\end{array}
$$

Since the reactions of R_2Mg in the presence of MgX_2 are the same as those of RMgX, we shall designate them as RMgX, while discussing their reactions.

8.12 Reactions of Grignard Reagents

The C - Mg bond in Grignard reagents is covalent but highly polar. The carbon atom is more electronegative than Mg. The electrons of the C - Mg bond are drawn towards the carbon atom. As a result, the carbon atom has a partial negative charge and the Mg atom has a partial positive charge.

$$
\overset{\delta-}{\underset{|}{-\text{C}}} \leftarrow \overset{\delta+}{\text{MgX}} \qquad \text{or} \qquad \overset{\delta-}{\text{R}} - \overset{\delta+}{\text{MgX}}
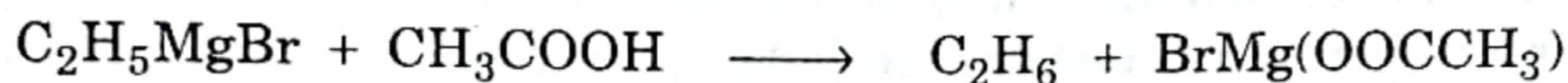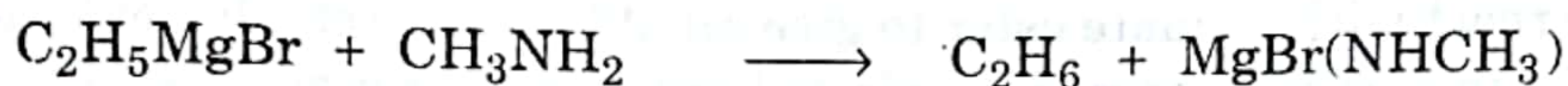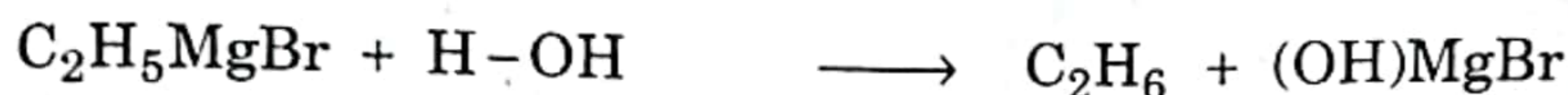$$
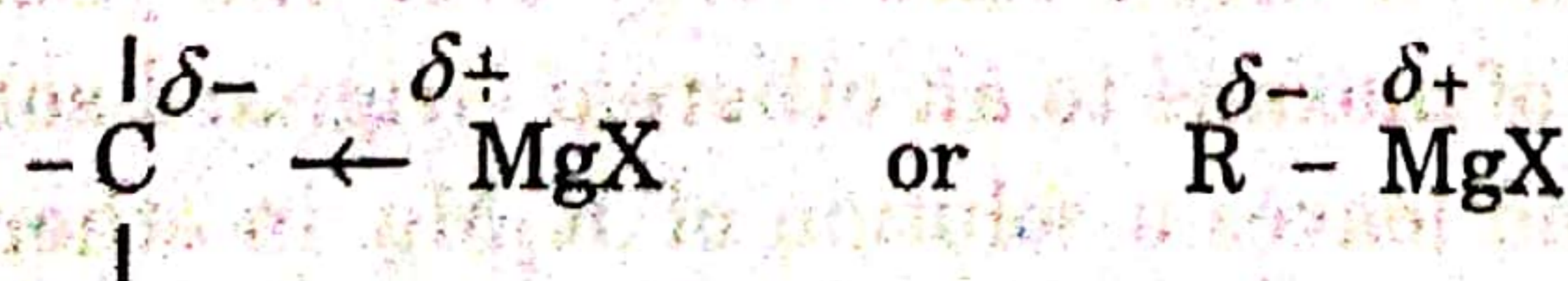
The alkyl groups in Grignard reagents being electron rich can act as carbanions or nucleophiles. Thus the characteristic reactions of Grignard reagents are nucleophilic substitution and nucleophilic addition reactions. (A carbon atom having a negative charge is called a carbanion).

Grignard reagents react with a variety of substances yielding almost the entire range of organic substances. The following reactions illustrate the synthetic importance of Grignard reagents.

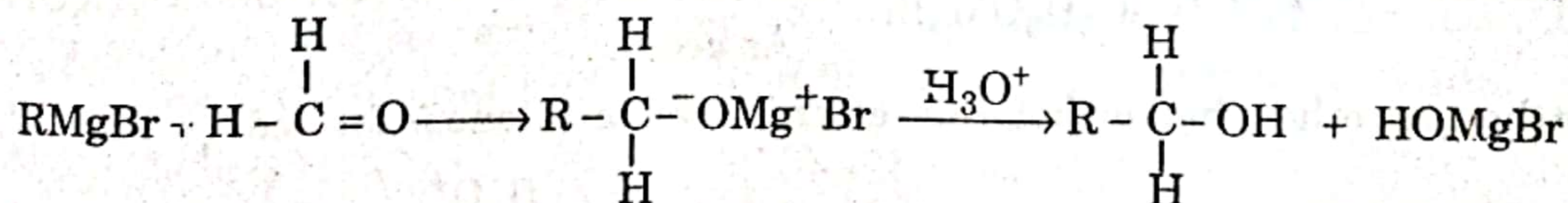## 1. Reaction with compounds containing Active hydrogen

Formation of Hydrocarbons: Any hydrogen that is acidic in nature is known as **active hydrogen.** Compounds like water, alcohols, amines, carboxylic acids and terminal alkynes which contain active hydrogen react with Grignard reagents to form Hydrocarbons.

$$C_2H_5MgBr + H-OH \longrightarrow C_2H_6 + (OH)MgBr$$

$$C_2H_5MgBr + C_2H_5OH \longrightarrow C_2H_6 + MgBr(OC_2H)_5$$

$$C_2H_5MgBr + CH_3NH_2 \longrightarrow C_2H_6 + MgBr(NHCH_3)$$

$$C_2H_5MgBr + CH_3COOH \longrightarrow C_2H_6 + BrMg(OOCCH_3)$$

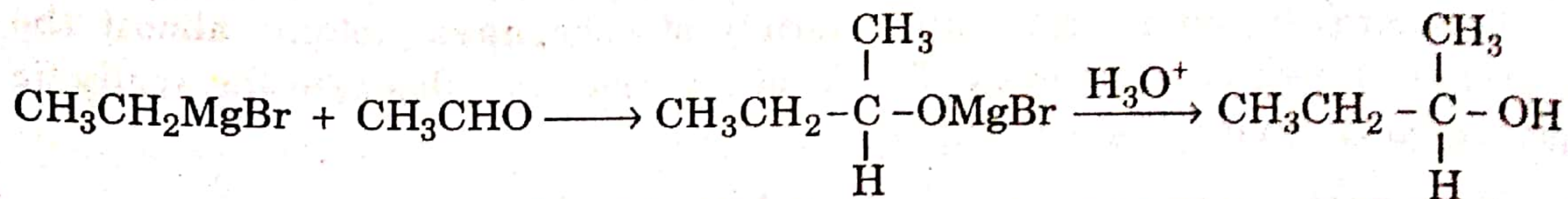$$C_2H_5MgBr + CH_3-C\equiv CH \longrightarrow C_2H_6 + CH_3-C\equiv CMgBr$$

The reaction of Grignard reagents with active hydrogen compounds can be used for the determination of number of active hydrogens in a compound. The procedure is known as **Zerewitnoff active hydrogen** determination. Methylmagnesium iodide is normally used and the methane that is liberated in the reaction, is measured by volume. One molecule of CH_4 being equivalent to one active hydrogen atom.

2. Reaction with Carbonyl Compounds: Nucleophilic Addition to Carbonyl Compounds.

Grignard reagents, being nucleophilic in character, add to carbonyl group of aldehydes, ketones, carboxylate ester, anhydrides and amides and the resulting complex on hydrolysis forms alcohol. In this reaction the alkyl group, having carbanionic character, is bonded to the carbonyl carbon and the MgX to the oxygen of the carbonyl group. The hydrolysis step is usually carried out with dil HCl or H_2SO_4 but this can not be done for tertiary alcohols because they are easily dehydrated under acidic conditions. For tertiary alcohols (and often for other alcohols as well) an aqueous solution of NH_4Cl is used instead of a strong acid.

(i) Reaction with formaldehyde; Formaldehyde reacts with Grignard reagents to give addition products which on hydrolysis gives primary alcohols.

$$RMgBr + H-\overset{\overset{\displaystyle H}{|}}{C}=O \longrightarrow R-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}{}^-OMg^+Br \xrightarrow{H_3O^+} R-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-OH + HOMgBr$$

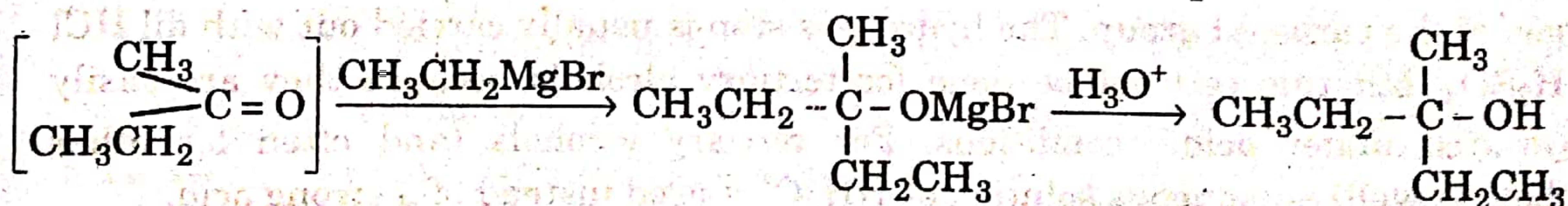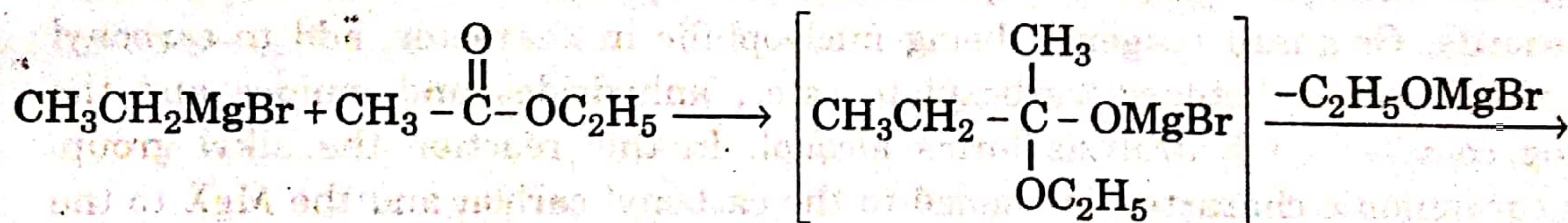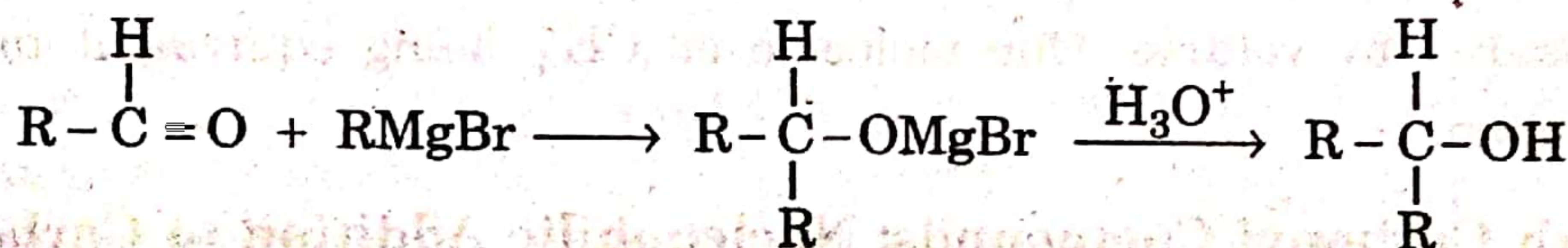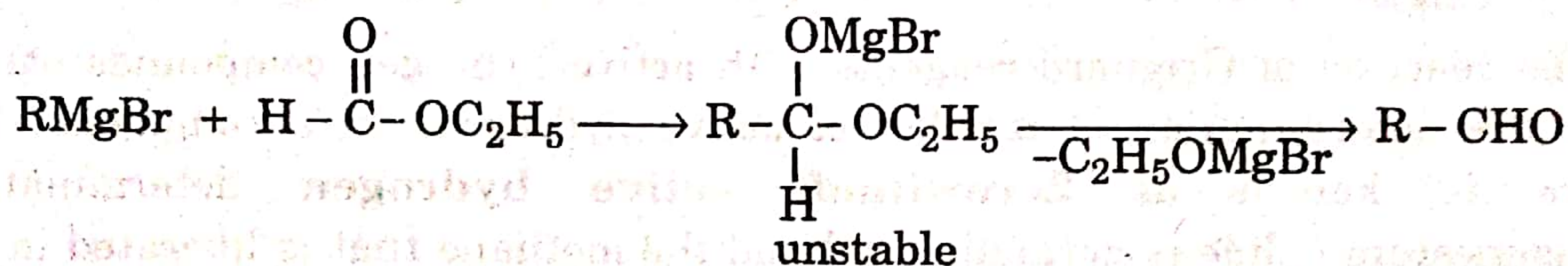**(ii) Reaction with aldehydes other than formaldehyde:** Synthesis of secondary alcohols. Aldehydes (except formaldehyde) react with Grignard reagents to give addition products which on hydrolysis give secondary alcohols.
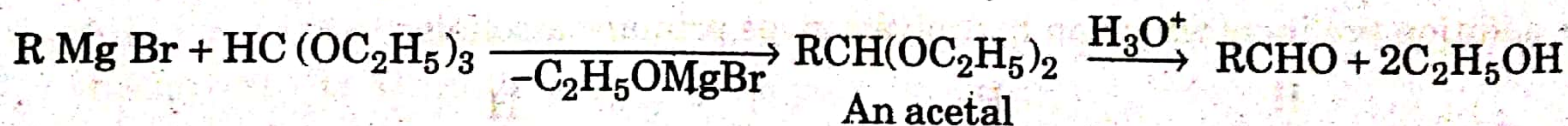
$$CH_3CH_2MgBr + CH_3CHO \longrightarrow CH_3CH_2 - \underset{\underset{H}{|}}{\overset{\overset{CH_3}{|}}{C}} - OMgBr \xrightarrow{H_3O^+} CH_3CH_2 - \underset{\underset{H}{|}}{\overset{\overset{CH_3}{|}}{C}} - OH$$

(iii) Reaction With ketones: Synthesis of tertiary alcohols. Ketones react with Grignard reagent to form tertiary alcohols.

$$RMgBr + \underset{R''}{\overset{R'}{>}}C=O \longrightarrow R - \underset{\underset{R''}{|}}{\overset{\overset{R'}{|}}{C}} - OMgBr \xrightarrow{aq.\ NH_4Cl} R - \underset{\underset{R''}{|}}{\overset{\overset{R'}{|}}{C}} - OH$$
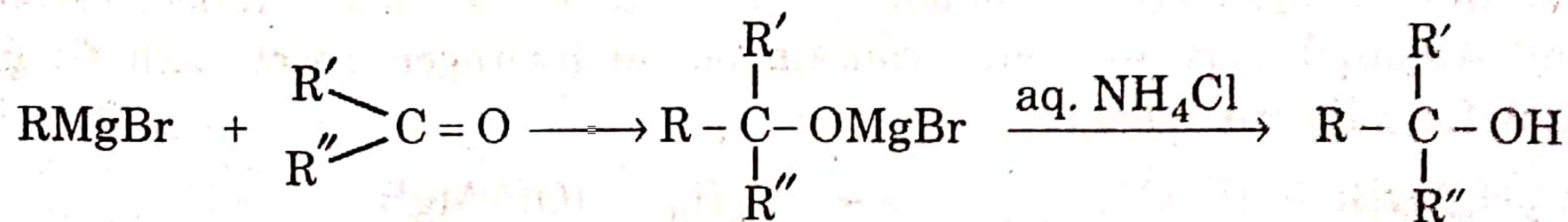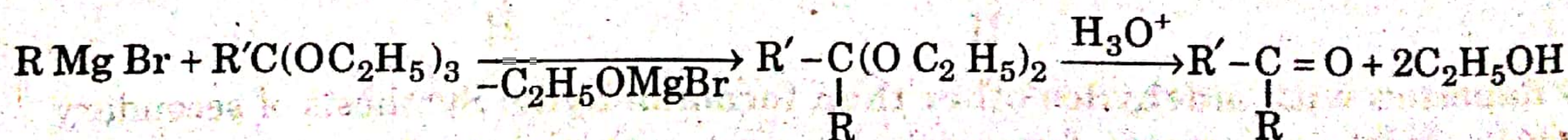
(iv) Reaction With esters: Synthesis of secondary and tertiary alcohols. Grignard reagents react with formate ester to give an aldehyde first. However, if the Grignard reagent is in excess, a secondary alcohol is formed. The other carboxylate ester with Grignard reagent gives tertiary alcohols.

$$RMgBr + H - \overset{\overset{O}{||}}{C} - OC_2H_5 \longrightarrow R - \underset{\underset{H}{|}}{\overset{\overset{OMgBr}{|}}{C}} - OC_2H_5 \xrightarrow[-C_2H_5OMgBr]{} R - CHO$$
$$\text{unstable}$$

$$R - \overset{\overset{H}{|}}{C} = O + RMgBr \longrightarrow R - \underset{\underset{R}{|}}{\overset{\overset{H}{|}}{C}} - OMgBr \xrightarrow{H_3O^+} R - \underset{\underset{R}{|}}{\overset{\overset{H}{|}}{C}} - OH$$

$$CH_3CH_2MgBr + CH_3 - \overset{\overset{O}{||}}{C} - OC_2H_5 \longrightarrow \left[CH_3CH_2 - \underset{\underset{OC_2H_5}{|}}{\overset{\overset{CH_3}{|}}{C}} - OMgBr \right] \xrightarrow[-C_2H_5OMgBr]{}$$

$$\left[\underset{CH_3CH_2}{\overset{CH_3}{>}} C = O \right] \xrightarrow{CH_3CH_2MgBr} CH_3CH_2 - \underset{\underset{CH_2CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}} - OMgBr \xrightarrow{H_3O^+} CH_3CH_2 - \underset{\underset{CH_2CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}} - OH$$

(v) Reaction with orthoesters. Grignard reagent reacts with ethyl orthoformate to form an acetal which on hydrolysis gives an aldehyde.

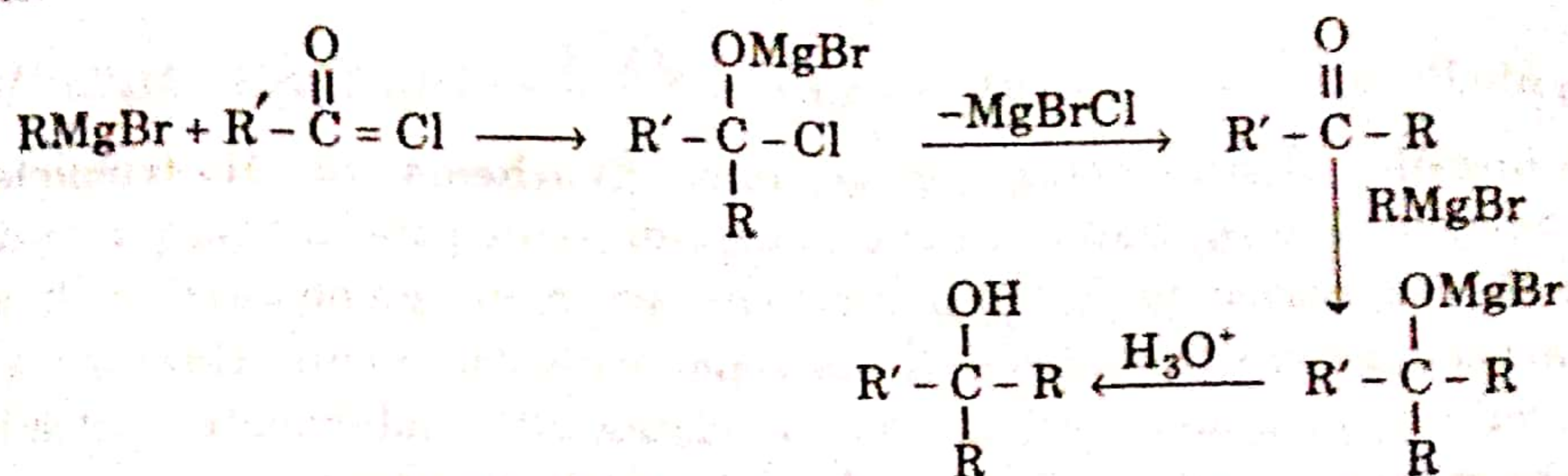$$R\,Mg\,Br + HC(OC_2H_5)_3 \xrightarrow[-C_2H_5OMgBr]{} RCH(OC_2H_5)_2 \xrightarrow{H_3O^+} RCHO + 2C_2H_5OH$$
$$\text{An acetal}$$

If an orthoester other than orthoformic ester is used, a ketone is formed.

$$R\,Mg\,Br + R'C(OC_2H_5)_3 \xrightarrow[-C_2H_5OMgBr]{} R' - \underset{\underset{R}{|}}{\overset{}{C}}(OC_2H_5)_2 \xrightarrow{H_3O^+} R' - \underset{\underset{R}{|}}{\overset{}{C}} = O + 2C_2H_5OH$$

(iv) Reaction with acid chlorides. Grignard reagents react with acid chloride

first to form ketone which further react with Grignard reagent to form tertiary alcohols.
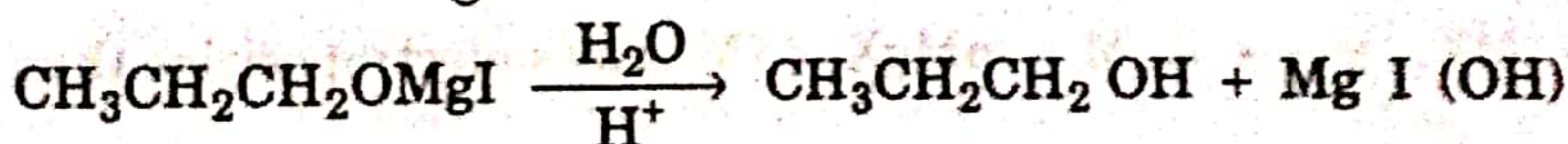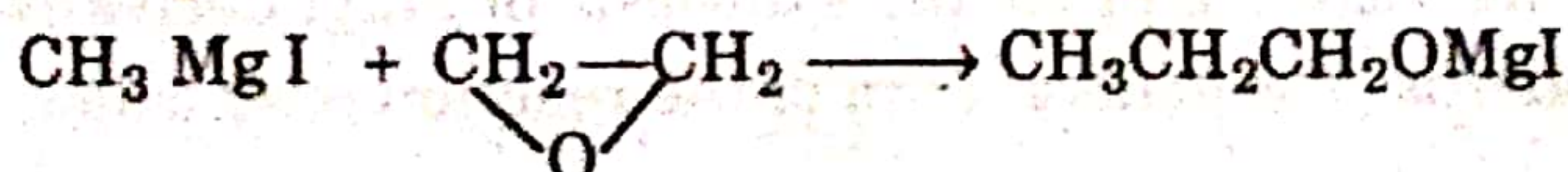
$$RMgBr + R' - \overset{\overset{\textstyle O}{\|}}{C} = Cl \longrightarrow R' - \overset{\overset{\textstyle OMgBr}{|}}{\underset{\underset{\textstyle R}{|}}{C}} - Cl \xrightarrow{-MgBrCl} R' - \overset{\overset{\textstyle O}{\|}}{C} - R$$

$$\xrightarrow{RMgBr}$$

$$R' - \overset{\overset{\textstyle OH}{|}}{\underset{\underset{\textstyle R}{|}}{C}} - R \xleftarrow{H_3O^+} R' - \overset{\overset{\textstyle OMgBr}{|}}{\underset{\underset{\textstyle R}{|}}{C}} - R$$

3. Reaction with Carbon Dioxide: Synthesis of Carboxylic acids: Grignard reagents react with CO_2 to give addition products which on hydrolysis yield carboxylic acids.

$$RMgBr + O = C = O \longrightarrow R - \overset{\overset{\textstyle O}{\|}}{C} - OMgBr \xrightarrow{H_3O^+} RCOOH$$

4. Reaction with Nitriles: Synthesis of Ketones: Nitrile group is polar with negative end on nitrogen and positive end on carbon. Due to this polarity the Grignard reagent adds as a nucleophile forming a ketimine salt which on hydrolysis gives the corresponding ketones.
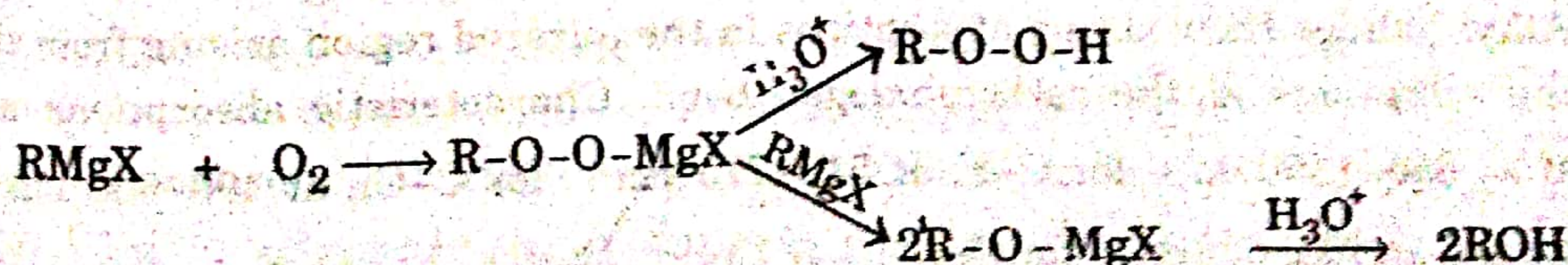
$$^-RMg^+Br + R' - C^{\delta+} \equiv N^{\delta-} \longrightarrow \overset{R}{\underset{R'}{>}}C = \bar{N}\overset{+}{M}gBr \xrightarrow[-HOMgBr]{H_3O^+} \overset{R}{\underset{R'}{>}}C = NH \xrightarrow{H_2O} \overset{R}{\underset{R'}{>}}C = O$$

ketimine
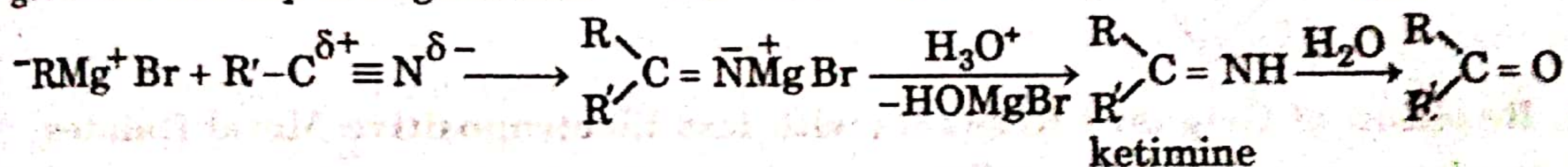
5. Reaction with ethylene oxide. Grigard reagents react with ethylene oxide to give an addition product which on hydrolysis gives primary alcohols.

$$CH_3MgI + \underset{\underset{\textstyle O}{\diagdown \diagup}}{CH_2 - CH_2} \longrightarrow CH_3CH_2CH_2OMgI$$

$$CH_3CH_2CH_2OMgI \xrightarrow[H^+]{H_2O} CH_3CH_2CH_2OH + MgI(OH)$$

6. Reaction with halogenated ethers. Grignard reagents react with lower halogenated ethers to form higher ethers.

$$CH_3CH_2MgBr + ClCH_2OCH_3 \longrightarrow CH_3CH_2CH_2OCH_3 + MgBr(Cl)$$

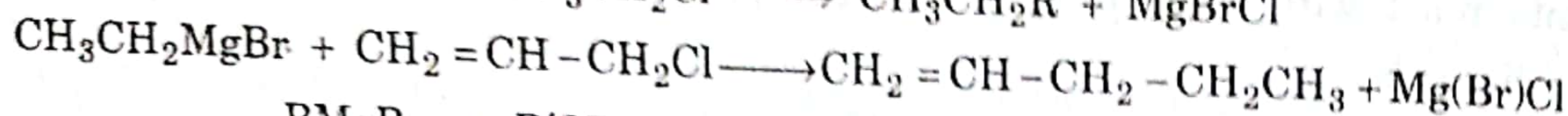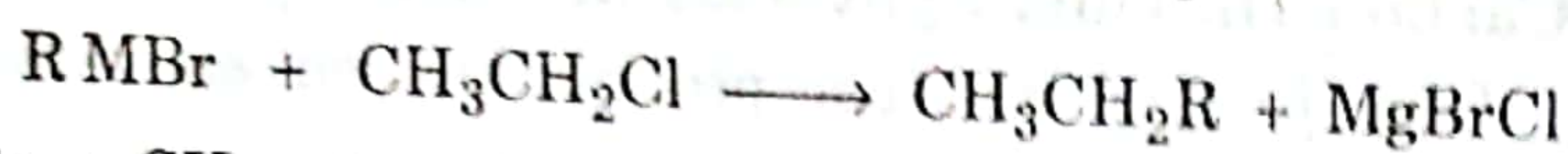$\qquad\qquad$ Chloromethyl ether $\qquad\qquad$ Methyl propyl ether

7. Reaction with oxygen: Synthesis of Alcohols and hydroperoxides: Oxygen reacts with Grignard reagents to give either hydroperoxides or alcohols. The reaction can be used to convert alkyl halides to alcohols without side reactions.

$$RMgX + O_2 \longrightarrow R - O - O - MgX \begin{array}{c} \overset{H_3O^+}{\nearrow} R - O - O - H \\ \underset{RMgX}{\searrow} 2R - O - MgX \xrightarrow{H_3O^+} 2ROH \end{array}$$

8. Reaction with Sulphur. Sulphur reacts with a Grignard reagent to give a product which on hydrolysis gives the corresponding thioalcohol.
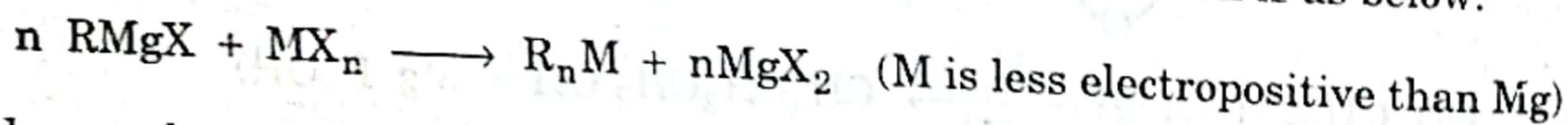
$$CH_3 CH_2 Mg Br + S \longrightarrow CH_3CH_2 S Mg Br \xrightarrow{H_2O, H^+} CH_3CH_2SH + MgBr(OH)$$
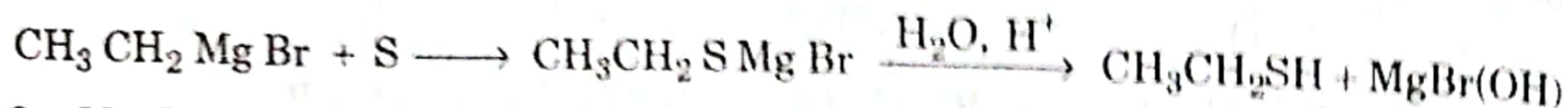
9. Nucleophilic Displacement Reactions: Synthesis of Hydrocarbons. Grignard reagents, being source of carbanions, can participate in SN2 reactions by providing R:⁻ as nucleophiles. Such reactions are more pronounced with alkyl halides having high reactivity towards nucleophilic displacements. However, a few other derivatives of alcohols such as alkyl sulphates, alkyl sulphonates which have good leaving groups can also undergo nucleophilic displacements.
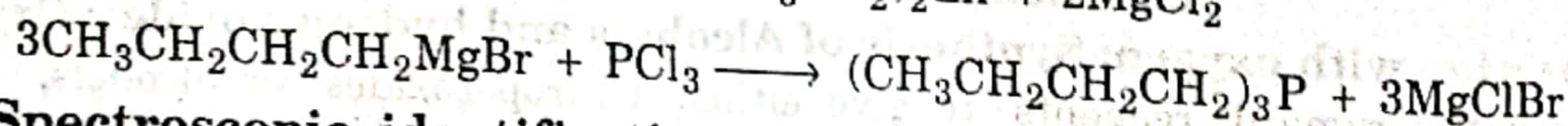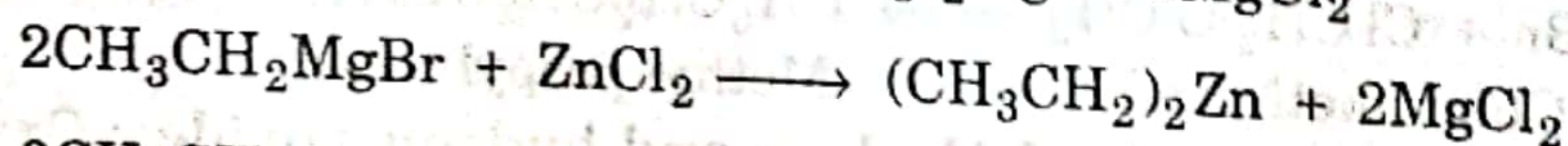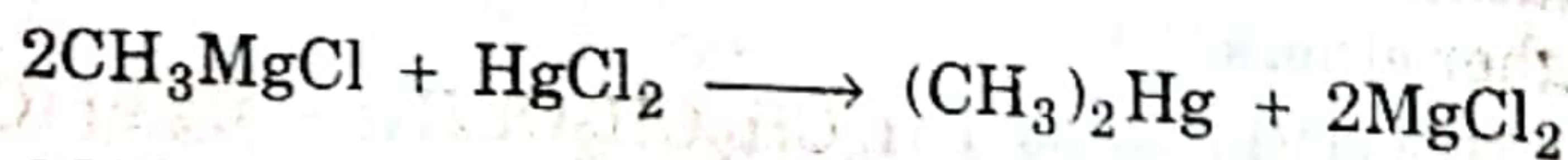
$$R MBr + CH_3CH_2Cl \longrightarrow CH_3CH_2R + MgBrCl$$

$$CH_3CH_2MgBr + CH_2 = CH - CH_2Cl \longrightarrow CH_2 = CH - CH_2 - CH_2CH_3 + Mg(Br)Cl$$

$$RMgBr + R'OTs \longrightarrow R-R' + TsOMgBr$$

10. Reaction with small- ring cyclic ethers (i.e, Epoxides): Synthesis of Alcohols: Grignard reagents react with small-ring cyclic ethers to form alcohols. The product contains two or three carbon atoms more than the alkyl or aryl group.

$$RMgBr + CH_2 - CH_2 \longrightarrow RCH_2CH_2OMgBr \xrightarrow{H_3O^+} RCH_2CH_2OH$$
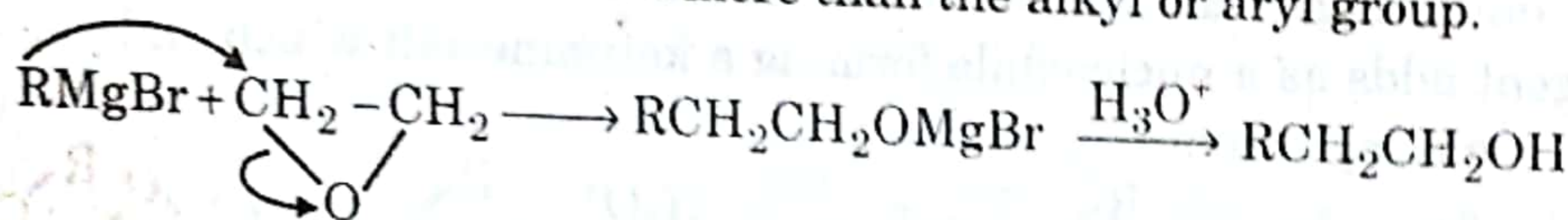
11. Reaction of Grignard Reagents with less Electropositive Metal Halides to produce new organometallic compounds: Grignard reagents react with a number of alkyl halides of less electropositive metals to form new organometallic compounds. These reactions are very useful for the synthesis of alkyl derivatives of Hg, Zn, Cd, Cu, Si and phosphorus. The general form of the reaction is as below:

$$n\ RMgX + MX_n \longrightarrow R_nM + nMgX_2 \quad \text{(M is less electropositive than Mg)}$$

Several examples are given:

$$2CH_3MgCl + HgCl_2 \longrightarrow (CH_3)_2Hg + 2MgCl_2$$

$$2CH_3CH_2MgBr + ZnCl_2 \longrightarrow (CH_3CH_2)_2Zn + 2MgCl_2$$

$$3CH_3CH_2CH_2CH_2MgBr + PCl_3 \longrightarrow (CH_3CH_2CH_2CH_2)_3P + 3MgClBr$$

8.13 Spectroscopic identification of alkyl halides

Alkyl halides show strong absorptions in the infrared region arising from the stretching vibrations of the carbon-halogen bond. Characteristic absorptions are observed at 950–1350 m⁻¹ for C–F, at 510–775 cm⁻¹ for C–Cl, at 490–650 cm⁻¹ for C–Br, and at 465–600 cm⁻¹ for C–I.

Questions

1. Discuss preparation of alkyl halides in details from:

(i) Alkenes   (ii) Alcohols   (iii) Allylic Bromination

(iv) Halogenation of alkanes   (v) Chlormethylation

2. Write short notes on the followings:

(a) The structure of Grignard Reagent   (b) $S_N 2$ reactions

(c) The Hofmann-Saytzeff rule   P.U. 1984

3. (a) Give five methods for the preparation of alkyl halides.

(b) What are Hofmann and Saytzeff rules? Discuss with relevant details.

P.U. 1988.

4. What are Elimination reactions? Discuss different mechanisms involved in the elimination reactions.   P.U. 1983

5. What is a Grignard Reagent? How is it prepared and give four of its synthetic applications in organic chemistry. Also, briefly discuss its structural aspects.

6. Write chemical equations with conditions for the preparation of the following compounds from Grignard Reagent:- (i) Carboxylic acid   (ii) Secondary alcohol (iii) Saturated hydrocarbons   (iv) Tertiary alcohol   P.U. 1995

7. Justify the statement, "Griganrd Reagent is an important synthetic tool in the hands of an Organic chemist".   P.U. 1994

8. Alkyl halides usually undergo nucleophilic displacement reactions by $S_N 1$ or $S_N 2$ mechanism. How do these two mechanism differ?   P.U. 1977

9. What is Grignard Reagent ? How is Grignard reagent used to prepare the folowing compounds:

(i) 3-hexanol (ii) 1-hexanol (iii) Ethanol (iv) 2-propanol   B.Z.U.1989

10. Give equations for the reactions of ethyl iodide with each of the following reagents:-(i) Mg (ii) KCN (iii) Na (iv) NH_S B.Z.U 1988

11. What are $S_N 1$ and $S_N 2$ reactions? Describe the factors which affect the rates of $S_N 1$ and $S_N 2$ reactions.

12. Which alkyl halides would you expect to react more rapidly by an $S_N 2$ mechanism? Explain your answer.

(i) 1- Bromopropane or 2-bromopropane

(ii) sec- butyl bromide or tert-buty bromide

(iii) 1- bromopropane or 1- chloropropane

13. Compare the nucleophilicity (rate of $S_N 2$ reactivity) of

(a) H_2O, OH^-, CH_3O^- and CH_3COO^-

    (b) NH_3 and PH_3

14.   Differentiate between S_N1 and S_N2 reactions.   P.U. 2002.

15.(a) Explain the structure of Grignard's reagent.

   (b) Give reactions of a suitable Grignard's reagent with each of the following:

      (i) Ethyl formate   (ii) Ethyl nitrile   (iii) Ethyl alcohol.

      (iv) Ethylene oxide   (v) Oxygen   P.U. 2001

16.   How will you differentiate nucleophilic substitution and elemination reactions. Discuss with suitable examples and reaction conditions. P.U. 1998

SHORT QUESTIONS

1.   Explain why neopentyl chloride, $(CH_3)_3CCH_2Cl$, a $1°RCl$, does not participate in typical S_N2 reactions.

Ans. The bulky $(CH_3)_3C$ group sterically hinders backside attack by a nucleophile, therefore, neopentyl chloride does not participate in typical S_N2 reactions.

2.   ROH does not react with NaBr, but adding H_2SO_4 forms RBr. Explain.

Ans. Br^-, an extremely weak Bronsted base, cannot displace the strong base OH^-. In acid, $R\overset{+}{O}H_2$ is first formed. Now, Br^- displaces H_2O, which is a very weak base and a good leaving group.

$$ROH + H_2SO_4 \xrightarrow[-HSO_4^-]{} R\overset{+}{O}H_2 \xrightarrow{Br^-} RBr + H_2O$$

3.   Compare the nucleophilicity (rate of S_N2 reactivity) of

    (a) $H_2O, OH^-, CH_3O^-, CH_3COO^-$ (b) NH_3 and PH_3

Ans. (a) When the nucleophilic site is the same atom (here an O), nucleophilicity parallel basicity. Therefore, $CH_3O^- > OH^- > CH_3COO^- > H_2O$.

    (b) When the attacking atoms are different but in the same periodic family, the one with the largest atomic mass is the most reactive. Therefore, $PH_3 > NH_3$. The order is the reverse of basicity.

4.   Give the solvolysis products for the reaction of $(CH_3)_3CCl$ with (a)C_2H_5OH, (b)CH_3COOH

Ans. (a)$(CH_3)_3C-OCH_3$, Methyl t-butyl ether (b) $(CH_3)_3COOCH_3$, t-butyl acetate.

5. $H_2C=CHCH_2Cl$ is solvolyzed faster than $(CH_3)_3CCl$. Explain.

Ans. Solvolyses go by an S_N1 mechanism. Relative rates of different reactants in S_N1 reaction depend on the stabilities of intermediate carbonium ions. $H_2C=CHCH_2Cl$ is more reactive because $[H_2C \cdots C \cdots CH_2]^+$ is more

stable than $(CH_3)_3C^+$.

6. In a polar solvent such as water the S_N1 and E_1 reactions of a tertiary alkyl halide have the same rate. Explain.

Ans. The rate-determining step both for EI and S_N1 is the same and is the first step of the reaction.

$$(H_3C)_3C-X \xrightarrow{\text{slow}} (CH_3)_3\overset{+}{C} + X^-$$

Therefore, both reactions proceed at the same rate.

7. Account for the observations: $(CH_3)_3CI + H_2O \longrightarrow (CH_3)_3COH + HI$ but $(CH_3)_3CI + OH^- \longrightarrow (CH_3)_2C=CH_2 + H_2O + I^-$

Ans. In a nucleophilic solvent in the absence of a strong base, a tert-alkyl halide undergoes as $S_N I$ solvolysis. In the presence of a strong base (OH^-) a tert-alkyl halide undergoes mainly E2 elimination.

8. Indicate the effect on the rate of $S_N I$ and $S_N 2$ reactions of the following:
(a) Doubling the concentration of substrate or Nu^-. (b) using a mixture of ethanol and H_2O or only acetone as solvent. (c) Increasing the number of R groups on the C bonded to the leaving group, L. (d) using a strong Nu^-.

Ans. (a) Doubling either [substrate] or [Nu^-] doubles the rate of $S_N 2$ reaction. For S_N1 reactions the rate is doubled only by doubling [substrate] and is not affected by change in [Nu^-].

(b) A mixture of ethanol and H_2O has a high dielectric constant and therefore enhances the rate of $S_N I$ reactions. This usually has little effect on S_N2 reactions. Acetone has a low dielectric constant and is aprotic and favours S_N2 reactions.

(c) Increasing the number of R groups on the reaction site enhances S_N1 reactivity through electron release and stabilization of R^+. The effect is opposite in S_N2 reactions because bulky alkyl R groups sterically hinder formation of the transition state.

(d) Strong nucleophiles favour S_N2 reactions and do not affect S_N1 reactions.

9. What happens when n-propyl bromide is treated with alcoholic KOH?

Ans. Propene is formed:

$$CH_3CH_2CH_2Br + \text{alc. KOH} \longrightarrow CH_3-CH=CH_2 + KBr + H_2O$$

10. Will the following reactions be primarily displacement or elimination?
(a) $CH_3CH_2CH_2Cl + I^- \longrightarrow$ (b) $(CH_3)_3CBr + CN^-(\text{ethanol}) \longrightarrow$
(c) $CH_3CHBrCH_3 + OH^-(H_2O) \longrightarrow$ (d) $(CH_3)_3CBr + H_2O \longrightarrow$

Ans. (a) S_N2 displacement. I^- is a good nucleophile and a poor base.

(b)   E2 elimination. A tert-alkyl halide reacts with a fairly strong base.

(c)   Mainly $S_N 2$ displacement.

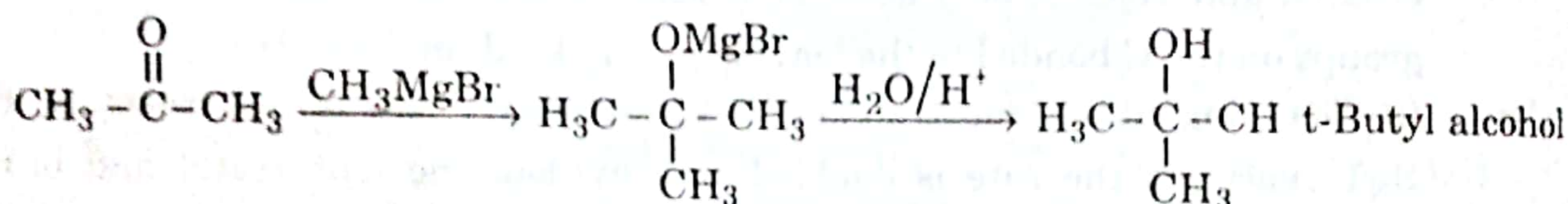(d) $S_N 1$ displacement. H_2O is not basic enough to remove a proton to give elimination.

11. $K^+ \bar{O}C(CH_3)_3$ is used as a base in E2 reactions. (a) How does it compare in effectiveness with $CH_3CH_2NH_2$? (b) Compare its effectiveness in the solvents tert-butyl alcohols and dimethylsulphoxide (DMSO).

Ans. (a) $K^+ \bar{O}C(CH_3)_3$ is more effective because it is more basic than $CH_3CH_2NH_2$. Its larger size also precludes $S_N 2$ reactions.

(b) Its reactivity is greater in aprotic DMSO because its basic anion is not solvated. $(CH_3)_3COH$ reduces the effectiveness of $(CH_3)_3CO^-$ by hydrogen bonding.

12. How will you synthesise tert-butyl alcohol from acetylene?

Ans. $HC \equiv CH \xrightarrow{NaNH_2} HC \equiv \overset{+}{C}Na \xrightarrow{CH_3Br} CH_3C \equiv CH \xrightarrow[HgSO_4]{H_2O/H_2SO_4}$

$$CH_3 - \overset{\overset{O}{\|}}{C} - CH_3 \xrightarrow{CH_3MgBr} H_3C - \overset{\overset{OMgBr}{|}}{\underset{\underset{CH_3}{|}}{C}} - CH_3 \xrightarrow{H_2O/H^+} H_3C - \overset{\overset{OH}{|}}{\underset{\underset{CH_3}{|}}{C}} - CH \text{ t-Butyl alcohol}$$

13. Explain why vinyl chloride is quite unreactive toward displacement in comparison with benzyl chloride?

Ans. Benzyl chloride, $\bigcirc\text{-}CH_2Cl$ gives a stable benzyl carbocation $(C_6H_5\overset{+}{C}H_2)$, because of the distribution of the positive charge over the benzene ring due to resonance. Therefore, it undergoes nucleophilic displacement reaction like the alkyl halide. The C–Cl bond in vinyl chloride is very strong due to the following resonance structures: $CH_2=CH-Br \leftrightarrow \bar{C}H_2-CH-Br^+$, and cannot be replaced easily. Therefore, it does not give displacement reactions.

14. Explain why thionyl chloride, $SOCl_2$, is the best reagent for the preparation of alkyl chloride from alcohols?

Ans. Thionyl chloride $(SOCl_2)$ is the best reagent for the preparation of alkyl chloride from alcohols, because the gaseous by-products leave the reaction mixture ensuring no reverse reaction.

$$ROH + SOCl_2 \longrightarrow RCl + SO_2(g) + HCl(g)$$
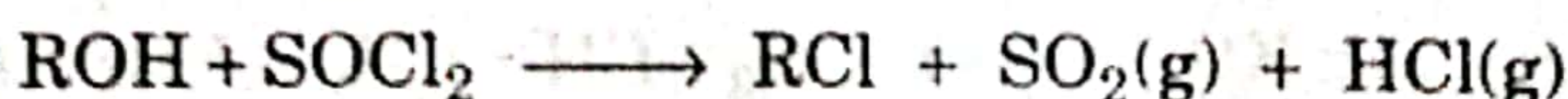
Multiple Choice Questions

1. Which one of the Grignard reactions below could give rise to $CH_3CH_2CH(OH)CH_2CH_3$?

(a) Propanone and methyl Grignard   (b) Butyl Grignard and acetaldehyde

(c) ethyl Grignard and propionaldehyde

(d) methyl ethyl ketone and methyl Grignard **Ans: (c)**

2. Indicate which one of the following statements regarding nucleophilicity is incorrect.

(a) Nucleophilicity is the affinity of a base for a carbon atom.

(b) The rate of S_N2 reaction may be markedly affected by the nucleophilicity of the attacking group.

(c) The more basic electron pairs tend to be more nucleophilic.

(d) F^- is more reactive towards CH_3I than Cl^-. **Ans. (d)**

3. Displacement reactions that proceed by the S_N2 mechanism are most successful with compounds that are:

(a) neopentyl system   (b) primary halides with braches at α-carbon

(c) primary halides with no branches at the β-carbon.

(d) secondary halides with branches at C-2. **Ans. (c)**

4. Which of the following is not true for the S_N2 reaction?

(a) The reaction is of second order   (b) Racemization is evident

(c) There is complete stereochmical inversion.

(d) There is absence of rearrangement. **Ans. (b)**

5. Which of the following would not react with propyl magnesium bromide?

(a) $CH_2 = CHCH_2Cl$ (b) HCHO

(c) $HC \equiv CH$ (d) $CH_3CH_2OCH_2CH_3$ **Ans. (d)**

6. Which of the following statements comparing the nucleophilicity of I^- and Cl^- is true?

(a) I^- is usually more nucleophilic than Cl^-.

(b) I^- is always more nucleophilic than Cl^-.

(c) I^- and Cl^- are approximately equal in nucleophilicity.

(d) I^- is always less nucleophilic than Cl^-. **Ans: (a)**

7. Which of the following is the most reactive in S_N2 reactions.

(a) $(CH_3)_3 CCN$ (b) $(CH_3)_3 CCl$

(c) CH_3CH_2CN (d) CH_3CH_2Cl **Ans: (d)**

8. Which of the following solvents is aprotic solvent?

(a) H_2O (b) $C_2H_5OC_2H_5$ (c) CH_3COOH (d) C_2H_5OH **Ans: (b)**

9. Which of the following solvents is protic solvent?

(a) CH_3OCH_3 (b) CH_3CN (c) HCOOH   (d) $(CH_3)_2SO$ **Ans: (c)**

10. Which of the following gives a tertiary alcohol when treated with Grignard reagents?

(a) HCHO   (b) CH_3CHO (c) CO_2 (d) CH_3COCH_3 **Ans: (d)**

11. n-Propylmagnesium bromide on treatment with CO_2 and further hydrolysis gives:

(a) Acetic acid

(b) Propanoic acid

(c) Butanoic acid

(d) 2-pentanone

Ans: (c)

12. Which of the following compounds does not react with phenylmagnesium bromide?

(a) CH_3COCH_3

(b) $\cdot CH_3CH_2OH$

(c) CH_3COOH

(d) $CH_3CH_2OCH_2CH_3$

Ans: (d)

13. Of the following, which lists the alkyl bromides shown below in order of decreasing reactivity with NaI in acetone.

$CH_3CH_2CH_2Br$ $\qquad$ $(CH_3)_3C-CH_2Br$ $\qquad$ $(CH_3)_2CHCH_2Br$

(1) $\qquad\qquad\qquad$ (2) $\qquad\qquad\qquad$ (3)

(a) 1>2>3 $\qquad$ (b) 1 > 3 > 2 $\quad$ (c) 2 > 3 > 1 $\quad$ (d) 3 > 2 > 1

Ans: (b)

14. Which of the following factors will not affect the S_N1 mechanism:

(a) The polarity of the solvent $\quad$ (b) The nature of the attacking nucleophile

(c) The stability of the carbocation

(d) Nature of leaving nucleophile

Ans: (b)

15. Which one of the following statement is incorrect about S_N1 and S_N2 reactions.

(a) S_N2 is a one step reaction $\qquad$ (b) S_N1 reaction is first order kinetics

(c) The polarity of solvent has no effect on the S_N1 rate reaction.

(d) S_N1 involves a carbocation intermediate

Ans: (c)

16. Which of the following factors will not affect the S_N2 mechanism:

(a) Steric hindrance to backside attack $\quad$ (b) Polarity of the solvent

(c) Nature of attacking nucleophile

(d) Nature of leaving nucleophile

Ans: (d)

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