# HALOALKANES AND HALOARENES

ALKYL HALIDES

Alkyl halides are halogen substituted alkanes. A monohaloalkane is written as R−X, where X is any halogen atom (F, Cl, Br and I). The general formula of monohaloalkanes is $C_nH_{2n+1}X$ while that of a dihaloalkane is $C_nH_{2n}X_2$.
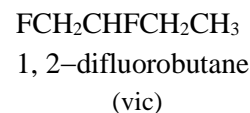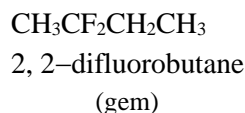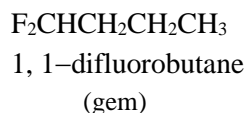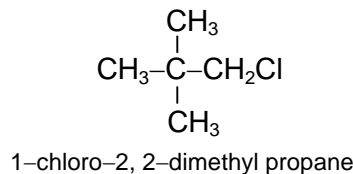
Alkyl halides of a particular kind, in which halogen atom is attached to a saturated carbon, which in turn is linked to unsaturated carbon, are called allyl halides. And when halogen atom is attached to an unsaturated (sp^2) carbon, they are called vinyl halides. For example,

$H_2C=CHCH_2–I$
(allyl iodide)

(vinyl chloride)

(vinyl chloride and allyl bromide)
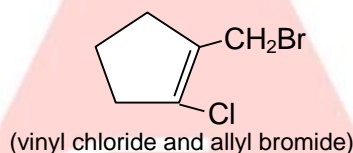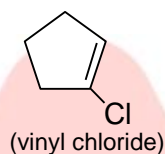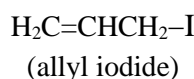
Alkyl halides are classified as primary (1°), secondary (2°) or tertiary (3°), depending upon the type of carbon to which X is bonded. When X is bonded to a carbon, which is bonded to one more carbon is called 1° halide and their general representation is RCH_2X. When X is linked to a carbon, which is bonded to two carbons is called 2° halides and is denoted by R_2CHX. When X is bonded to a carbon, which is attached to 3 carbons is called 3° halides and is designated as R_3CX. CH_3X is unique (not classified as 1°, 2° or 3°) as carbon is bonded to only hydrogens and is simply called methyl halide. Dihaloalkanes with both halogens on same carbon are called gemdihalides and with halogens on adjacent carbons are called vicinal dihalides.
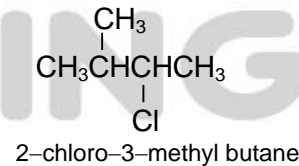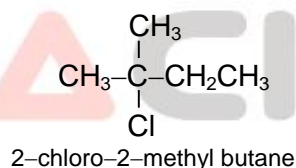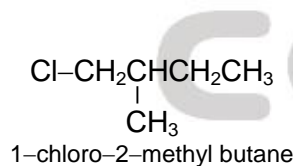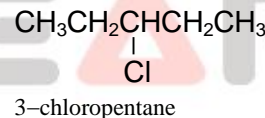
1   IUPAC NOMENCLATURE OF ALKYL HALIDES
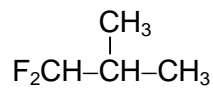
IUPAC nomenclature of alkyl halides with one halogen is haloalkanes and with two similar halogens is dihaloalkanes. If the halogens present are different, they are prefixed in alphabetical order. For example,

$Cl–CH_2CH_2CH_2CH_2CH_3$
1−chloropentane

$CH_3CHCH_2CH_2CH_3$
          |
         Cl
2−chloropentane

$CH_3CH_2CHCH_2CH_3$
              |
             Cl
3−chloropentane

$Cl–CH_2CHCH_2CH_3$
              |
             CH_3
1−chloro−2−methyl butane

$CH_3–\overset{\displaystyle CH_3}{\underset{\displaystyle Cl}{C}}–CH_2CH_3$
2−chloro−2−methyl butane

$CH_3\overset{\displaystyle CH_3}{CH}\underset{\displaystyle Cl}{CH}CH_3$
2−chloro−3−methyl butane

$CH_3–\overset{\displaystyle CH_3}{CH}CH_2CH_2–Cl$
1−chloro−3−methyl butane

$CH_3–\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}–CH_2Cl$
1−chloro−2, 2−dimethyl propane

$F_2CHCH_2CH_2CH_3$
1, 1−difluorobutane
(gem)

$CH_3CF_2CH_2CH_3$
2, 2−difluorobutane
(gem)

$FCH_2CHFCH_2CH_3$
1, 2−difluorobutane
(vic)

FCH$_2$CH$_2$CHFCH$_3$
1, 3–difluorobutane
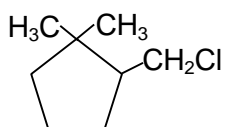
FCH$_2$CH$_2$CH$_2$CH$_2$F
1, 4–difluorobutane
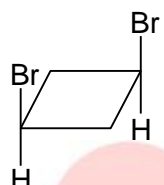
CH$_3$CHFCHFCH$_3$
2, 3–difluorobutane
(vic)

F$_2$CH–CH(CH$_3$)–CH$_3$
1,1–difluoro–2–methyl propane
(gem)

FCH$_2$–CF(CH$_3$)–CH$_3$
1,2–difluoro–2–methyl propane
(vic)

BrCH$_2$CHClCHCl$_2$
3–bromo–1, 1, 2–trichloropropane

2–chloromethyl–1, 1–dimethyl cyclopentane
(with H$_3$C, CH$_3$ and CH$_2$Cl cyclopentane structure)

cis–1, 3–dibromocyclobutane
(cyclobutane with Br, Br, H, H)

(CH$_3$)$_2$C=CHCH$_2$Cl
1–chloro–3–methyl–2–butene.

2 METHODS OF PREPARATION OF ALKYL HALIDES

2.1 FROM ALCOHOLS

2.1.1 By using hydrogen halides

$$R-OH \xrightarrow{HX} R-X + H_2O$$
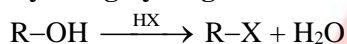
It must be noted that the HX used should be dry, which is produced, in situ, as follows

$$2NaCl + H_2SO_4 \xrightarrow{heat} 2HCl\uparrow + Na_2SO_4$$

$$2NaBr + H_2SO_4 \xrightarrow{heat} 2HBr\uparrow + Na_2SO_4$$

$$6NaI + 2H_3PO_4 \xrightarrow{heat} 6HI\uparrow + 2Na_3PO_4$$
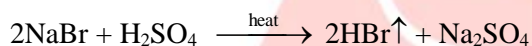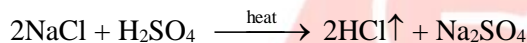
It may be noted that H$_3$PO$_4$ is used in place of H$_2$SO$_4$ to prepare HI. This is because HI is a reducing agent and H$_2$SO$_4$ being an oxidising agent can oxidize it.

The above conversion of alcohol to alkyl halides proceeds via S$_N$1 or S$_N$2 mechanism. Both the mechanisms are operative during the reaction, having competition between them. The type of mechanism followed by an alcohol depends on the structure of alcohol and the type of solvent used for carrying out reaction.
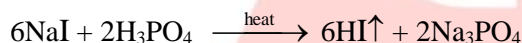
$$R-OH \xrightarrow{H^+} R\overset{\oplus}{-O}H \xrightarrow[-H_2O]{S_N1} R^{\oplus} \xrightarrow{+X^-} R-X + \text{(Some rearranged product, if possible)}$$

(with X$^-$ | S$_N$2 pathway leading to)

$$R-X + H_2O$$
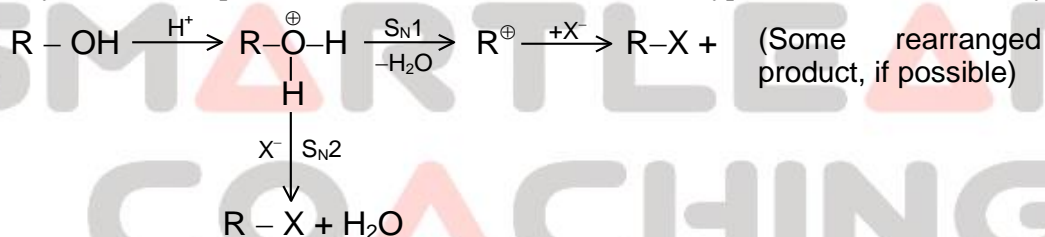
Details about S$_N$1 and S$_N$2 mechanism will be discussed later in this topic.

2.1.2 By using phosphorous halides

$$R-OH + PCl_5 \longrightarrow R-Cl + POCl_3 + HCl$$

$$3R-OH + PCl_3 \longrightarrow 3R-Cl + H_3PO_3$$

$$3R-OH + PBr_3 \longrightarrow 3R-Br + H_3PO_3$$

$$3R-OH + PI_3 \longrightarrow 3R-I + H_3PO_3$$
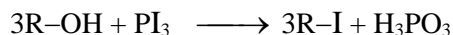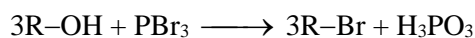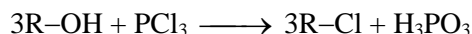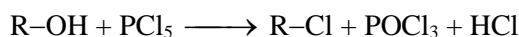
Phosphorous halides are prepared by treating red phosphorous and halogen. The advantage of using phosphorous halides is that the reaction does not involve carbocation intermediate so, it is free from rearrangement.

2.1.3 By using SOCl$_2$ (thionyl chloride)

$$R–OH + SOCl_2 \xrightarrow{\text{Pyridine}} R–Cl + SO_2\uparrow + HCl\uparrow$$
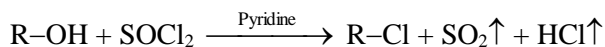
The usefulness of this method is that there is no side product, which has to be separated. The side products are gaseous SO_2, which escapes from the reaction mixture and HCl, which forms a salt with the base (pyridine), named pyridinium chloride ($C_5H_5N^+Cl^-$). The product alkyl chloride has a configuration inverted with respect to the reactant alcohol (if it is chiral) in the presence of pyridine base. In absence of a base and polar solvent, the chiral alcohol gives alkyl chloride with retention of configuration.

Mechanism:

Alcohol first reacts with $SOCl_2$ to form an intermediate chlorosulphite ester, which gives alkyl chlorosulphite and HCl. In presence of pyridine, HCl reacts with it to give pyridinium (PyH^+) ion and chloride (Cl^-) ion. The Cl^- displaces the leaving group $ClSO_2^-$ and chloro sulphite ester decomposes to SO_2, Cl^- and $R–Cl$ with inversion of configuration.

Alkyl chlorosulphite

$$Py + HCl \longrightarrow PyH^+ + Cl^-$$
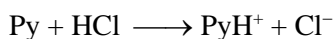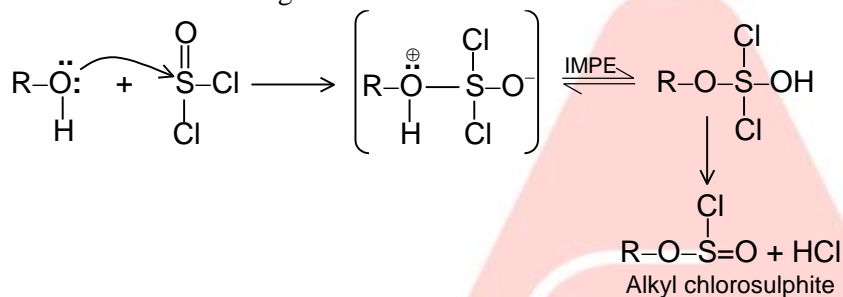
In the absence of a base and polar solvent, the chlorosulphite ester dissociates into an intimate ion–pair. The Cl of the anion of ion–pair attacks from the front side of R^+ to give retention of configuration. The retention is observed because Cl cannot reach the rear of the R^+ group but is close to its front side.

Intimate ion–pair
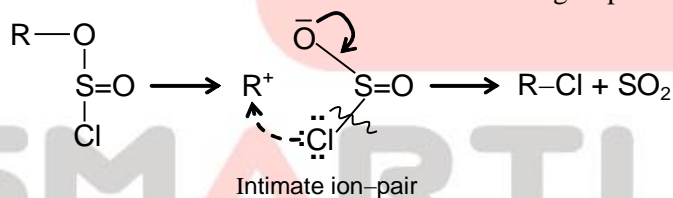
This is referred as S_Ni (substitution nucleophilic internal) mechanism because a part of the leaving group detaches itself from the rest of the leaving group during the process and attacks the substrate.
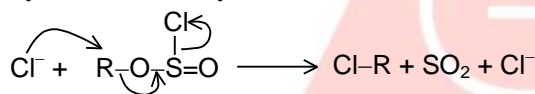
2.2 BY DIRECT HALOGENATION OF HYDROCARBONS

$$R–H \xrightarrow{X_2/h\nu} R–X + HX$$
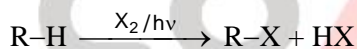
Reactivity of above reaction with respect to type of hydrogen to be replaced follows following order

Tertiary hydrogen > Secondary hydrogen > Primary hydrogen

As far as the reactivity of halogen is concerned, F_2 is most reactive while I_2 is least reactive. Infact, reaction with I_2 is reversible and is carried out in the presence of some oxidising agents like HIO_3, HNO_3 etc. to oxidise HI. Mechanism of this reaction has already been discussed in the lesson "*alkanes*".

2.3 BY HALIDE EXCHANGE

Alkyl iodides can be prepared from alkyl chlorides and alkyl bromides by nucleophilic substitution. This can be achieved by treating them with NaI, using acetone as a solvent. Feasibility of this reaction is due to the solubility of NaI in acetone and more nucleophilic character of I^- ion.

$$R-Cl \xrightarrow[\text{Acetone}]{\text{NaI}} R-I + NaCl$$

$$R-Br \xrightarrow[\text{Acetone}]{\text{NaI}} R-I + NaBr$$
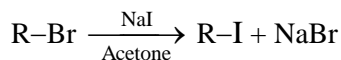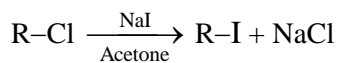
The reaction proceeds by S_N2 mechanism and is possible because NaCl and NaBr are precipitated in the reaction, as they are not soluble in weakly polar aprotic solvent.

2.4 BY ADDITION OF H–X TO ALKENES

Alkyl chlorides, bromides and iodides can be prepared by treating an alkene with corresponding hydrogen halide (HCl, HBr or HI). The addition of these compounds to alkene takes place according to Markownikov's rule. The reaction proceeds by electrophilic addition of H^+ to give more stable carbocation followed by attack of X^-. Anti−Markownikov addition of HBr can be achieved, if the reaction is carried out in presence of peroxides (H_2O_2 or benzoyl peroxide or di−tert−butyl peroxide). Addition of HBr to alkenes in the presence of peroxide follows free radical mechanism.

$$CH_3-CH=CH_2 \xrightarrow{HX} CH_3-\overset{\oplus}{C}H-CH_3 \xrightarrow{X^-} CH_3-\underset{\underset{X}{|}}{C}H-CH_3$$
$$\text{(2° carbocation)}$$

$$CH_3-CH=CH_2 \xrightarrow[\text{Peroxide}]{HBr} CH_3-\overset{\bullet}{C}H-CH_2-Br \xrightarrow{HBr} CH_3-CH_2-CH_2Br + \overset{\bullet}{B}r$$
$$\text{(2° radical)}$$
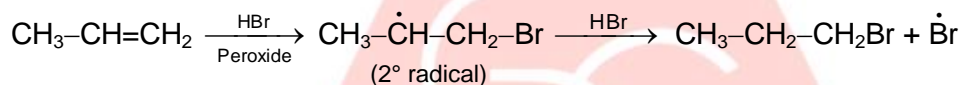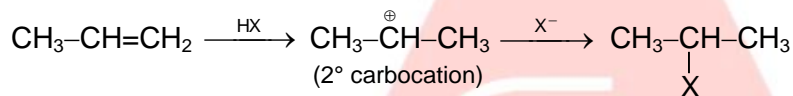
2.5 FROM SILVER SALT OF CARBOXYLIC ACID

$$RCOOAg + X_2 \xrightarrow{CCl_4} R-X + AgX\downarrow + CO_2$$

$(X_2 = Cl_2$ or $Br_2)$
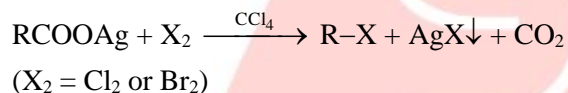
This reaction is called *Hunsdieker reaction.*

Mechanism:

The mechanism is uncertain but probably in the first step acyl hypohalite is formed which then decomposes into free radicals.

$$RCOOAg + X_2 \longrightarrow RCOOX + AgX$$

Initiation step: $RCOOX \longrightarrow RCOO^\bullet + X^\bullet$

Propagation step: $RCOO^\bullet \longrightarrow R^\bullet + CO_2$

$$R^\bullet + RCOOX \longrightarrow R-X + RCOO^\bullet$$
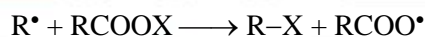
Then, the propagation steps are repeated again. Chain can be terminated at any stage, when any two radicals will collide to form a neutral molecule.

In Hunsdieker reaction, the yield of R−Br is better than R−Cl because O−Br bond is weaker than O−Cl bond as well AgBr is less soluble than AgCl.

The yield and ease of formation of R−X is

1°RX > 2°RX > 3°RX

2.6 PREPARATION OF ALLYLIC OR BENZYLIC HALIDES

(i) Direct halogenation of any aromatic hydrocarbon preferably gives benzylic halide. This is because benzyl radical is resonance stabilized.
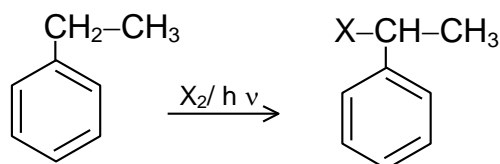
The reaction follows free radical mechanism.

(ii) When alkenes are reacted with halogens at high temperature or in the presence of radiations or any reagent, which is able to provide halogen radicals in low concentrations, then allyl halides are produced.

$$CH_3-CH=CH_2 \xrightarrow{X^\bullet} X-CH_2-CH=CH_2$$

$$CH_3-CH=CH_2 + Cl_2 \xrightarrow[400\ to\ 500^\circ C]{High\ temperature,} \underset{\underset{Cl}{|}}{CH_2}-CH=CH_2$$

$$CH_3-CH=CH_2 + Br_2 \xrightarrow[CCl_4]{NBS\ in} \underset{\underset{Br}{|}}{CH_2}-CH=CH_2$$

$$CH_3-CH=CH_2 \xrightarrow{SO_2Cl_2/h\nu} \underset{\underset{Cl}{|}}{CH_2}-CH=CH_2$$

2.7 PREPARATION OF POLYHALIDES

(i) Addition of halogen to alkenes produces vicinal dihalides.

$$CH_2=CH_2 + X_2 \xrightarrow[in\ CCl_4]{(X_2=Cl_2\ or\ Br_2)} \underset{\underset{X}{|}}{CH_2}-\underset{\underset{X}{|}}{CH_2}$$

(ii) Addition of halogen (Cl_2 or Br_2) to alkynes produces tetrahaloalkanes.

$$HC\equiv CH \xrightarrow[in\ CCl_4]{X_2} \underset{\underset{X}{|}}{CH}=\underset{\underset{X}{|}}{CH} \xrightarrow[in\ CCl_4]{X_2} H-\underset{\underset{X}{|}}{\overset{\overset{X}{|}}{C}}-\underset{\underset{X}{|}}{\overset{\overset{X}{|}}{C}}-H$$
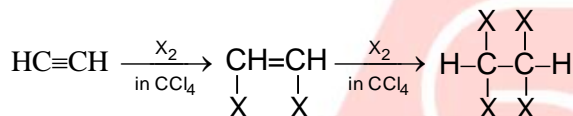
Mechanism of addition of halogen to alkenes and alkynes has been discussed in the lesson "*alkenes*".

2.8 PREPARATION OF VINYL HALIDES

$$CH\equiv CH \xrightarrow[CuCl_2]{HCl} \underset{\underset{Cl}{|}}{CH_2}=CH$$
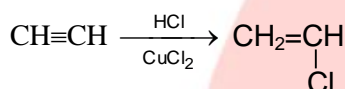
The above reaction proceeds via electrophilic addition as follows

$$CH\equiv CH \xrightarrow{Cu^{2+}} CH\cdots CH \xrightarrow{Cl^-} \underset{\underset{Cl}{|}}{\overset{\ominus}{C}H}=CH \xrightarrow[-H_2O]{H_3O^+} \underset{\underset{Cl}{|}}{CH_2}=CH$$
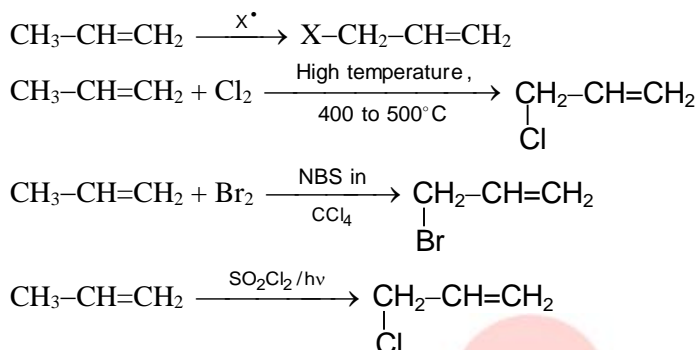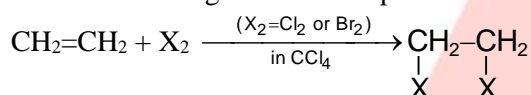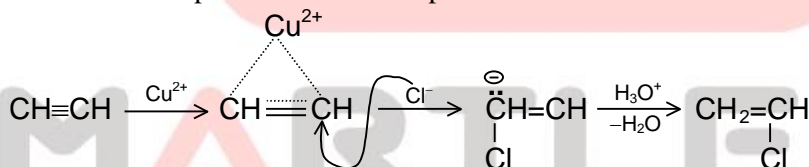
3 GENERAL PHYSICAL PROPERTIES OF ALKYL HALIDES

The physical properties of alkyl halides are influenced by the polarity of C−X bond.
The bond length of C−X bond in alkyl halides follow the order MeI > MeBr >MeCl > MeF. Vapour phase dipole moments in Me−X varies as MeCl > MeF > MeBr > MeI. This is because dipole moment depends on electronegativity of halogen as well as on the bond length.

The order of boiling points of alkyl halides is MeI > MeBr > MeCl > MeF, which is influenced by the decreasing van der Waal forces of attraction between them. Among polyhalogen compounds, boiling point decreases as CCl_4 > $CHCl_3$ > CH_2Cl_2 > CH_3Cl. This is due to accumulation of Cl's on CH_4, increases the molecular mass and size, thus van der Waals forces increases and boiling point also increases.

The densities of alkyl iodides and bromides is more than that of H_2O that the densities of alkyl chlorides and fluorides in less than that of H_2O. The order of densities of alkyl halides and H_2O is RI > RBr > H_2O > RCl > RF and the densities of polychloro methane varies as CCl_4 > $CHCl_3$ > CH_2Cl_2 > H_2O > CH_3Cl. The alkyl halides are in general insoluble in water.

4 **GENERAL CHEMICAL PROPERTIES OF ALKYL HALIDES**

Carbon−halogen bond in alkyl halides is polar owing to the partial positive charge on carbon and partial negative charge on halogen. Due to the positive charge on carbon, any nucleophile can attack the molecule and if it is a stronger nucleophile than halide, it can substitute halide ion. So, nucleophilic substitution reactions are the most common reactions of alkyl halides. Other common reaction shown by them is elimination reaction.

4.1 PREPARATION OF ORGANOMETALLIC COMPOUNDS

$$R-X \xrightarrow[\text{Dry ether}]{\text{Mg}} RMgX$$

(Grignard reagent)

$$R-X \xrightarrow[\text{ether}]{\text{2Li}} R-Li + LiX$$

(Organo lithium compound)

Mechanism:

$$R-X + Li \longrightarrow [R-X]^- Li^+$$

$$[R-X]^- \longrightarrow R^{\bullet} + X^-$$

$$R^{\bullet} + Li \longrightarrow R-Li$$
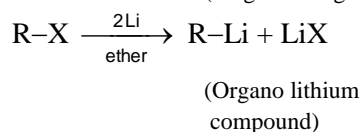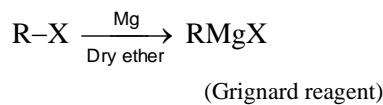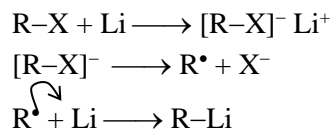
The extra electron in free radical anion occupies an antibonding molecular orbital.

It must be noted that the reactivity of alkyl halides to form organometallic compounds increases from alkyl fluorides to alkyl iodies. Infact, alkyl fluorides do not respond to the reaction and alkyl chloride and aryl halides give considerable yield only if THF (tetrahydrofuran) is used as a solvent. Further, more the stability of free radical, more will be reactivity of alkyl halide to form organometallic compound.

Alkyl organometallic compounds are good source of carbanions (as carbon is more electronegative than the metals) and are very useful in organic synthesis.

4.2 REDUCTION OF ALKYL HALIDES
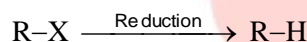
$$R-X \xrightarrow{\text{Reduction}} R-H$$

The reagents used for the reduction of alkyl halides to alkanes are Zn and CH_3COOH, Zn and HCl, Zn and NaOH, Zn − Cu couple and alcohol, aluminium amalgam and alcohol etc.

4.3 WURTZ REACTION

$$2R-X + Na \xrightarrow{\text{Dry ether}} R-R$$

4.4 ELIMINATION REACTIONS OF ALKYL HALIDE

E2 ELIMINATION:

$$CH_3-\underset{\underset{Br}{|}}{CH}-CH_2CH_3 + CH_3O^- \xrightarrow{CH_3OH} \underset{(80\%)}{CH_3CH=CHCH_3} + \underset{(20\%)}{CH_2=CHCH_2CH_3}$$
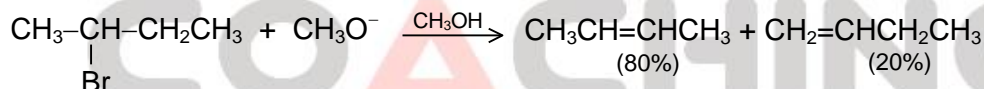
2−bromobutane has two structurally different β−carbons from which a proton can be removed. Thus, it leads to the formation of 2 products (2−butene and 1−butene). The anti−coplanar transition state for the formation of two products is

Transition state leading to 2−butene

Transition state leading to 1−butene
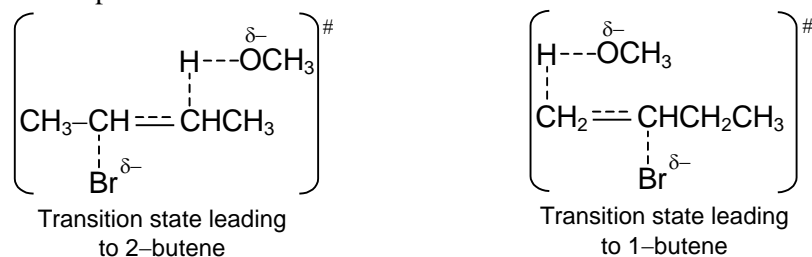
The transition state leading to 2–butene is more stable than that leading to the formation of 1–butene, as this transition state has more hyperconjugable hydrogens. Thus, 2–butene is a more stable product than 1–butene and is formed in greater quantity than 1–butene. The stability of the product is governed by Saytzeff's rule (according to which more substituted alkene is the major product).

If the base in an E2 reaction is sterically bulky and hindered, it will preferentially remove the most accessible hydrogen. For example, when 2–bromo–2–methyl butane is treated with bulky t–butoxide ion, base removes one of the more exposed terminal hydrogens, which leads to the less substituted alkene.

$$CH_3-\underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2CH_3 + CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-O^- \xrightarrow{(CH_3)_3C-OH} \underset{(28\%)}{CH_3\overset{\overset{CH_3}{|}}{C}=CHCH_3} + \underset{(72\%)}{CH_2=\overset{\overset{CH_3}{|}}{C}-CH_2CH_3} + (CH_3)_3COH + Br^-$$

The less substituted product is called Hoffmann's product and is governed by Hoffmann's rule (according to which less substituted alkene is the major product).

Although the major product of the E2 dehydrohalogenation of alkyl chlorides, alkyl bromides and alkyl iodides is most substituted alkene (except in case of bulkier base) but the major product of E2 dehydrohalogenation of alkyl fluorides is the least substituted alkene, even with less hindered bases.

$$CH_3-\underset{\underset{F}{|}}{\overset{\overset{F}{|}}{C}H}-CH_2CH_2CH_3 + CH_3O^- \xrightarrow{CH_3OH} \underset{70\%}{CH_2=CHCH_2CH_2CH_3} + \underset{30\%}{CH_3CH=CHCH_2CH_3}$$
$$+ CH_2OH + F^-$$

Of the halogen ions, F^- is the strongest base and is thus the poorest leaving group. So, when a base begins to remove a proton from an alkyl fluorid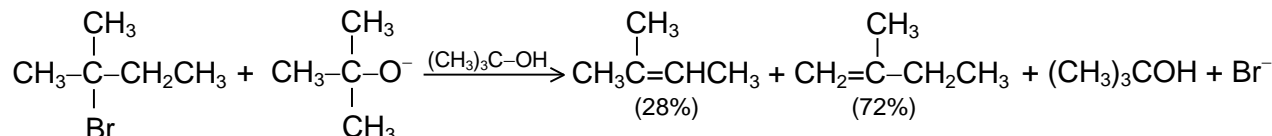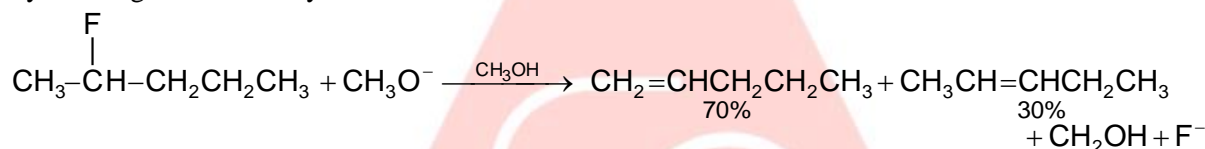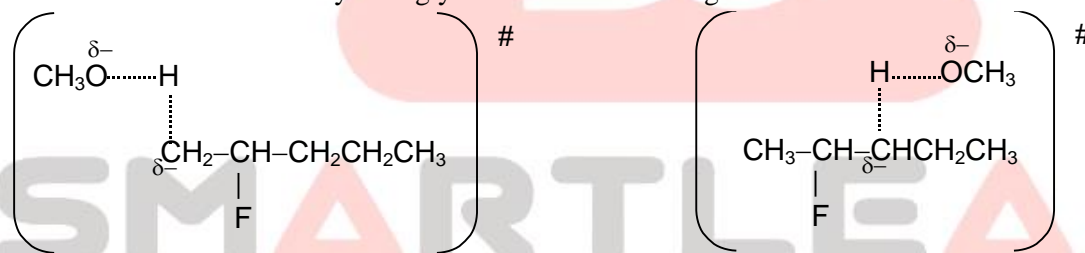e, the F^- has less tendency to leave than do the other halide ions. As a result negative charge develops on the carbon that is losing the proton, giving the transition state a carbanionic character rather than an alkene character. This kind of mechanism is called E1cB mechanism. The carbanionic transition state is stabilized by strongly electron–withdrawing fluorine.

$$\left[\begin{array}{l} \overset{\delta-}{CH_3O}\cdots\cdots H \\ \quad\quad | \\ \underset{\delta-}{CH_2}-CH-CH_2CH_2CH_3 \\ \quad\quad\quad | \\ \quad\quad\quad F \end{array} \right]^{\#}$$

$$\left[\begin{array}{l} \quad\quad\quad H\cdots\cdots\overset{\delta-}{OCH_3} \\ \quad\quad\quad | \\ CH_3-CH-\underset{\delta-}{C}HCH_2CH_3 \\ \quad\quad\quad | \\ \quad\quad\quad F \end{array} \right]^{\#}$$

Transition state leading to 1–pentene   **Transition state leading to 2–pentene**

The transition state leading to 1–pentene has the developing negative charge on a primary carbon. This is more stable than the transition state leading to 2–pentene, which has the developing negative charge on a secondary carbon. Because the transition state leading to the formation of 1–pentene is more stable, thus 1–pentene is the major product in this reaction.

$$CH_2=CHCH_2\underset{\underset{Cl}{|}}{\overset{\overset{CH_3}{|}}{C}H}CHCH_3 \xrightarrow{OH^-} \underset{\substack{(major\ product - a \\ conjugated\ diene)}}{CH_2=CHCH=\overset{\overset{CH_3}{|}}{C}HCHCH_3} + \underset{(minor\ product - an\ isolated\ diene)}{CH_2=CHCH_2CH=\overset{\overset{CH_3}{|}}{C}CH_3} + H_2O + Cl^-$$

$$C_6H_5-CH_2\underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{C}H}CHCH_3 \xrightarrow{OH^-} \underset{(major\ product)}{C_6H_5-CH=\overset{\overset{CH_3}{|}}{C}HCHCH_3} + \underset{(minor\ product)}{C_6H_5-CH_2CH=\overset{\overset{CH_3}{|}}{C}CH_3} + H_2O + Br^-$$
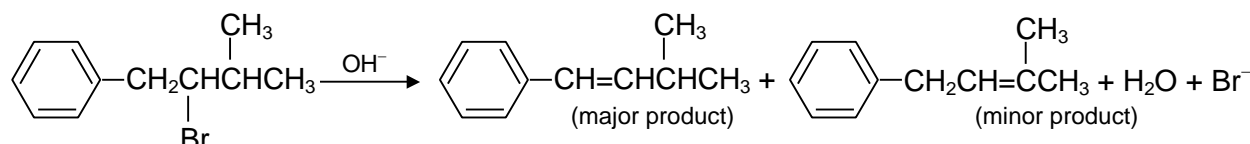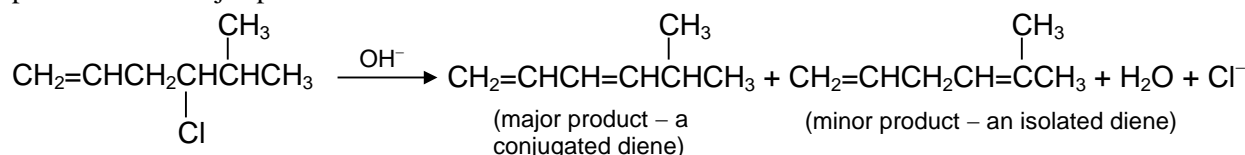
In the given reactions, Saytzeff's rule is not followed, although the substrates are alkyl chlorides/bromides and bases are also small, because the rule does not take into account the fact that conjugated double bonds are more stable than isolated double bonds.

E1 ELIMINATION:

$$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br + H_2O \longrightarrow CH_3-\overset{\overset{CH_3}{|}}{C}=CH_2 + H_3O^+ + Br^-$$
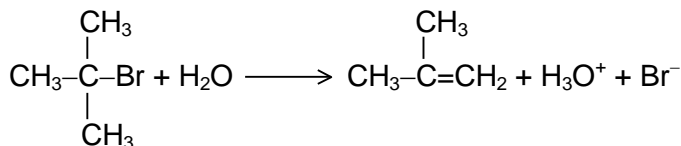
t–Butyl bromide undergoes hydrolysis in two steps. In the first rate–limiting step, the alkyl halide dissociates heterolytically. In the second step, the base forms an elimination product by removing a proton from a carbon adjacent to the positively charged carbon. Increasing the concentration of base has no effect on the rate of the reaction.

Step I : $$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br \underset{slow}{\rightleftharpoons} CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}\oplus + Br^-$$

Step II : $$CH_3-\underset{\underset{CH_2}{|}\overset{}{-}H \;\; H_2\ddot{O}:}{\overset{\overset{CH_3}{|}}{C}}\oplus \xrightarrow{fast} CH_3-\underset{\underset{CH_2}{\|}}{\overset{\overset{CH_3}{|}}{C}} + H_3O^+$$

When two elimination products can be formed, the major product is generally the one obtained by following Saytzeff's rules.
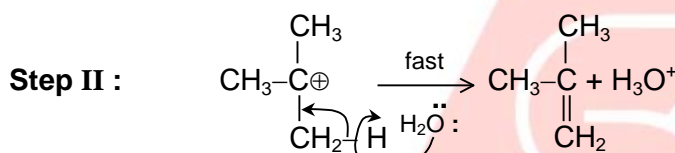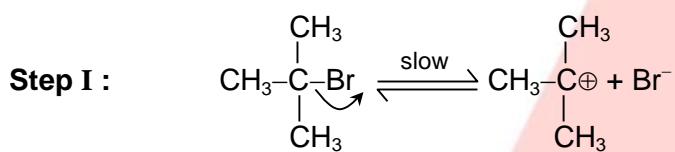
$$CH_3CH_2-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Cl + H_2O \longrightarrow \underset{\text{(major product)}}{CH_3CH=\overset{\overset{CH_3}{|}}{C}-CH_3} + \underset{\text{(minor product)}}{CH_3CH_2\overset{\overset{CH_3}{|}}{C}=CH_2} + H_3O^+ + Cl^-$$
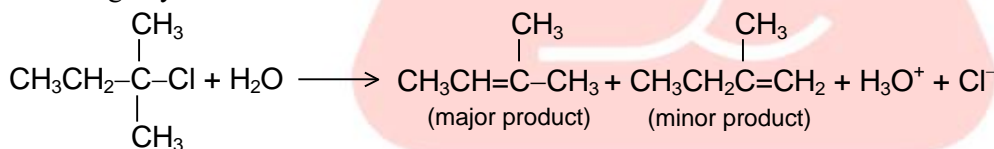
The energy profile diagram for this reaction is
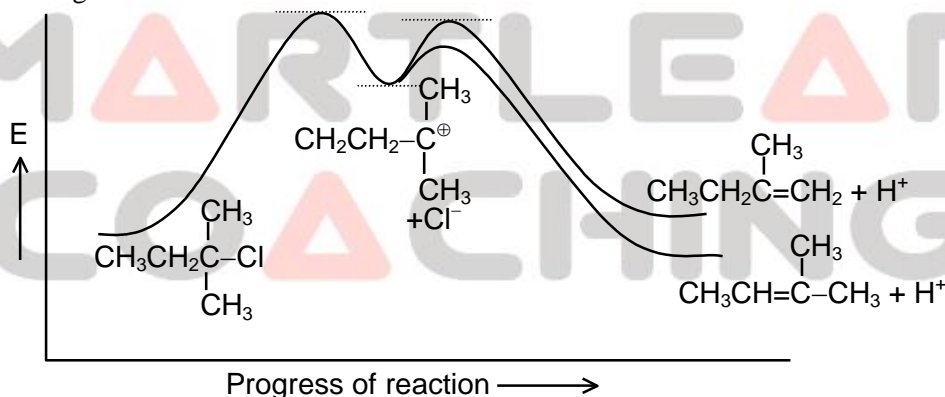
Rate of E1 reaction depends on the ease with which the leaving group leaves and the stability of the carbocation formed. Thus, the relative reactivities of a series of alkyl halides with the same leaving group parallels the relative stabilities of carbocations and the order is represented as

3° benzylic ≈ 3° allylic > 2° benzylic ≈ 2° allylic ≈ 3° alkyl > 1°benzylic ≈ 1° allylic ≈ 2° > 1° > vinyl

Because E1 reaction involves formation of carbocation as intermediate, so rearrangement of the carbon skeleton is also frequently observed. For example,

2° carbocation

3° carbocation

2° carbocation

1, 2–hydride shift

$CH_3CH=CH-CH=CHCH_2CH_3$ $\xleftarrow{-H^+}$ $CH_3CH=CH\overset{\oplus}{C}HCH_2CH_2CH_3$ $\longleftarrow$

2° allylic carbocation
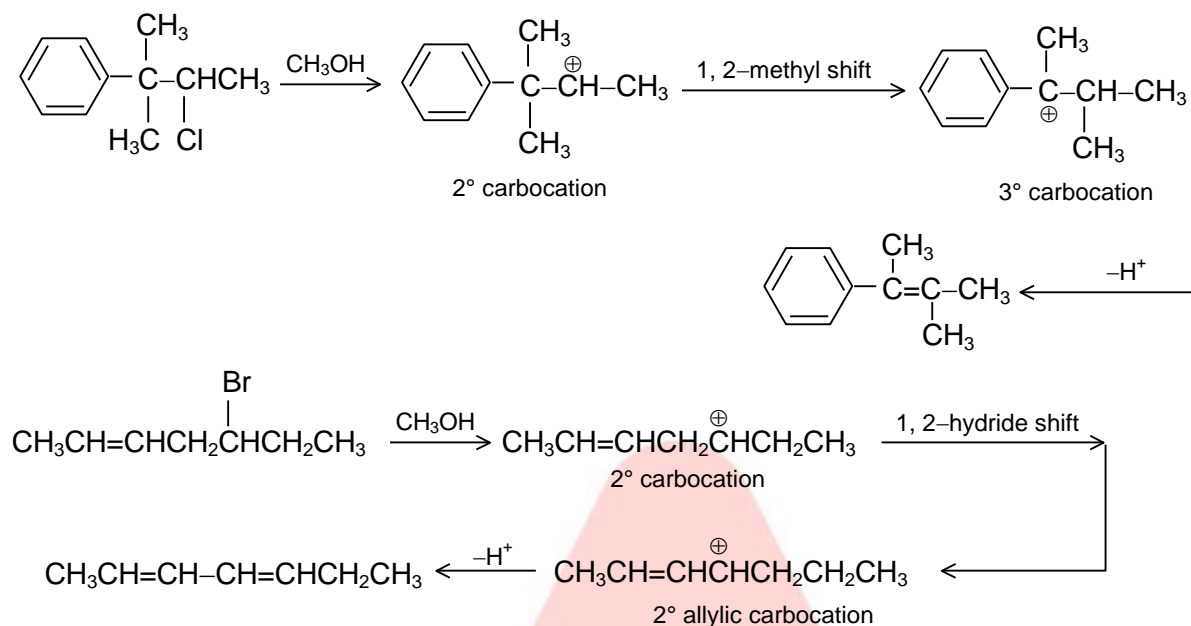
In this example, the secondary carbocation undergoes a 1, 2–hydride shift to form a more stable secondary allylic carbocation.

COMPETITION BETWEEN E1 AND E2 REACTIONS:

Primary alkyl halides undergo only E2 elimination reactions. They cannot undergo E1 reactions because of the difficulty encountered in forming primary carbocations. Secondary and tertiary alkyl halides can undergo either E1 or E2 reactions.

For those alkyl halides that can undergo both E1 and E2 reactions, the E2 reaction is favoured by a high concentration of a strong base and polar aprotic solvent while E1 reaction is favoured by a weak base and a polar protic solvent.

An important reaction of alkyl halides i.e. aliphatic nucleophilic substitution is dealt as a separate heading.

5 ALIPHATIC NUCLEOPHILIC SUBSTITUTION

In nucleophilic substitutions, the attacking reagent (nucleophile) brings an electron pair to the substrate, which uses this pair to form a new bond and the leaving group goes away with an electron pair. When nucleophile is a solvent, the reaction is called *solvolysis*.

$R-X + Y \longrightarrow R-Y + X$

Y is a nucleophile, which may be neutral or negatively charged while RX may be neutral or positively charged.

$R-I + HO^- \longrightarrow R-OH + I^-$

$R-I + NMe_3 \longrightarrow R-\overset{+}{N}Me_3 + I^-$

$R-\overset{+}{N}Me_3 + OH^- \longrightarrow R-OH + NMe_3$

$R-\overset{+}{N}Me_3 + {}^+H_2S \longrightarrow R-\overset{+}{S}H_2 + NMe_3$

The reaction scheme for R–X:

$$R-X \xrightarrow{\text{aq. NaOH or KOH or moist Ag}_2O} R-OH + NaX \text{ or } KX + AgX$$

$$\xrightarrow{R'O^-Na^+} R-O-R' + NaX$$

$$\xrightarrow{\text{KSH or NaSH}} R-SH + KX \text{ or } NaX$$

$$\xrightarrow{R'S^-Na^+} R-S-R' + NaX$$

$$\xrightarrow{NH_3} R-NHR' + HX$$

$$\xrightarrow{R'NH_2} R-NR'_2 + HX$$

$$\xrightarrow{R'_2NH_2} R-NR'_2 + HX$$

$$\xrightarrow{AgCN/KCN} R-C\equiv N + R-N{=}C + X^-$$

$$\xrightarrow{^-C\equiv C-R'} R-C\equiv C-R' + X^-$$

$$\xrightarrow{I^-,\ acetone} R-I + X^-$$

$$\xrightarrow{NO_2^-} R-NO_2 + R-ONO + X^-$$
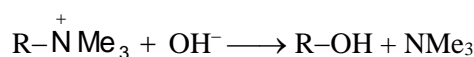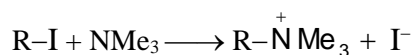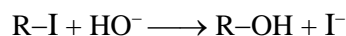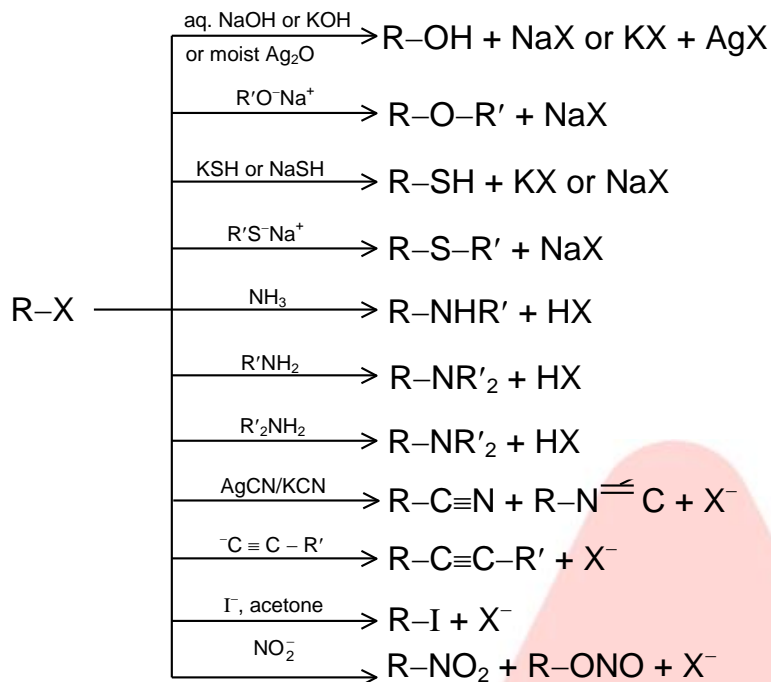
Before embarking on the mechanism of nucleophilic substitution reactions in alkyl halides, we must know certain basic terms.

5.1 HSAB (HARD AND SOFT ACID–BASE) PRINCIPLE

According to hard and soft acid–base principle of Pearson, hard acids are those species, which have less tendency to accept an electron pair (like H^+, Li^+, Mg^{2+}, Cr^{3+}, Al^{3+} etc.)
and hard bases are those species, which have less tendency to donate electron pair (like F^-, O^{2-} etc.) A hard base prefers a hard acid whereas a soft base prefers a soft acid.

5.2 BASICITY AND NUCLEOPHILICITY

A negatively charged species can function as nucleophile as well as like base but its nucleophilicity and basicity are different. Nucleophilicity of the species is the ability of the species to attack an electrophilic carbon while basicity is the ability of the species to remove H^+ from an acid. Let us have a species, B^-. Its function as a nucleophile is shown as

and its role as base is indicated as

$$B^{\ominus} + H{-}A \rightleftharpoons B{-}H + A^{\ominus}$$

The nucleophilicity is determined by the kinetics of the reaction, which is reflected by its rate constant (k) while basicity is determined by the equilibrium constant, which is reflected by its K_b.

The order of nucleophilicity of different species depends on the nature of solvent used.
For instance, let us take F^-, Cl^-, Br^- and I^- with their counter cation as Na^+ and see their nucleophilicity order in different solvents. There are four categories of solvents, namely non–polar (CCl_4), polar protic (H_2O), polar aprotic (CH_3SOCH_3) and weakly polar aprotic(CH_3COCH_3).

Polar solvents are able to dissociate the salts i.e. ion–pairs can be separated. On the other hand, non–polar and weakly polar solvents are unable to dissociate salts, so they exist as ion–pairs. The ion–pairing is strong when ions are small and have high charge density.

In non–polar and weakly polar aprotic solvents, all the salts will exist as ion–pairs.

The ion–pairing will be strongest with the smallest anion (F^-) and weakest with the largest anion (I^-), thus the reactivity of X^- decreases with decreasing size. Thus, the nucleophilicity order of X^- in such solvents would be

$$I^- > Br^- > Cl^- > F^-$$
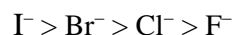
In polar protic solvents, hydrogen bonding or ion–dipole interaction diminishes the reactivity of the anion. Stronger the interaction, lesser is the reactivity of anion. F^- ion will form strong H–bond with polar protic solvent while weakest ion–dipole interaction will be with I^- ion. Thus, the nucleophilicity order of X^- in polar protic solvent would be $I^- > Br^- > Cl^- > F^-$.

Polar aprotic solvents have the ability to solvate only cations, thus anions are left free.

The reactivity of anions is then governed by their negative charge density (i.e. their basic character). Thus, the order of nucleophilicity of X^- in polar aprotic solvents would be

$$F^- > Cl^- > Br^- > I^-$$
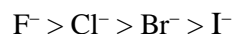
On this basis, certain nucleophilicity orders are

  (i) In polar protic solvents, $HS^- > HO^-$

  (ii) In weakly polar aprotic solvents, $CsF > RbF > KF > NaF > LiF$

 (iii) Bases are better nucleophiles than their conjugate acids. For example,

     $OH^- > H_2O$ and $NH_2^- > NH_3$

  (iv) In non–polar solvents, $^-CH_3 > {}^-NH_2 > {}^-OH > {}^-F$

  (v) When nucleophilic and basic sites are same, nucleophilicity parallels basicity. For example,

     $RO^- > HO^- > R - CO - O^-$

  (vi) When the atom bonded to nucleophilic site also has an unshared pair of electrons, nucleophilicity of species increases. For example,
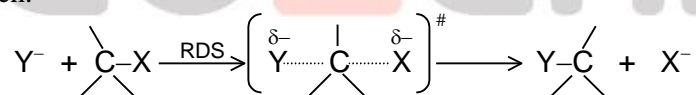
     $HOO^- > HO^-$ and $H_2\ddot{N}{-}\ddot{N}H_2 > \ddot{N}H_3$
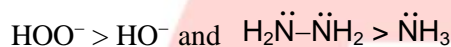
Edwards and Pearson gave following order of nucleophilicity for S_N2 reactions in protic solvents.

   $RS^- > ArS^- > I^- > CN^- > OH^- > N_3^- > Br^- > ArO^- > Cl^- > pyridine > AcO^- > H_2O.$
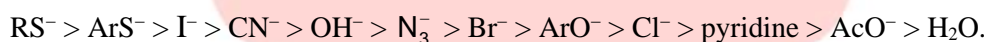
Several distinct mechanisms are possible for aliphatic nucleophilic substitution reactions. By far the most common are S_N1 and S_N2 mechanisms.

6 S_N2 REACTION

S_N2 stands for substitution nucleophilic bimolecular. In this mechanism, there is a backside attack of the nucleophile. The nucleophile approaches the substrate from a position 180° away from the leaving group. The reaction is a one–step process with no intermediate, it involves a transition state. The C–Y bond is formed as C–X bond is broken.

$$Y^- + \overset{|}{\underset{|}{C}}{-}X \xrightarrow{RDS} \left[\overset{\delta-}{Y} \cdots \overset{|}{\underset{|}{C}} \cdots \overset{\delta-}{X} \right]^{\#} \longrightarrow Y{-}\overset{|}{\underset{|}{C}} + X^-$$

The energy necessary to break C–X bond is supplied by the simultaneous formation of C–Y bond. The group X must leaves as Y comes in, because at no time can the carbon atom have more than 8 electron in its outermost shell. In the transition state, bond forming and bond breaking are simultaneous.

In the transition state, the carbon is sp^2 hybridized with a p–atomic orbital available for overlapping of its lobes with an orbital of the incoming $:Nu^-$ while the other lobe overlaps with an orbital of the leaving group X^-. The reaction is initiated by $:Nu^-$ beginning to overlap with the small lobe (tail) of the sp^3 hybrid orbital bonding with X. In order to provide more bonding volume to give a stronger bond, the tail becomes the larger lobe (head) and the head becomes the tail, inverting the configuration of carbon. The configuration of the original compound

is opposite than the compound obtained. Inversion in configuration implies change in configuration from R to S or

S to R and not from $(+)$ to $(-)$ or $(-)$ to $(+)$. This inversion in configuration would be observed only when the leaving group and incoming nucleophile have same priority relative to other atoms or group of atoms.

As **:Nu⁻** starts to bond to carbon, it loses some of its full charge and in the transition state has a δ^- charge, as does X as it begins to leave as an anion.

In S_N2 mechanism, the front side attack has never been observed. In a hypothetical front side attack, both the nucleophile and nucleofuge (leaving group) would have to overlap with the same lobe of p−orbital whereas the backside attack involves the maximum amount of overlap throughout the course of reaction. During the transition state, the three non−reacting groups and the central carbon atom are approximately co−planar.

sp³ hybridized — S configuration

sp² hybridized with p orbital — Transition State

sp³ hybridized — R configuration (if Nu and X are of same priority)
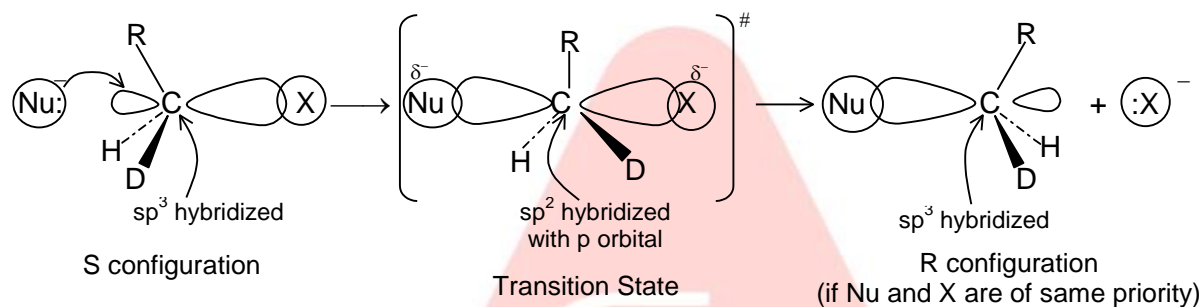
In the given representation it is clear that the carbon atom is linked to five groups, so it is highly overcrowded. Due to high overcrowding, it is easier to make a decision that bigger the groups attached to carbon, more unstable will be the transition state. Hence, steric factors play

an important role in S_N2 mechanism. Thus, the reactivity of alkyl halides towards S_N2 reaction is as follows,
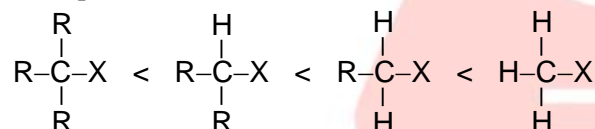
The rate law for the S_N2 reaction is

$$\text{Rate} = k\,[R{-}X]\,[Nu^-]$$

Rate of the S_N2 reaction is dependent on the concentration of RX and Nu⁻ both.

S_N2 reactions are stereospecific because stereoisomeric reactants give stereochemically different products. They are also stereoselective because they form exclusively or predominantly only one of a possible pair of enantiomers or one of the possible diastereoisomers.

Let us see the effect of solvent polarity on the rate of S_N2 reactions. For most of the S_N2 reactions, the rate decreases with the increasing polarity of solvents, so S_N2 reactions are more favoured in non−polar solvents.

We know that successful S_N2 displacements are exothermic in nature and its energy profile can be shown as

Progress of reaction ⟶
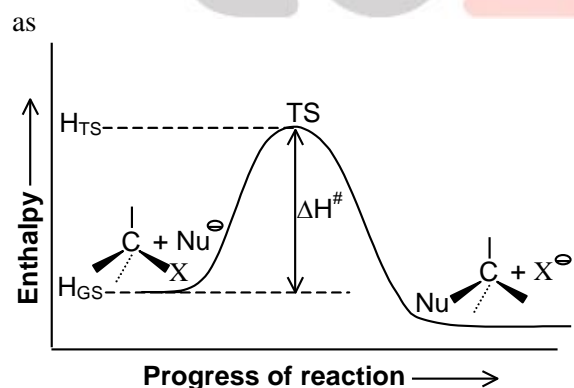
In general, if we change solvent that increases $\Delta H^{\#}$ would decrease the rate of S_N2 reaction. $\Delta H^{\#}$ can be inc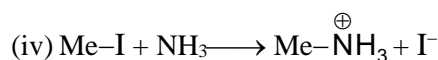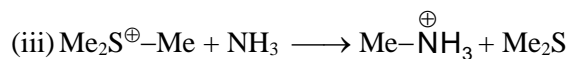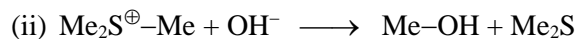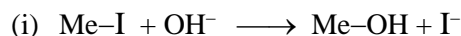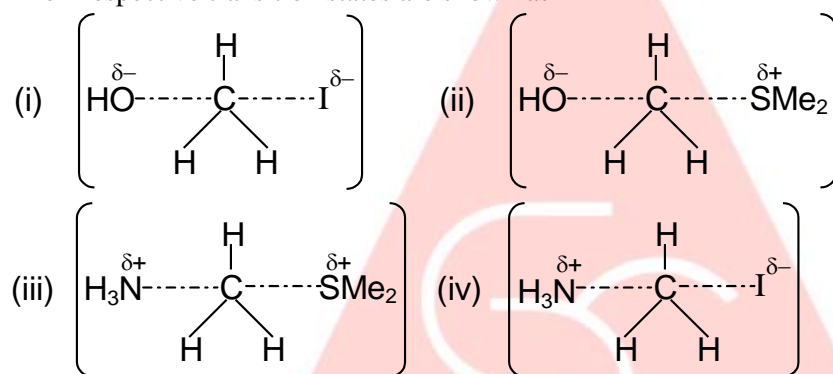reased by decreasing H_{GS} or by increasing H_{TS} or by doing both. Conversely, any change in solvent that decreases $\Delta H^{\#}$ will increase the S_N2 rate and the decrease in $\Delta H^{\#}$ can be achieved by increasing H_{GS} or by decreasing H_{TS} or by doing both.

Let us consider four charge−type of S_N2 reactions and see the effect of change of solvent polarity on them.

(i) $Me{-}I + OH^- \longrightarrow Me{-}OH + I^-$

(ii) $Me_2S^{\oplus}{-}Me + OH^- \longrightarrow Me{-}OH + Me_2S$

(iii) $Me_2S^{\oplus}{-}Me + NH_3 \longrightarrow Me{-}\overset{\oplus}{N}H_3 + Me_2S$

(iv) $Me{-}I + NH_3 \longrightarrow Me{-}\overset{\oplus}{N}H_3 + I^-$

Their respective transition states are shown as

(i) $\left[\begin{array}{c} H \\ \overset{\delta-}{HO}{-}{-}{-}{-}{-}\overset{|}{C}{-}{-}{-}{-}{-}\overset{\delta-}{I} \\ H \quad\quad H \end{array}\right]$ (ii) $\left[\begin{array}{c} H \\ \overset{\delta-}{HO}{-}{-}{-}{-}{-}\overset{|}{C}{-}{-}{-}{-}{-}\overset{\delta+}{SMe_2} \\ H \quad\quad H \end{array}\right]$

(iii) $\left[\begin{array}{c} H \\ \overset{\delta+}{H_3N}{-}{-}{-}{-}{-}\overset{|}{C}{-}{-}{-}{-}{-}\overset{\delta+}{SMe_2} \\ H \quad\quad H \end{array}\right]$ (iv) $\left[\begin{array}{c} H \\ \overset{\delta+}{H_3N}{-}{-}{-}{-}{-}\overset{|}{C}{-}{-}{-}{-}{-}\overset{\delta-}{I} \\ H \quad\quad H \end{array}\right]$

Increasing the polarity of the solvent stabilizes charged ground state species, thereby lowering H_{GS} and also stabilizes charged transition state that would lower H_{TS}. The enthalpy of a fully charged ion is lowered more than a species with diffused charge.

In case of reactions (i), (ii) and (iii), the charge in the transition state is more diffused than the charge on the reactant species. Thus, increasing the polarity of the solvent lowers H_{GS} more than H_{TS}. Thus, increasing $\Delta H^{\#}$ and decreasing the rate. Hence, such reactions proceed with faster rate in non−polar solvents.

But in reaction (iv), the reactants are uncharged while the transition state has diffused charge. Thus, increasing solvent polarity lowers H_{TS} but not H_{GS}. So, $\Delta H^{\#}$ decreases and the rate increases. Hence, such reactions proceed with a faster rate in polar solvents than in non−polar solvents.

Thus, in general reactions with charged reactants, the rate of S_N2 reactions decreases with increasing polarity of solvent while for reactions with uncharged reactants, the S_N2 rate increases with increasing polarity of solvent.

7 S_N1 REACTION

S_N1 stands for substitution nucleophilic unimolecular. The ideal version of S_N1 consists of two steps. The first step is the slow ionization of the substrate and is rate limiting step. The second step is the rapid reaction between the carbocation and nucleophile.

$R{-}X \xrightarrow{\text{RDS}} R^+ + X^-$ Step 1 (slow)

$R^+ + Y^- \longrightarrow R{-}Y$ Step 2 (fast)
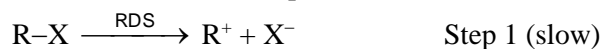
Solvent assists the ionization process, since the energy of activation required for breaking of the bond is largely recovered from solvation of ions produced. In pure S_N1 reactions, solvent molecules assist the departure of leaving group from the front side.

The carbocation generated by first step has an sp^2 hybridized carbon i.e. the structure is flat (trigonal planar). Thus, nucleophile will be able to attack the carbocation from the front side as well as from the rear side with equal ease, leading to the formation of two isomers, if the chiral carbon is present in the substrate.

The basic difference in S_N1 and S_N2 mechanisms is in the timing of the steps. In the S_N1 mechanism, first X^- leaves and then Y^- attacks while in an S_N2 process, the two things happen simultaneously. The following order of reactivity for S_N1 is observed,

$$R–I > R–Br > R–Cl > R–F$$
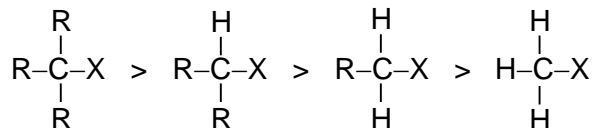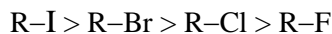
The rate law for the S_N1 reaction is

$$Rate = k [R–X]$$

The rate of S_N1 reaction is independent of the nucleophile used. Moreover, the carbocation formed are sp^2 hybridized and planar, so the attack of nucleophile has almost equal chances of attack from both the sides. So, any optically active alkyl halide will give a partial racemic mixture since before the formation of carbocation, the nucleophile attacks from rear side.
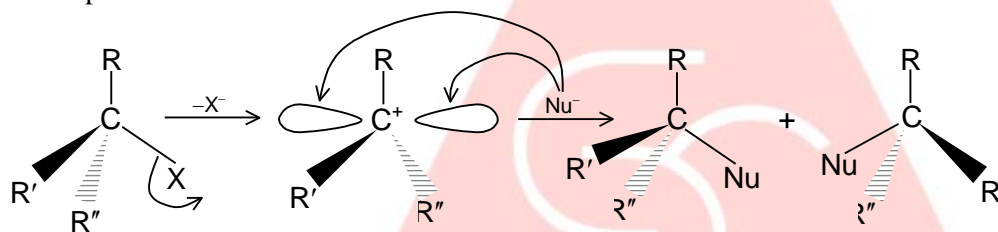
Now, let us observe the effect of solvent polarity on the rate of S_N1 reaction. It is generally said that the rate of S_N1 reactions is favoured in polar solvents than in non–polar solvents. Successful S_N1 reactions are exothermic in nature and their general energy profile can be shown as

Progress of reaction ⟶
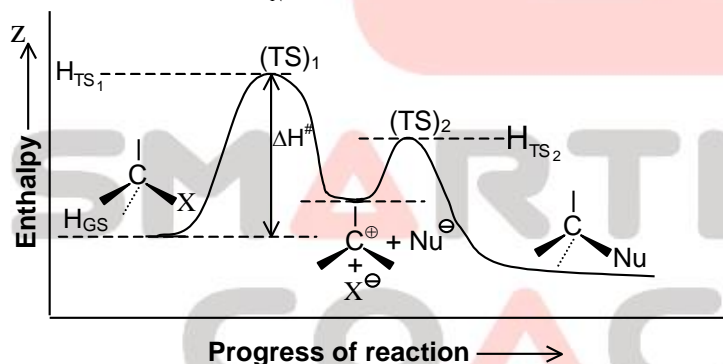
Let us consider the rate of solvolysis of t–BuCl and $Me_3C – \overset{\oplus}{S}Me_2$. The solvolysis reaction of t–BuCl and $Me_3C – \overset{\oplus}{S}Me_2$ can be represented as

(i) $Me_3C–Cl \xrightarrow[\substack{\text{solvent } (H_2O) \\ \text{Slow step}}]{\text{Polar}} Me_3\overset{\oplus}{C} + Cl^{\ominus}$

$$\downarrow \substack{H_2O \\ (–H^+) \text{ fast step}}$$

$$Me_3C{-\!-}OH$$

(ii) $Me_3C\overset{\oplus}{-}SMe_2 \xrightarrow{H_2O} Me_3\overset{\oplus}{C} + Me_2S$

$\downarrow H_2O\ (-H^+)$

Me_3C-OH
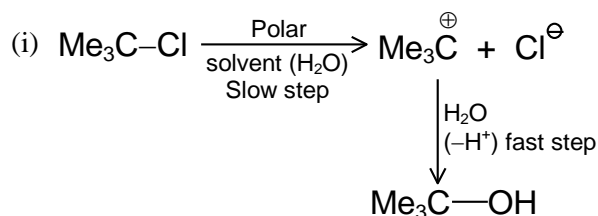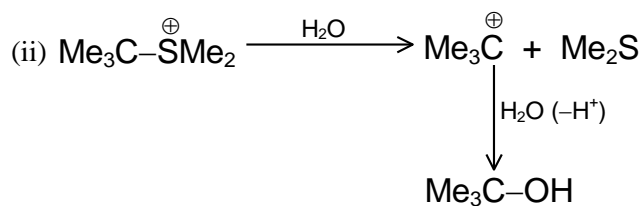
The transition states for the two reactions in the slow step can be shown as

(i) $\left[Me_3\overset{\delta+}{C}\text{-----}\overset{\delta-}{Cl}\right]$ 　　　　(ii) $\left[Me_3\overset{\delta+}{C}\text{-----}\overset{\delta+}{SMe_2}\right]$

In reaction (i), the ground state has no charge but transition state has diffused charge. Thus, an increase in solvent polarity decreases H_{TS_1}, which also decreases $\Delta H^{\#}$ and thereby increasing the rate of reaction.

In reaction (ii), the reactants carry full–fledged positive charge, while the transition state has diffused positive charge. Thus, increase in solvent polarity lowers H_{GS} more than H_{TS_1}, which increases $\Delta H^{\#}$. Hence, such reactions proceed with slower rate in solvents with high polarity.

8　COMPARISION OF S_N1 AND S_N2 REACTION

|		S_N1	S_N2
(a)	Number of steps	2 steps : (i) $R : L \xrightarrow{slow} R^+ + :L^-$ (ii) $R^+ + :NuH \xrightarrow{fast} R:Nu + H^+$	1 step : $R : L + : Nu^- \rightarrow R:Nu + :L^-$ Or $R : L + :NuH \rightarrow R : N^+uH + :L^-$
(b)	Reaction rate & order	Rate = $k_1[RL]$; first order	Rate = $k_1[RL]\ [:Nu^-]$; second order
(c)	Molecularity	Unimolecular	Bimolecular
(d)	TS of slow step	$\overset{\delta+}{R}\ ......\ \overset{\delta-}{L}\ ......HNu:$	$^{\delta-}Nu......C......\ L^{\delta-}$ (with : Nu^-) $^{\delta+}HNu......C....\ L^{\delta-}$ (with : HNu)
(e)	Stereochemistry	Inversion and retention (Partial racemization)	Inversion of configuration (backside attack)
(f)	Reacting nucleophile	Nucleophilic solvent; stable R^+ may react with added nucleophile	Added nucleophile
(g)	Structure of R	$3° > 2° > 1° > Me$	$Me > 1° > 2° > 3°$
(h)	Nature of Leaving group	Weakest base is best leaving group, i.e. $I^- > Br^- > Cl^- > F^-$	Weakest base is best leaving group, i.e. $I^- > Br^- > Cl^- > F^-$
(i)	Nature of nucleophile	For HNu: (solvent), rate α basicity of HNu:	In protic solvents, (i) Within a periodic table group, rate α polarizability of Nu (ii) For same nucleophilic site, rate α basicity of Nu In polar aprotic solvents, rate α basicity of Nu
(j)	Solvent effect	Rate α H–bonding ability and dielectric constant	Depends on charge type. Polar aprotic solvents leave "freest" most reactive Nu.
(k)	Determining factor	Stability of R^+	Steric hindrance
(l)	Rearrangement	Observed	Not observed, except for allylic
(m)	Catalysis	Lewis and Bronsted acids: Ag^+, $AlCl_3$, $ZnCl_2$ etc.	No specific catalyst

9　AMBIDENT NUCLEOPHILES

Some nucleophiles have lone pair of electrons on more than one atom and can attack through more than one site. Such nucleophiles are called *ambident nucleophiles*. In such cases, different products are possible due to attack through different sites. Attack by a specific site can be promoted under special conditions. Two well–known examples are discussed in detail.

9.1 ATTACK BY CN^- NUCLEOPHILE ($:^-C \equiv N:$)

$$R–X \xrightarrow{\;CN^-\;} R–CN \;\; + \;\; R–NC + X^-$$
$$\text{nitriles} \qquad \text{isonitriles}$$

In CN^-, carbon (negatively charged) will be a soft base as compared to nitrogen. So, if the reaction proceeds via S_N1 mechanism, which produces a free carbocation (a hard acid), then attack through nitrogen (hard base) will take place. But if the reaction proceeds via S_N2 mechanism (small positively charged carbon is soft acid) then attack through carbon (soft base) will take place. So, if we want to increase relative yield of nitriles, we can use NaCN or KCN etc in a less polar solvent, which facilitates S_N2 substitution. Similarly, if we want to increase the yield of isonitriles, we can use AgCN. Ag^+ has very strong affinity for X^-, so it favours the formation of R^+ and the reaction proceeds via S_N1 mechanism. This will result in attack by hard base giving R–NC. Further if we compare primary, secondary and tertiary alkyl halides, formation of R–NC should be more favoured in tertiary alkyl halide. But in actual practice, tertiary alkyl halides undergo elimination and the yield of R–NC decreases. This is because CN^- is a strong base, which causes elimination reaction.

9.2 ATTACK BY NO_2^- NUCLEOPHILE ($^-O–N=O$)

$$R–X \xrightarrow{\;NO_2^-\;} \quad R–O–N=O \;\; + \;\; R–NO_2 + X^-$$
$$\text{alkane nitrite} \qquad \text{nitro alkane}$$
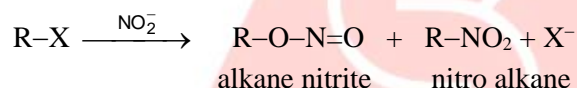
In NO_2^-, the negative charge is shared by two oxygen atoms. So nitrogen will be a hard base as compared to oxygen. If the reaction proceeds via S_N1 mechanism, then attack through nitrogen (hard base) will take place to produce nitro alkane. But if the reaction takes place via S_N2 mechanism then attack through oxygen (soft base) takes place to give alkane nitrite.

If we want to increase the yield of alkane nitrite, the reaction should proceed via S_N2 mechanism. i.e. we can use $NaNO_2$, KNO_2 etc. Moreover, the yield will be best if we use primary alkyl halide and less polar solvent. Formation of nitro alkane will dominate, if we use tertiary alkyl halide, more polar solvent and $AgNO_2$ because Ag^+ has strong affinity for X^- and can form a carbocation to force the reaction to proceed via S_N1 mechanism. Primary alkyl halide with $AgNO_2$ chiefly gives nitro alkane but if secondary and tertiary alkyl halides are used then $AgNO_2$ will yield nitro alkane as the major product.

10 INTERMOLECULAR VERSUS INTRAMOLECULAR DISPLACEMENT REACTIONS

A molecule with two functional groups is called a bifunctional molecule. If the two functional groups are able to react with each other, two kinds of reactions can take place. In case of a molecule having both, a nucleophile and a leaving group, the nucleophile of one molecule can displace the leaving group of a second molecule of the compound. Such reactions, which take place between two different molecules, are called intermolecular reactions.

$$BrCH_2(CH_2)_nCH_2O^- + Br - CH_2(CH_2)_nCH_2O^-$$

An intermolecular reaction

$$BrCH_2(CH_2)_nCH_2OCH_2(CH_2)_nCH_2O^- + Br^-$$
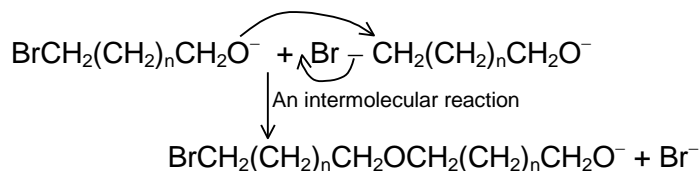
Alternatively, the nucleophile of a molecule can displace the leaving group of same molecule, leading to the formation of a ring compound. So, such reactions, which takes place within a single molecule are called intramolecular reactions.

$$Br - CH_2(CH_2)_nCH_2O^- \xrightarrow[\text{reaction}]{\text{An intramolecular}} H_2C \overset{(CH_2)_n}{\underset{O}{\diagup}} CH_2 + Br^-$$
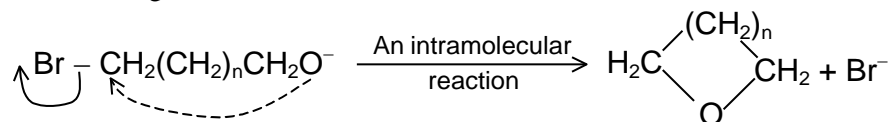
In such cases, when the nucleophile and the leaving group are part of the same molecule, inter as well as intramolecular reactions, both can takes place. Which reaction is more likely to occur, can be determined by the concentration of the bifunctional molecule and by the size of the ring that will be formed by intramolecular reactions.

Intramolecular reactions has an advantage in that the reacting groups are tethered close together (entropy factor) and thus do not have to wander through the solvent to find a group with which it react. As a result, a low concentration of reactant favours an intramolecular reaction because the two functional groups have a better chance of finding one another if they are in the same molecule. When an intramolecular reaction would form a five or six membered ring, it would be highly favoured over the intermolecular reaction because of the stability of 5 and 6 membered rings as they are less strained. Three and four membered rings are highly strained, thus they are less stable than 5 and 6 membered rings. The entropy factor in 3 membered ring is so highly favoured that 3 membered rings are also formed with ease inspite of the fact that they are too strained. The high activation energy for the formation of 4 membered rings cancels the advantage gained by tethering, thus they are not easily formed.

The likelihood that the reacting groups can find each other decreases sharply for the formation of 7 membered and larger rings, so the intramolecular reaction becomes less favoured as the ring size increases beyond 6.

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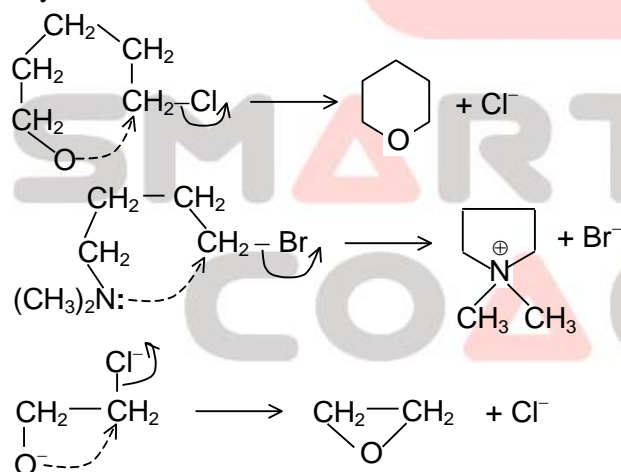
11   SUBSTITUTION VERSUS ELIMINATION REACTIONS

We know that an alkyl halide can undergo four types of reactions; S_N1, S_N2, E1 and E2.
A given alkyl halide under the given conditions will follow which pathway, can be decided in following manner.

The first thing you must look at is the alkyl halide, is it 1°, 2° or 3°. If the reactant were a primary alkyl halide, it would undergo E2/S_N2 reactions (as their carbocations are not stable).

If the reactant is a secondary or a tertiary alkyl halide, then it can undergo E1/S_N1 or E2/S_N2 reactions depending

upon reaction conditions. E2/S_N2 reactions are favoured by a high concentration of a good nucleophile/strong base, whereas a poor nucleophile/weak base favours E1/SN1 reactions.

Once you have decided whether the conditions will favour E2/S_N2 reactions or E1/S_N1 reactions, then you should decide how much of the product will be substitution and how much will be the elimination product. The relative amount of substitution and elimination product can be decided again on the basis of structure of alkyl halide (i.e. 1°, 2° or 3°) and on the nature of the nucleophile/base. Relative reactivities of alkyl halides in various reactions are:

In an S_N2 reaction: $\quad$ 1° > 2° > 3°
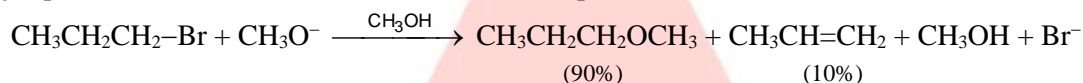
In an E2 reaction: $\quad$ 3° > 2° > 1°

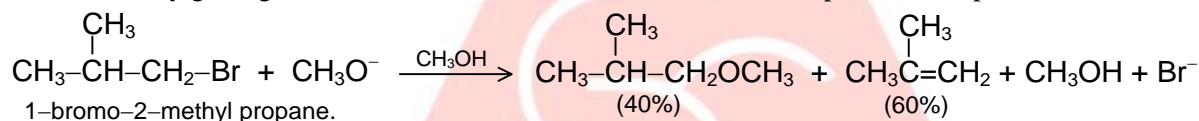In an S_N1 reaction: $\quad$ 3° > 2° > 1°

In an E1 reaction: $\quad$ 3° > 2° > 1°

For instance, propyl bromide when treated with methoxide ion in methanol can undergo either substitution reaction to give methyl propyl ether or elimination reaction to give propene.
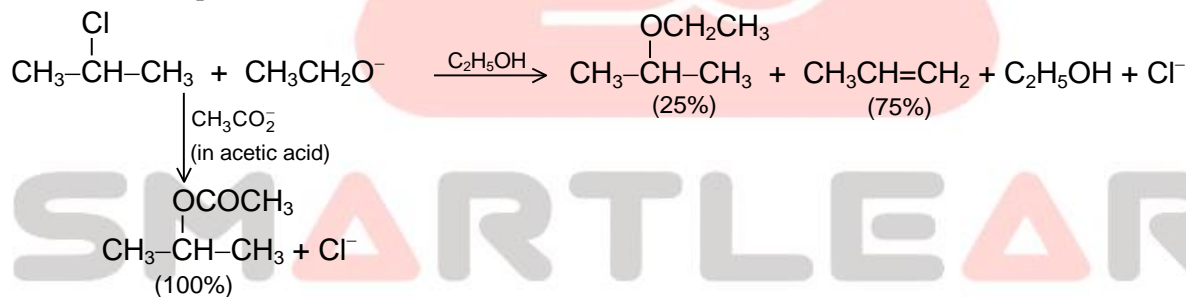The major product of the reaction would be substitution product.

$$CH_3CH_2CH_2-Br + CH_3O^- \xrightarrow{CH_3OH} CH_3CH_2CH_2OCH_3 + CH_3CH=CH_2 + CH_3OH + Br^-$$
$$\text{(90\%)} \qquad\qquad \text{(10\%)}$$

But when the primary alkyl halide or the nucleophile / base is sterically hindered, the nucleophile will have difficulty getting to the back of α−carbon and thus, elimination product will predominate. For example,

$$\overset{\overset{\displaystyle CH_3}{|}}{CH_3-CH-CH_2-Br} + CH_3O^- \xrightarrow{CH_3OH} \overset{\overset{\displaystyle CH_3}{|}}{CH_3-CH-CH_2OCH_3} + \overset{\overset{\displaystyle CH_3}{|}}{CH_3C=CH_2} + CH_3OH + Br^-$$

1−bromo−2−methyl propane. $\qquad\qquad$ (40%) $\qquad\qquad$ (60%)

A secondary alkyl halide can form both substitution and elimination products, whose relative amount depend on the base strength of the nucleophile. The stronger and bulkier the base, greater will be the percent of the elimination product.

$$\overset{\overset{\displaystyle Cl}{|}}{CH_3-CH-CH_3} + CH_3CH_2O^- \xrightarrow{C_2H_5OH} \overset{\overset{\displaystyle OCH_2CH_3}{|}}{CH_3-CH-CH_3} + CH_3CH=CH_2 + C_2H_5OH + Cl^-$$

$\qquad\qquad\qquad\qquad\qquad$ (25%) $\qquad\qquad$ (75%)

$$\downarrow \overset{\displaystyle CH_3CO_2^-}{\text{(in acetic acid)}}$$

$$\overset{\overset{\displaystyle OCOCH_3}{|}}{CH_3-CH-CH_3} + Cl^-$$
$$\text{(100\%)}$$

Increasing the temperature at which the reaction is carried out increases the rates of both the substitution and elimination reactions but increase in the rate of elimination reaction is more than that of substitution reaction. Thus, if the substitution product is desired, the reaction should be carried out at low temperature and high temperature promotes elimination product.

A tertiary alkyl halide is least reactive towards S_N2 reaction but most reactive towards E$_2$ reaction. Thus, only elimination product is formed.
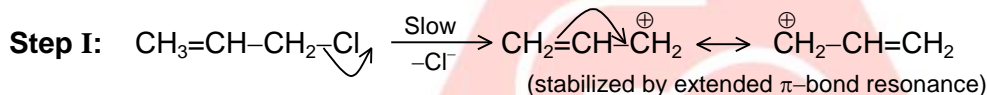
When the nucleophile is poor or base is weak, E1/S_N1 reactions will be preferred. Both E1/S_N1 reactions will take place through the formation of carbocation, formed by the heterolytic dissociation of alkyl halide. Alkyl halides have the same order of reactivity in E1 and S_N1 reaction because they have the same rate−determining step. Thus, all alkyl halides that react by E1/S_N1 reactions would give both elimination and substitution products. Substitution is favoured over elimination at lower temperatures and with the increase of temperature, the percentage of elimination product increases. Primary alkyl halides do not undergo E1/S_N1 reactions because primary carbocations are not too stable.

12 NUCLEOPHILIC SUBSTITUTION IN ALLYL & VINYL HALIDES

Let us compare the S_N1 and S_N2 rates of allyl chloride and n−Pr chloride. Both allyl chloride ($CH_2=CHCH_2Cl$) and n−Pr chloride are 1° RX. Towards S_N2 rate, allyl chloride is more reactive than n−Pr chloride because the transition state of allyl chloride is stabilized by the overlap of p−atomic orbital of the transition state with π−bond while such stabilization is not possible in n−propyl chloride.
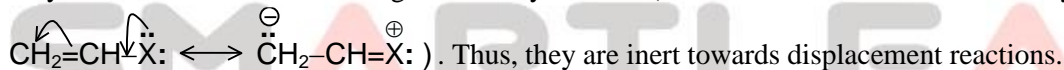

Transition state of allyl chloride   Transition state of n−Pr chloride
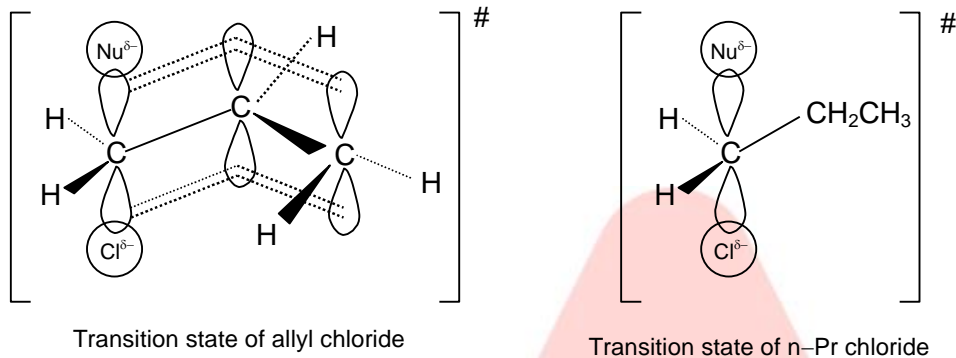
Towards S_N1 rate also, allyl chloride is more reactive than n−Pr chloride because the allyl carbocation is resonance stabilized while n−propyl carbocation is stabilized by induction.

Step I: $CH_3=CH-CH_2-Cl \xrightarrow[-Cl^-]{Slow} CH_2=CH-\overset{\oplus}{C}H_2 \longleftrightarrow \overset{\oplus}{C}H_2-CH=CH_2$
(stabilized by extended π−bond resonance)

Step I: $CH_3CH_2CH_2-Cl \xrightarrow[-Cl^-]{Slow} CH_3CH_2-\overset{\oplus}{C}H_2$
(stabilized +I effect of $-C_2H_5$ group)

The rate of S_N1 reaction for allyl chloride is faster than the S_N2 rate while for n−propyl chloride, S_N2 rate is faster than S_N1 rate.

Now let us see the S_N1 and S_N2 reaction possibility in vinyl halides.

In general, vinyl halides are less reactive than alkyl halides because C−X bond in vinyl halides is shorter and stronger than alkyl halides (this is because of resonance in vinyl halides,
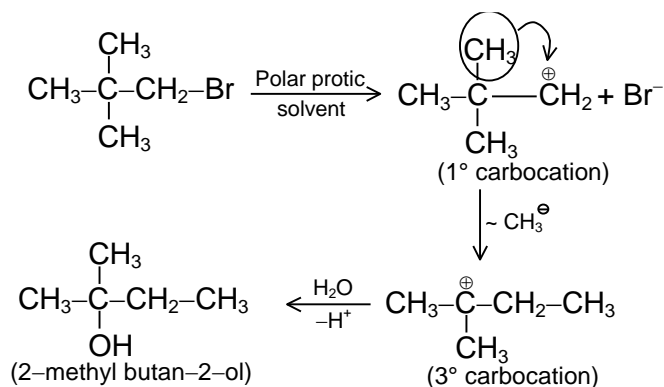
$CH_2=CH-\overset{..}{\underset{..}{X}}: \longleftrightarrow \overset{\ominus}{C}H_2-CH=\overset{\oplus}{\underset{..}{X}}:$). Thus, they are inert towards displacement reactions.

When they show S_N1 reaction, they would ionize to give vinyl cations, which are very unstable because the carbon bearing positive charge is sp hybridized. More the s−character in carbocation, the less stable it would be.

During S_N2 attack, backside attack of nucleophile is difficult because it would approach in the plane of the molecule where it would be repelled by the π−electron density and if there is mono or dialkylation at C^2, it would cause steric hindrance also. Thus, vinyl halides have little or no tendency to undergo S_N1 and S_N2 reactions.

13 NUCLEOPHILIC SUBSTITUTION IN NEOPENTYL HALIDES

Although neopentyl halide is a 1° halide, it does not undergo nucleophilic substitution by S_N2 mechanism because it is highly sterically crowded to be able to form a transition state. So, neopentyl halide has a greater tendency to undergo nucleophilic substitution by S_N1 mechanism. Although the initially formed carbocation is a primary carbocation, it rearranges to give a more stable carbocation, which is then attacked by nucleophile to give corresponding product. For example,
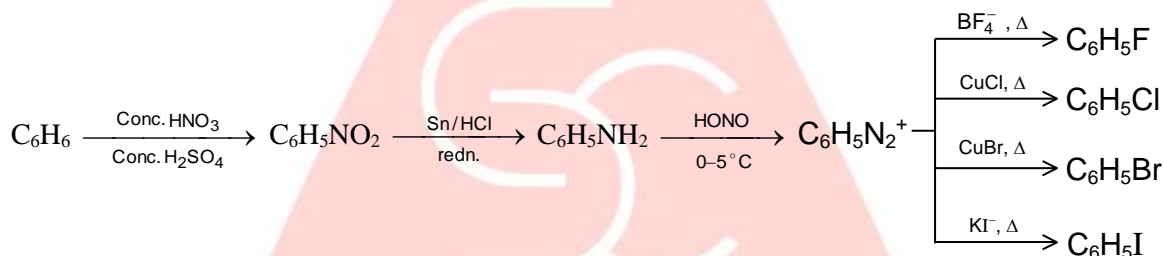
$$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2-Br \xrightarrow[\text{solvent}]{\text{Polar protic}} CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}\overset{\oplus}{-}CH_2 + Br^-$$

(1° carbocation)

$\sim CH_3^{\ominus}$

$$CH_3-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2-CH_3 \xleftarrow[-H^+]{H_2O} CH_3-\overset{\oplus}{\underset{\underset{CH_3}{|}}{C}}-CH_2-CH_3$$

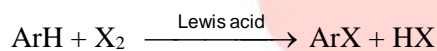(2–methyl butan–2–ol)   (3° carbocation)

ARYL HALIDES

Aryl halides are the compounds in which the halogen atom (F, Cl, Br and I) is directly attached to benzene. They are less reactive compounds than alkyl halides.

15 PREPARATION OF ARYL HALIDES
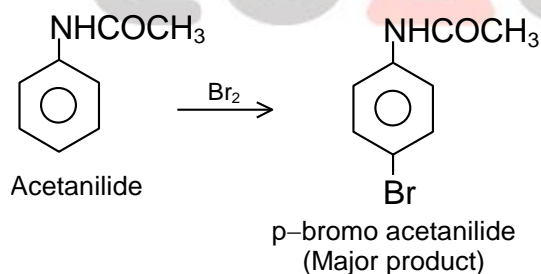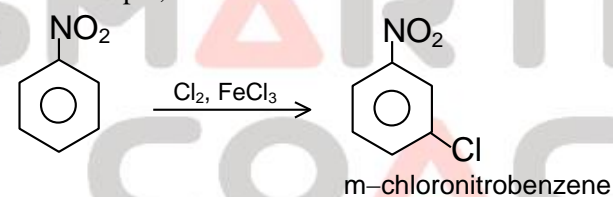
15.1 FROM DIAZONIUM SALTS

$$C_6H_6 \xrightarrow[\text{Conc. }H_2SO_4]{\text{Conc. }HNO_3} C_6H_5NO_2 \xrightarrow[\text{redn.}]{Sn/HCl} C_6H_5NH_2 \xrightarrow[0-5\,^\circ C]{HONO} C_6H_5N_2^+$$

$$\begin{array}{l} \xrightarrow{BF_4^-,\,\Delta} C_6H_5F \\ \xrightarrow{CuCl,\,\Delta} C_6H_5Cl \\ \xrightarrow{CuBr,\,\Delta} C_6H_5Br \\ \xrightarrow{KI^-,\,\Delta} C_6H_5I \end{array}$$

15.2 BY HALOGENATION OF ARENES OR SUBSTITUTED ARENES

$$ArH + X_2 \xrightarrow{\text{Lewis acid}} ArX + HX$$

where $X_2 = Cl_2$ or Br_2

Lewis acid = $FeCl_3$, $AlCl_3$ etc.

For example,

m–chloronitrobenzene

Acetanilide → p–bromo acetanilide (Major product)

(Note: Acetanilide group is majorly p–director)

16 GENERAL CHEMICAL PROPERTIES OF THE ARYL HALIDES

16.1 LOW REACTIVITY OF ARYL AND VINYL HALIDES

An alkyl halide can be conveniently detected by the precipitation of insoluble silver halides when it is warmed with alcoholic $AgNO_3$. The reaction occurs instantaneously with tertiary alkyl or benzyl halides and within five minutes or so with primary and secondary halides. But halobenzene or vinyl halides can be heated with alcoholic $AgNO_3$ for days without the slightest trace of silver halide being detected.
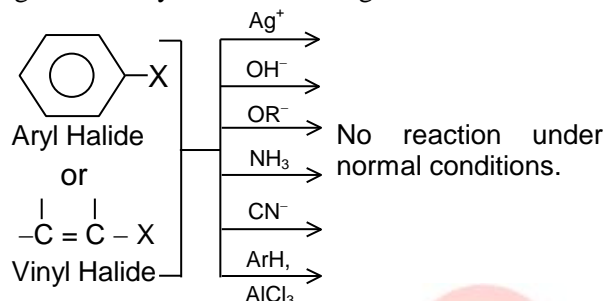
The typical reaction of alkyl halides is nucleophilic substitution.

$$R\text{–}X + :Z^- \longrightarrow R\text{–}Z + :X^-$$

where $Z = OH^-, OR^-, NH_3, CN^-, NH_2^-, ROH, H_2O$ etc.

But aryl halides undergo nucleophilic substitution reactions only in extreme conditions. Except for certain industrial processes where very severe conditions are feasible, one does not ordinarily prepare phenols (ArOH), ethers (ArOR), amines ($ArNH_2$) or nitriles (ArCN) by nucleophilic attack on aryl halides. The aryl halides cannot be used in the Friedel−Craft's alkylation reaction just like alkyl halides.

However, aryl halides do undergo nucleophilic substitution readily if the aromatic ring contains, in addition to halogen, certain other properly placed groups, which can activate the ring towards nucleophilic substitution. The presence of electron withdrawing groups like $-NO_2$, $-CF_3$ at ortho or para position to the halogen atom makes the aryl halides more susceptible to nucleophilic attack.

The reactions of unactivated and deactivated aryl halides with strong bases or at high temperature proceed via the benzyne intermediate. The Dow's process used for the manufacture of phenol involves benzyne intermediate.

Aryl halides can also undergo typical electrophilic aromatic substitution reactions like nitration, sulphonation, halogenation, Friedel−Craft's alkylation. Halogen is unusual in being deactivating but ortho and para−directing.
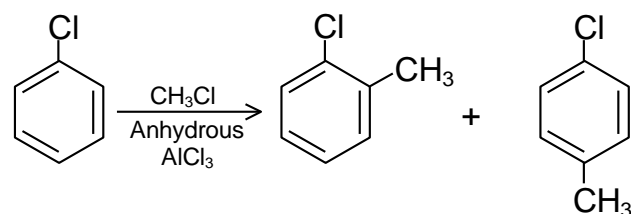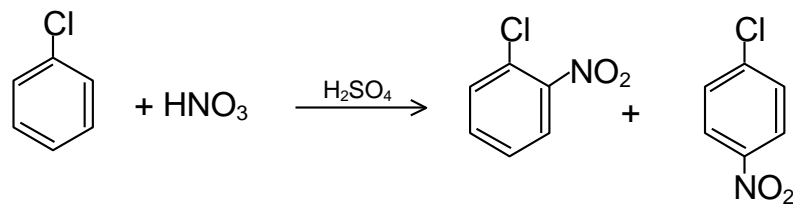
16.2 FORMATION OF GRIGNARD REAGENT

$$ArBr + Mg \xrightarrow{\text{dry ether}} ArMgBr$$

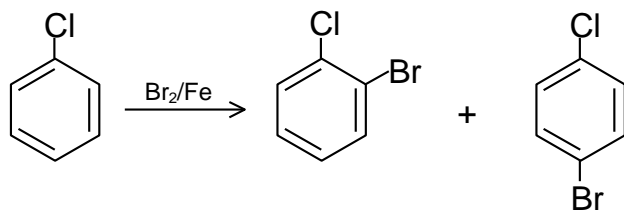$$ArCl + Mg \xrightarrow{\text{tetrahydrofuran}} ArMgCl$$
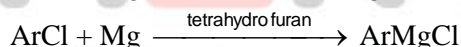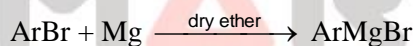
16.3 ELECTROPHILIC AROMATIC SUBSTITUTION

Although halogen is deactivating but it directs the incoming electrophile to ortho and para position.
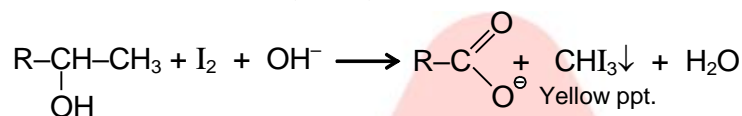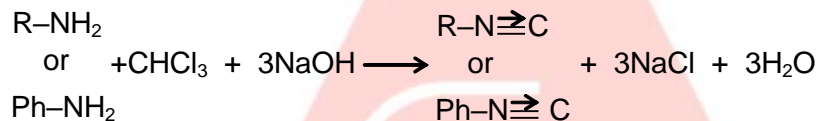For example,

17 ADDITIONAL INPUTS

1. Compounds containing $CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-$ or $CH_3-\overset{\overset{\displaystyle OH}{|}}{CH}-$ link will undergo reaction with X_2 and alkali (OH^-) to give an acid salt and haloform (CHX_3). The reaction is referred as Haloform reaction.

$$R-\underset{\underset{\displaystyle OH}{|}}{CH}-CH_3 + I_2 + OH^- \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}\underset{\underset{\displaystyle O^\ominus}{}}{} + CHI_3\downarrow + H_2O$$
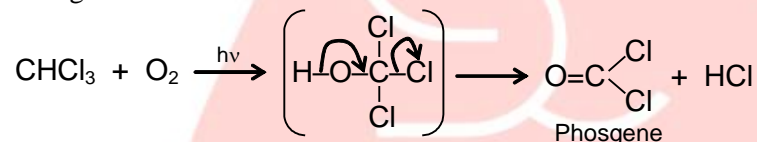Yellow ppt.

2. Primary aliphatic and primary aromatic amines on reaction with $CHCl_3$ and alkali (NaOH or KOH) undergo carbylamine or isocyanide reaction, to give alkyl or aryl isocyanide.

$$\begin{matrix} R-NH_2 \\ or \\ Ph-NH_2 \end{matrix} + CHCl_3 + 3NaOH \longrightarrow \begin{matrix} R-N{\equiv}C \\ or \\ Ph-N{\equiv}C \end{matrix} + 3NaCl + 3H_2O$$

The reaction proceeds via the formation of dichlorocarbene as an intermediate.

3. On exposure to air and sunlight chloroform undergoes slow oxidation to give phosgene–a highly poisonous gas

$$CHCl_3 + O_2 \xrightarrow{h\nu} \left[H-O-\underset{\underset{\displaystyle Cl}{|}}{\overset{\overset{\displaystyle Cl}{|}}{C}}-Cl \right] \longrightarrow O=C\underset{Cl}{\overset{Cl}{\big\langle}} + HCl$$
Phosgene

In order to prevent the formation of phosgene, chloroform is stored in brown bottles to cut off light and the bottles are filled completely to exclude air. A small amount of ethanol (0.6 to 1%) is also added to retard the oxidation of chlorine. Ethanol also converts phosgene, if formed, into harmless diethylcarbonate.