ALKYL HALIDES

PREPARATION OF ALKYL HALIDES

1. FROM ALCOHOLS

1. From Alcohols :

a) In presence of $ZnCl_2 / Hcl$ → Lucas reagent

b) In presence of Phosphorus pentachloride Pcl_5

c) In presence of Thionyl chloride ($Socl_2$)

a) Ethyl alcohol on treating with Hcl in presence of Anhy $ZnCl_2$ to form Ethyl chloride

$$C_2H_5OH + Hcl \xrightarrow{Anh\ ZnCl_2} C_2H_5cl + H_2O$$

Ethyl alcohol on refluxing with HBr in presence of little amount of Conc H_2SO_4 gives Ethyl Bromide

$$C_2H_5OH + HBr \xrightarrow{\Delta, Conc\ H_2SO_4} C_2H_5Br + H_2O + H_2SO_4$$

b) Ethyl alcohol reacts with phosphorus pentachloride (Pcl_5) to yield Ethyl chloride

$$C_2H_5OH + Pcl_5 \longrightarrow C_2H_5cl + Pocl_3 + Hcl$$

c) Ethyl alcohol reacts with thionyl chloride ($Socl_2$) in presence of Pyridine gives Ethyl Chloride:

$$C_2H_5OH + Socl_2 \xrightarrow[Reflux]{Pyridine} RC_2H_5cl + SO_2\uparrow + Hcl\uparrow$$

2. FROM ALKANES:

By direct halogenation of Alkanes

Alkyl halides were prepared by the direct halogenation of alkanes in diffused sunlight, heat (400°C) (or) in presence of Catalyst $Cucl_2$, $Fecl_3$, $FeBr_3$ - -)

$$CH_4 + Cl_2 \xrightarrow{h\nu} CH_3cl + (CH_2cl_2 + CHcl_3 + CCl_4)..$$

If excess of alkane is taken, then monochlorinated product is in high yield.

3. FROM ALKENES:

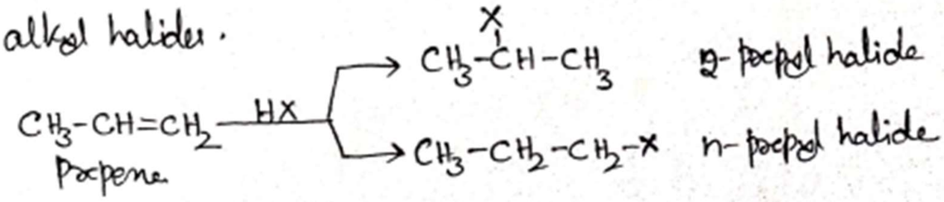
Alkenes reacts with Hydrogen halides to form alkyl halides. This reaction is called Hydrohalogenation

$$\underset{\text{Alkene}}{CH_2=CH_2} + HX \longrightarrow \underset{\text{Alkyl halide}}{CH_3-CH_2-X}$$

Symmetrical alkene on reaction with hydrogen halide produces only one type of alkyl halide.

$$CH_2=CH_2 + HX \longrightarrow CH_3-CH_2-X$$

Unsymmetrical alkene on reaction with HX produces two different types of alkyl halides.



$$CH_3-CH=CH_2 \xrightarrow{HX} CH_3-\overset{X}{\overset{|}{C}}H-CH_3$$

$$CH_3-CH=CH_2 \xrightarrow{HX} CH_3-CH_2-CH_2-X$$

NUCLEOPHILIC SUBSTITUTION REACTIONS

Nucleophilic substitution reactions are classified into 2 types

i Unimolecular Nucleophilic substitution reactions (SN^1)

ii Bimolecular Nucleophilic substitution reactions (SN^2)

1. UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^1)

1.1 MECHANISM FOR UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^1)

i) UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^1)

In unimolecular substitution substitution reactions, the rate of reaction depends only on the Concentration of Alkyl halide (RX) and is independent on the Concentration of base (on Nucleophile

$$\text{Rate} \propto [RX]$$

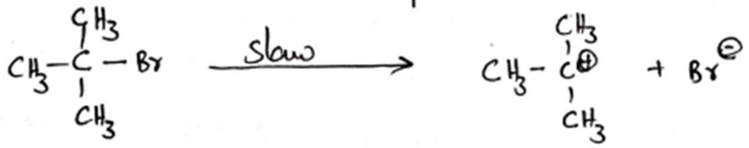
This reaction takes place in two steps.

Example for SN^1 reaction

Hydrolysis of t-butyl bromide to give t-butyl alcohol is taken as a typical example for SN^1 reaction.

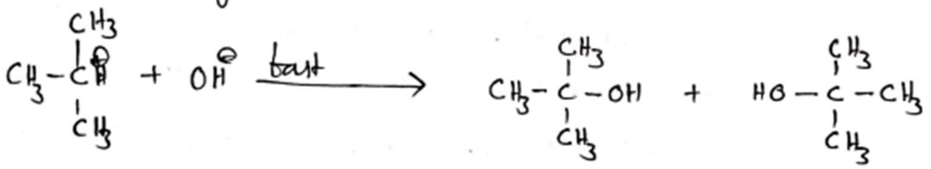
$$(CH_3)_3CBr + OH^{\ominus} \longrightarrow (CH_3)_3C-OH + Br^{\ominus}$$

In the first step t-butyl Bromide ionises to give t-butyl Carbocation and bromide ion, This is the slowest step and rate determining step.



$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-Br \xrightarrow{\text{slow}} CH_3-\underset{CH_3}{\overset{CH_3}{C^{\oplus}}} + Br^{\ominus}$$

In the second step attack of Nucleophile ($OH^{\ominus}$) on the Carb t-butyl Carbocation takes place resulting in the formation of t-butyl alcohol



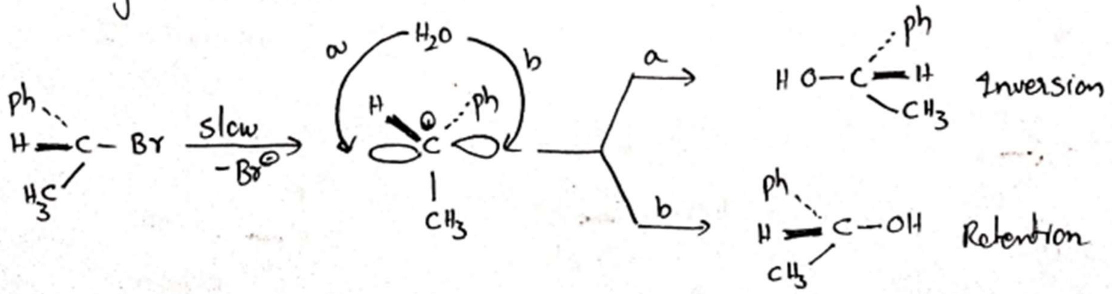
$$CH_3-\underset{CH_3}{\overset{CH_3}{C^{\oplus}}} + OH^{\ominus} \xrightarrow{\text{fast}} CH_3-\underset{CH_3}{\overset{CH_3}{C}}-OH + HO-\underset{CH_3}{\overset{CH_3}{C}}-CH_3$$

1.2 STEREOCHEMISTRY OF UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTIONS (SN^1)

Stereochemistry of SN^1 reaction

we know that the first step is formation of Carbocation, which is sp^2 hybridised the three groups in a Carbocation remain in one plane and making an angle of 120° with each other. The empty orbital of the central Carbon of Carbocation remains at right angles to the plane of sp^2 orbitals. Thus, the nucleophile Can attack equally to either of the two lobes of the empty p-orbitals to form two different products.

It the reactant is optically active, the Carbocation will form equal amount of the two isomer (one with retention and one with inversion) leading to racemisation of optically active substrate.

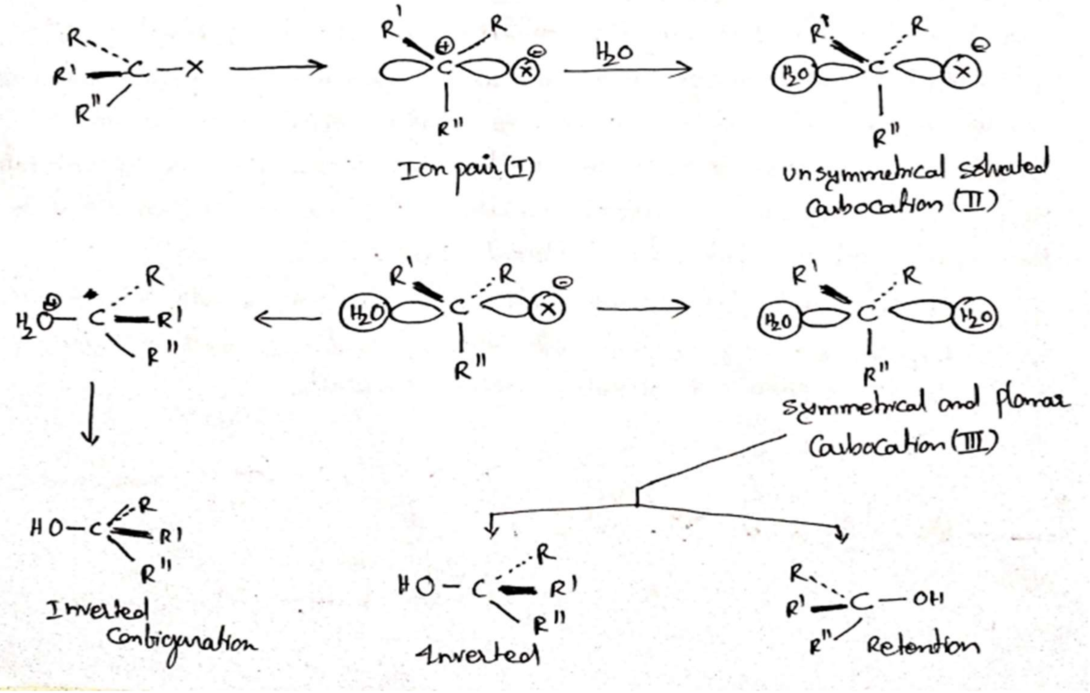


It is important to note that the complete racemisation as appear from the above representation is uncommon. The number of inverted isomer predominates over that with the same Configuration.

The incomplete racemisation is explained by the fact that ionization of an alkyl halide does not involve the formation of free Carbocation. The two Charged ions (Carbocation and halide) remain close together as ion pair (I). This halide ion close to Carbocation in ion pair shield the attack of $Nu^{\ominus}$ from front side and thus the $Nu^{\ominus}$ attacks only from the back side forming unsymmetrical solvated Carbo cation (II) which form the product with inverted Configuration.

the solvent

The halide ion from the ion pair (I) is replaced by another solvent molecule forming symmetrical and planar solvated ion (III), which is attacked by the nucleophile equally on both sides giving equal amounts of two isomer (inverted & retained configuration). Thus in short SN^1 reaction proceeds with racemisation plus some net inversion.



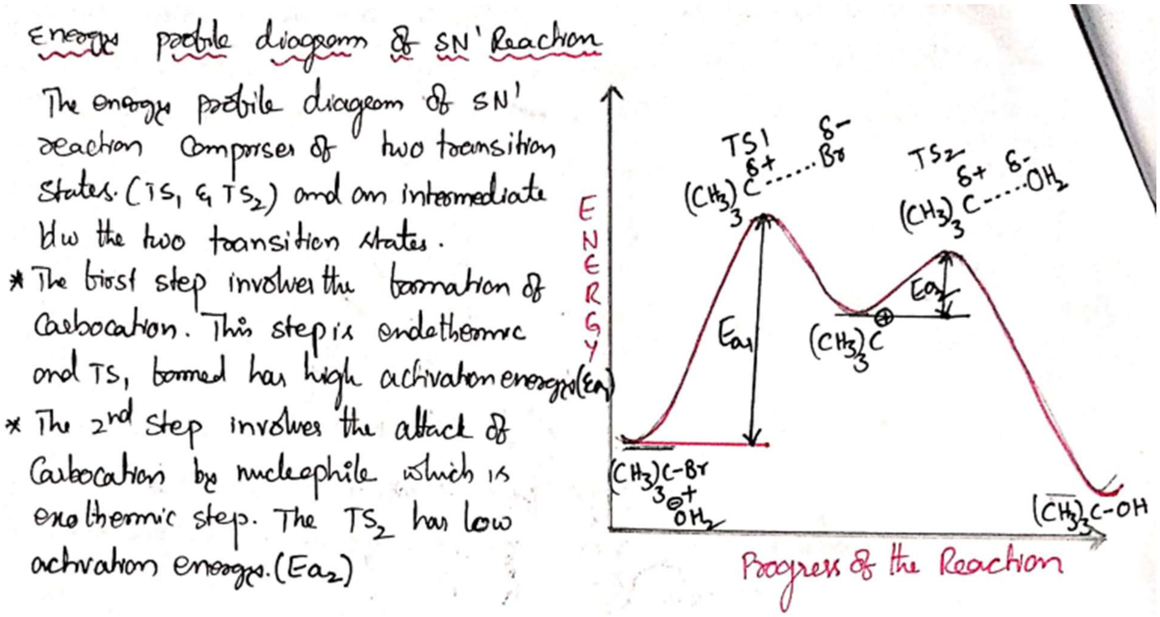
1.3 EFFECT OF SOLVENT ON UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^1)

Solvent effect: SN^1 reaction occurs more rapidly in polar solvents (high dielectric constant) than in non-polar solvents.

$$Me_3C-Cl + C_2H_5OH \xrightarrow{\text{Solvent}} Me_3C-OC_2H_5 + HCl.$$

Relative reactivity		Solvent
1,00,000	→	H_2O
5000	→	HCOOH
4	→	CH_3OH
≤1	→	CH_3COOH.

1.4 ENERGY PROFLE DIAGRAM OF UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^1)



Energy profile diagram of SN' Reaction

The energy profile diagram of SN' reaction comprises of two transition states. (TS_1 & TS_2) and an intermediate b/w the two transition states.

- The first step involves the formation of carbocation. This step is endothermic and TS_1 formed has high activation energy (Ea_1)
- The 2nd step involves the attack of carbocation by nucleophile which is exothermic step. The TS_2 has low activation energy. (Ea_2)

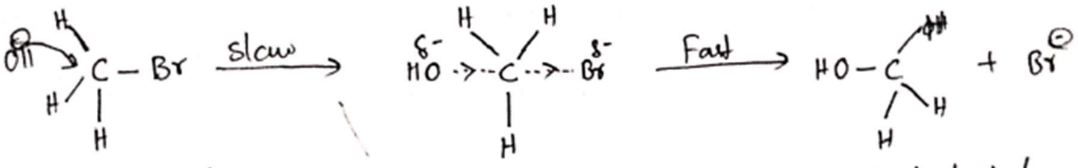
2. BIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^2)

2.1 MECHANISM FOR BIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^2)

In bimolecular nucleophilic substitution reaction, the rate of reaction depends on the Concentration of Alkyl halide (RX) and Nucleophile ($Nu^{\ominus}$)

$$\text{Rate} \propto [RX][Nu^{\ominus}]$$

The reaction takes place in one step.
Let us consider the hydrolysis of Methyl bromide by aq. NaOH. The Nucleophile (OH^-) starts to share its electrons with the substrate Carbon from the side opposite to the bromine atom. Simultaneously the bromine atom starts parting away with its shared pair of electrons from the Carbon. This state is represented in the form of transition state in which Carbon is sp^2 hybridised. the three hydrogen atoms lie in a plane with a bond angle 120°.

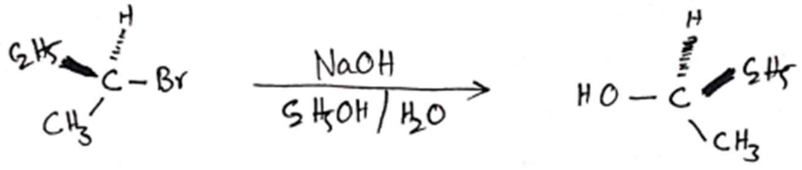


methyl bromide Transition state Methyl alcohol

Finally the C–Br bond is fully cleaved and C–OH bond is fully formed occupying the opposite position to –Br. Thus the alcohol formed is with inverted Configuration is called Walden inversion.

2.2 STEREOCHEMISTRY OF BIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^2)

stereo chemistry of SN^2 reactions can be best demonstrated by taking Alkyl halide having Chiral Carbon eg: 2-Bromobutane when (+)-2-Bromobutane is allowed to react with Aq NaOH under SN^2 condition (-)-2-Butanol is obtained.



(+)-2-Bromobutane

(-)2-Butanol.

The change in specific rotation (sign) from (+) to (-) indicates that the configuration changes during the reaction. The inversion of configuration is referred as walden inversion.

It is proved by the fact that a sample of 83% pure optically pure (+)-2-Bromo butane give 83% optically pure (-)-2-Butanol on SN^2 reaction.

2.3 EFFECT OF SOLVENT ON BIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^2)

Effect of solvent :

The rate of SN^2 reactions is increased in polar aprotic solvents (Acetonitrile, DMF, DMSO)

$$CH_3-CH_2-CH_2-CH_2-Br + N_3^{\ominus} \longrightarrow CH_3-CH_2-CH_2-CH_2-N_3 + Br^{\ominus}$$

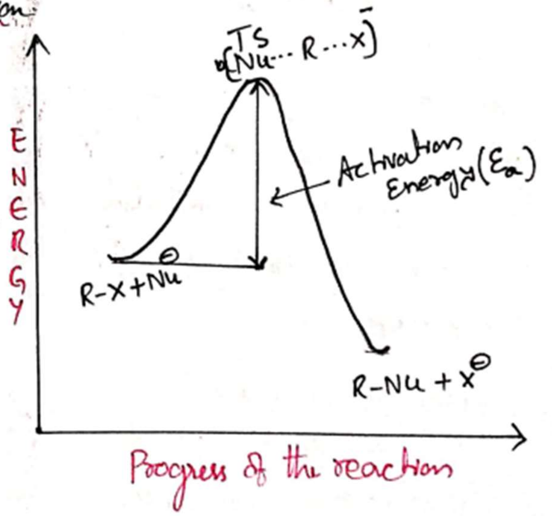
The rate of SN^2 reaction changes with solvent

solvent	Relative reactivity	solvent	Relative reactivity
CH_3OH	1	DMF	2800
H_2O	7	CH_3CN	5000
DMSO	1300		

2.4 ENERGY PROFLE DIAGRAM OF BIMOLECULAR NUCLEOPHILIC SUBSTITUTION REACTION (SN^2)

Energy profile diagram of SN^2 reaction

The potential energy diagram of SN^2 reaction shows single transition state without any intermediates. This step is exothermic. The T.S represents the highest energy state as Carbon is linked to five atoms. The TS is then converted product with inverted configuration.



WILLIAMSON'S SYNTHESIS

It is used for the preparation of ethers by heating alkyl halide with sod. or pot. alkoxide. It is used for preparation of simple and as well as mixed ethers.

$$CH_3I + NaOC_2H_5 \longrightarrow CH_3-O-C_2H_5 + NaI$$

For the preparation of $(CH_3)_3-C-O-C_2H_5$ we have to start the reaction with $(CH_3)_3CONa$ and C_2H_5Br Not with $(CH_3)_3-C-Br + C_2H_5ONa$

$$(CH_3)_3CONa + C_2H_5Br \longrightarrow (CH_3)_3-COC_2H_5 + NaBr.$$

Ethyl and methyl sulphate can also be used in place of halide

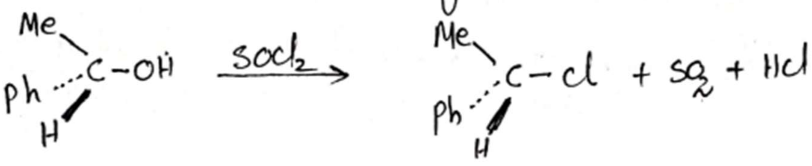
$$C_2H_5O^{\ominus} + CH_3-O-SO_3-CH_3 \longrightarrow C_2H_5OCH_3 + CH_3SO_3O^{\ominus}$$

SUBSTITUTION NUCLEOPHILIC INTERNAL REACTION (SNi)

In internal Nucleophilic substitution reactions rate of reaction depends on Concentration of ROH and $SOCl_2$.

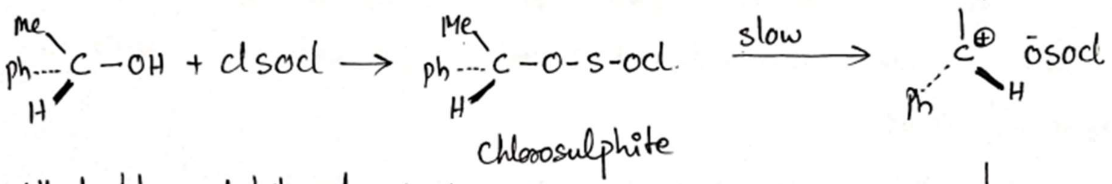
$$\text{Rate} \propto [ROH][SOCl_2]$$

But let us Consider the following example



Mechanism

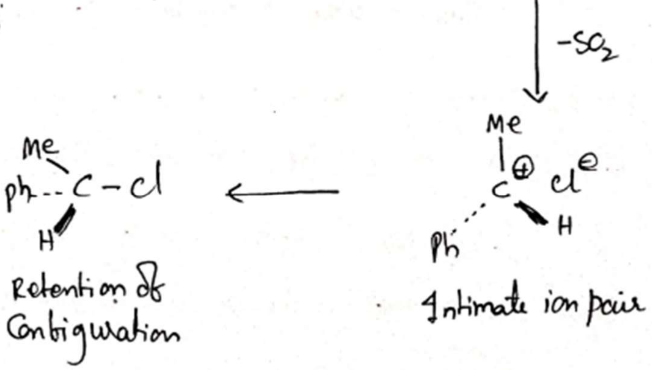
The mechanism of this SNi involves the formation of a true intermediate called alkyl chlorosulphite (ROSOCl), which is isolated under mild conditions. The chlorosulphite is formed with retention of configuration because R–O (or) C–O bond is not broken.



Chlorosulphite

Alkyl chloro sulphite decomposes instantaneously into SO_2 & $Cl^\ominus$

The Carbocation and $Cl^\ominus$ ion Constitute an intimate ion pair. and hence attack by $Cl^\ominus$ ion is likely to occur only on the same side of the R^+ from which OSOCl is departed.



Retention of Configuration

Intimate ion pair

The Configuration of the reactant is retained in the product.

ARYL HALIDES

PREPARATION OF ARYL HALIDES

1. FROM PHENOLS

Reaction with PCl_5

Phenol reacts with PCl_5/Δ to form chlorobenzene

$$\underset{\text{phenol}}{C_6H_5OH} \xrightarrow{PCl_5/\Delta} \underset{\text{chlorobenzene}}{C_6H_5-Cl}$$

2. FROM BENZENE DIAZONIUM SALTS

. By decomposition of diazonium salts.

SondMayer reaction

i Benzene diazonim chloride on reacting with CuCl / HCl gives chlorobenzene

$$C_6H_5N_2Cl \xrightarrow{CuCl/HCl} C_6H_5Cl + N_2$$

ii Benzene diazonim chloride on reacting with CuBr / HBr gives Bromobenzene

$$C_6H_5N_2Cl \xrightarrow{CuBr/HBr} C_6H_5Br + N_2$$

Balz Schiemann reaction

iii Benzene diazonium chloride on reacting with KI gives Iodobenzene

$$C_6H_5N_2Cl + KI \xrightarrow{Warm} C_6H_5-I +$$

IV Benzene diazonim chloride on reacting with Fluoroboric acid (HBF_4) gives fluorobenzene

$$C_6H_5N_2Cl + HBF_4 \longrightarrow C_6H_5\overset{\oplus}{N_2}\,\overset{\ominus}{BF_4} \xrightarrow{\text{gentle heat}} C_6H_5F + BF_3 + N_2$$

NUCLEOPHILIC SUBSTITUTION REACTIONS IN ARYL HALIDES

Unlike alkyl halides, Aryl halides does not undergo nucleophilic substitution reactions easily., this is because the lone pair of electrons on halogen are in conjugation with π-electron, hence these compounds undergo resonance which stabilizes the molecule. and Carbon carrying halogen is in sp^2 hybridization so, the Carbon-halogen bond is shorter & stronger than C-X bond in Alkyl halides.

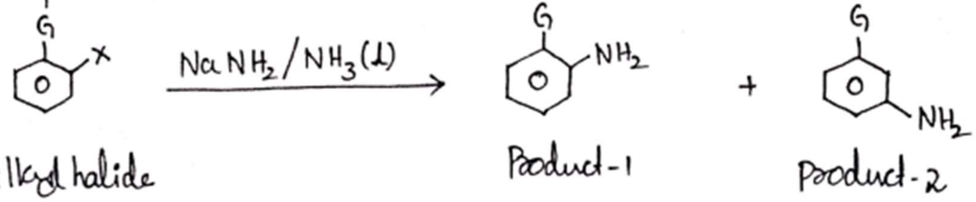
The nucleophilic substitution reactions in Aryl halides occurs under drastic conditions (high temp, pressure and strong Nucleophiles).

NUCLEOPHILIC SUBSTITUTION REACTIONS IN ARYL HALIDES VIA BENZYNE MECHANISM

Aryl halides with at least one hydrogen at ortho-position undergo Aromatic nucleophilic substitution reaction via Benzyne in presence of strong base like $NaNH_2$ or KNH_2 in liq. ammonia.

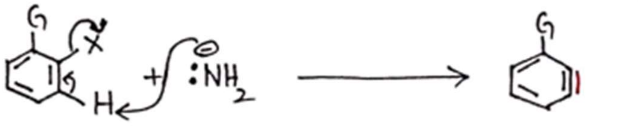
Benzynes are neutral and highly reactive intermediates

Example:



Mechanism

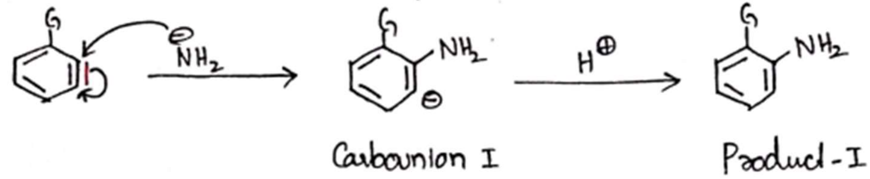
1. Alkyl halide reacts with $NaNH_2/NH_3$ gives benzyne



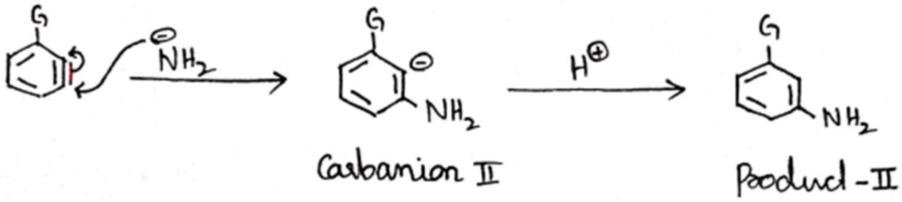
Benzyne

2. The available nucleophile ($\overset{\ominus}{N}H_2$) reacts with generated benzyne gives two different substituted products.

a.

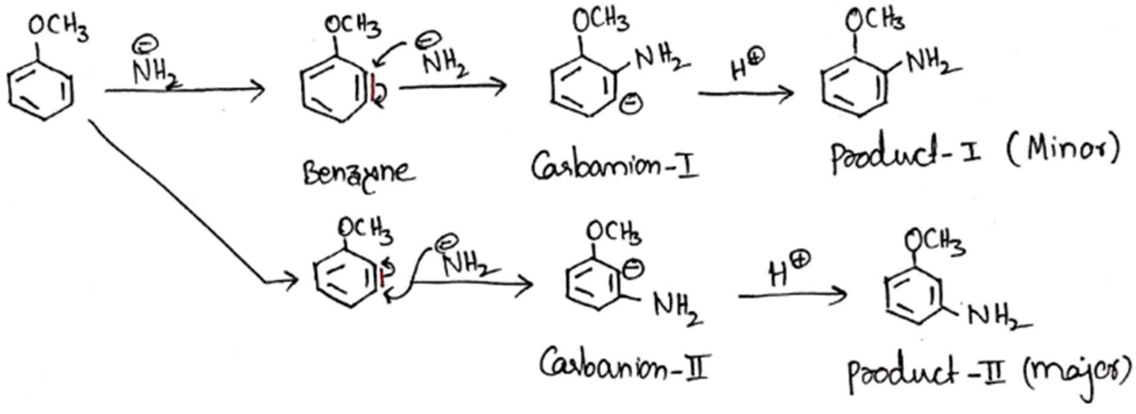


b.

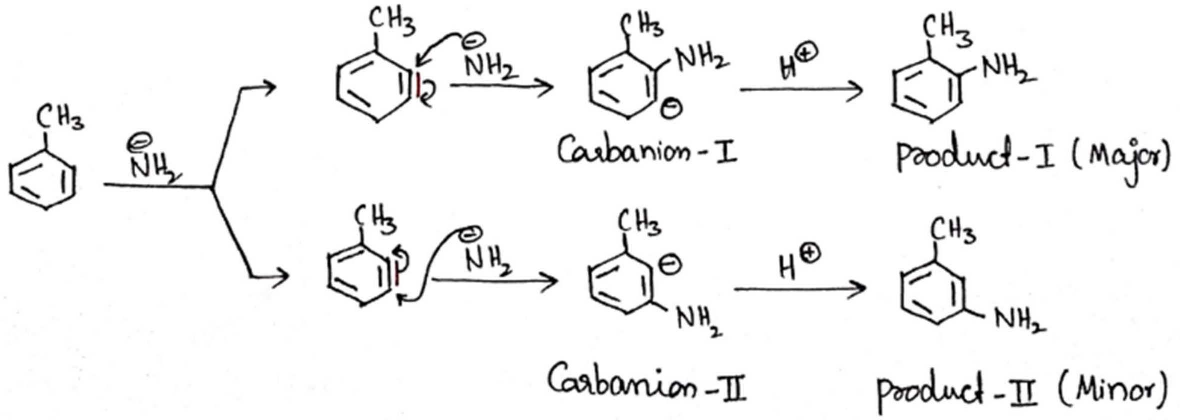


The type of product formed, either I or II depends on the stability of the Carbanion formed. The stability of carbanion depends upon the nature of the group (G). either electron releasing group (ERG) or electron withdrawing group (EWG).

If "G" is electron withdrawing group which shows –I effect and stabilises Carbanion – II resulting in the formation of product – II in major quantity.



If "G" is electron releasing group, which exerts +I effect and stabilizes Carbanion-I resulting in the formation of product-I in major quantity.



RELATIVE REACTIVITY OF ALKYL, ARYL, VINYL, ALLYL AND BENZYL HALIDES

ALKYL HALIDE

$CH_3-\underset{\uparrow}{CH_2}-X$

sp^3 hybridisation

Alkyl halides are very reactive for nucleophilic substitution Reactions. Carbon-Halogen bonds in Alkyl halide is weak & long. so small amount of energy is sufficient to break C-X bond.

ALLYL HALIDE

$CH_2=CH-\underset{\uparrow}{CH_2}-X$

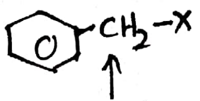
sp^3 hybridisation

In allyl halides, the p orbital of C_2 is seperated from the p-orbital of Halogen atom by a saturated sp^3 hybrid Carbon atom. Due to this the halogen atom in allyl halide is more reactive.

Moreover, the allyl Carbocation formed is stabilized by resonance

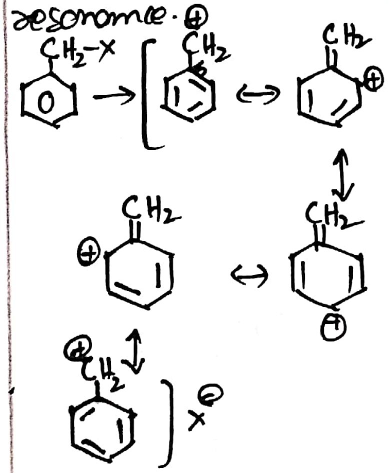
$$CH_2=CH-CH_2-X \rightarrow \left[CH_2=CH-\overset{\oplus}{C}H_2 \leftrightarrow \overset{\oplus}{C}H_2-CH=CH_2\right]X^{\ominus}$$

BENZYL HALIDE



sp^3 hybridisation

In Benzyl halides the πes of the benzene ring are seperated from the lone pair of electrons on the halogen atom by a sp^3 hybridised Carbon. The Benzyl halide undergo ionisation to form benzyl Carbocation which is stabilised by resonance.



VINYL HALIDE

$CH_2=\underset{\uparrow}{CH}-X$

sp^2 hybridisation

Carbon-halogen bonds in vinyl halide is strong & shorter.

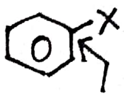
i) The halide attached Carbon is sp^2 hybridised and therefore the e^-s of the Carbon orbital are closer to the nucleus which requires more energy to break C-X bond.

ii) Resonance:

$$CH_2=CH-\ddot{\underset{..}{X}}: \leftrightarrow \overset{\ominus}{C}H_2-CH=\overset{\oplus}{\underset{..}{X}}$$

Electron pair on the halogen ion is in Conjugation with the πe^- pair of double bond. Due to double bond b/w Carbon & Halogen in structure (II) the bond strength increases and bond cleavage becomes difficult.

ARYL HALIDE



sp^2 hybridisation

Carbon-halogen bonds in Aryl halide is shorter & stronger

i) The halide attached Carbon is sp^2 hybridised and therefore the e's of the Carbon orbital are closer to the nucleus which requires more energy to break C-X bond.